FATS AND OILS
A SERIES OF MONOGRAPHS

FATTY ACIDS

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A SERIES OF MONOGRAPHS ON THE CHEMISTRY AND TECHNOLOGY OF FATS, OILS, AND RELATED SUBSTANCES

FATTY ACIDS

THEIR CHEMISTRY AND PHYSICAL PROPERTIES

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1 9 4 7
INTERSCIENCE PUBLISHERS, INC., NEW YORK
INTERSCIENCE PUBLISHERS LTD., LONDON

INTERSCIENCE PUBLISHERS, INC., 250 Fifth Avenue, New York 1, N. Y.
For Great Britain and Ireland:
INTERSCIENCE PUBLISHERS LTD., 2a Southampton Row, London, W. C. 1

PRINTED IN THE UNITED STATES OF AMERICA

PREFACE

The higher fatty acids have been the subject of continuous research and investigation since about 1815, when Chevreul established the constitution of natural fats as the glycerol esters of these long chain aliphatic compounds. During the interval of nearly one and a half centuries which has elapsed since Chevreul's discovery a vast literature has accumulated dealing with the chemical and physical properties of the fatty acids and their simple derivatives. Moreover, the increment of this knowledge during the past twenty-five years has exceeded that of the entire preceding history of these substances. This accumulated literature is not only voluminous but it is widely scattered and relatively unorganized. Although all books and monographs on fats, oils, or waxes devote some space to a description of the more common properties and reactions of the fatty acids as a background to the main subject, none has been devoted solely to an exposition of our knowledge of the fatty acids *per se*.

The purpose of this volume has been to bring together in an organized and readily accessible form as much as possible of the present accumulation of facts and data pertaining to the chemical reactions and physical properties of the fatty acids and, especially, of the long chain fatty acids which comprise the building stones of all natural fats, oils, and waxes. The material thus made available should obviate many hours of searching the literature by the large and growing body of chemists, physicists, engineers, and technologists who are interested in the fatty acids and their numerous products and by-products.

While it has not been the primary purpose to discuss the lower members of the fatty acid series at length, it has nevertheless been impossible to ignore them entirely. Although the lower members of this series are not generally encountered as components of the fatty glycerides or the solid waxes, they do occur as simple esters in fruit essences and many ethereal oils. Furthermore, many of the reactions and derivatives of the fatty acids have been investigated only for the lower members of the series. This is especially true with respect to various physical properties of these acids and their derivatives. Moreover, it is only when the reactions and properties of the complete series are examined that it becomes apparent to what extent additional work is necessary to fill the missing gaps in our knowledge of these substances. It has likewise not been the primary purpose to discuss the chemical and physical properties of the glyceride esters and natural fats, because a comprehensive treatment of these subjects would require a volume at least the same size and scope as the present one. Here too, however, it has been impossible to ignore them entirely.

In the process of assembling the data with respect to the physical properties of the fatty acids and their derivatives, a number of anomalies has come to light. For example, many of the most useful and important properties were determined twenty-five or more years ago when it was most improbable that even moderately pure fatty acids were available. Also, very many of the reported constants have been obtained incidentally and not as a result of planned or systematic investigations. Owing to the incidental manner in which many physical properties have been determined, there is often no way of selecting the most reliable value from among several which may have been recorded by different investigators for the same compound. However, an effort has been made to include only the most accurate values available for the various properties, but in some instances these may be in error. Where no choice appeared to be preferable, two or more values are sometimes given without comment.

It is hoped that, in addition to the purposes mentioned above, the present work will result in the stimulation of qualified individuals to undertake investigations designed to fill the missing gaps in our knowledge of the subject and to re-examine those reactions and properties which obviously are in need of review.

While the plan and contents of the present volume are the author's and any defects found therein are attributable to him alone, he has had the assistance of many individuals in its preparation and desires to make grateful acknowledgment to them. For their invaluable assistance in reading and criticizing the individual chapters, he is deeply indebted to A. M. Altschul, A. E. Bailey, S. T. Bauer, F. G. Dollear, Mrs. M. G. Lambou, R. T. O'Connor and E. L. Skau. Sincere thanks are also expressed to R. O. Feuge who prepared many of the original drawings, to C. H. Billett for assistance in preparing photographs for illustrations, to B. Ashby Smith who checked the calculated molecular weights, neutralization values, iodine values, etc., of the many tables of such data, to Mrs. E. L. Skau for checking and verifying all literature citations, to M. E. Jefferson and Mrs. F. B. Kreeger for preparation of the original x-ray photographs, and to Mrs. Calla L. Markley and Mrs. Ruth R. Warren for an inordinate amount of typing of the various drafts of the manuscript. The author also wishes to thank the editors of *The Journal of the American Oil Chemists' Society* and *Industrial and Engineering Chemistry* as well as various industrial concerns and publishing houses for permission to reproduce illustrations from their publications.

K. S. MARKLEY

New Orleans, Louisiana
May 1, 1947

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A. THE NATURE AND HISTORY OF FATS AND WAXES

CHAPTER I

HISTORICAL AND GENERAL

1. Introduction

The three most important classes of compounds which occur in nature are the proteins, the carbohydrates, and the fats. All vital processes are involved primarily in the elaboration or degradation of these substances, assisted or activated by various natural catalysts such as enzymes, vitamins, hormones, and other vital agents. Each of these classes of compounds is represented by numerous and varied individual members which are elaborated by nature from a small number of simpler compounds. The proteins, no matter how complex, are all built up from simple amino acids, the carbohydrates from glucose residues or other simple monosaccharides, and the fats and waxes from a small number of fatty acids.

The fats differ from the proteins and carbohydrates by the fact that the latter consist solely of condensation products of similar structural units, whereas in the fats the component acids are attached to a common skeleton, namely, the trihydric alcohol, glycerol. The natural fats also differ from proteins and carbohydrates by virtue of the fact that their complexity is due, in part, to mechanical admixture or mutual solubility of several components of relatively low molecular weight rather than to the existence of highly condensed systems.

The large number and complexity of the natural fats have their origin in two sources, namely, in the number, kind, and mode of arrangement of the individual fatty acids which are attached to the glycerol skeleton to form specific glycerides, and in the number and relative proportions of such glycerides in the mixture or solution comprising the fat. The natural waxes likewise consist of mixtures of esters of fatty acids, but these esters are derived, not from one polyhydroxy alcohol, but from a number of alcohols having relatively long hydrocarbon chains and only one replaceable hydroxyl group. Their complexity is due, therefore, to the variety of combinations which may result from esterifying different fatty acids with different monohydroxy alcohols, and from the relative proportions of these esters in the mixture comprising the wax.

Although the present volume is concerned primarily with the fatty acids and their derivatives rather than with the natural fats and waxes, nevertheless, the latter represent the natural source of these substances and provide the stimulus for investigating their chemical and physical properties. Consequently, in discussing the fatty acids, frequent references to and comparisons with the natural fats and waxes will be made throughout the text and, especially in the introductory chapter, where the related histories of the two are set forth against a common background.

2. Definitions

The words *fats and oils* have been applied both in the technical and lay literature with so many different meanings that it is necessary to define them at the outset to avoid subsequent misunderstanding regarding their usage in the present instance. Throughout this work, the term *fats and oils* will be used to refer to that class of lipoidal materials consisting of the glycerol esters of the fatty acids and their associated phosphatides, sterols, alcohols, hydrocarbons, pigments, etc., which are obtained from plants and animals by such industrial processes as pressing, cooking with steam and water, extraction with organic solvents, or any combination of these processes.

No chemical distinction exists between *fats and oils*, and by an oil is meant a liquid fat, and by a fat is meant a solidified oil. These changes in physical state may occur more or less spontaneously as a result of change in environment (temperature, light, etc.), or as a result of chemical treatment (hydrogenation, isomerization, etc.). For example, a liquid oil at room temperature may be hydrogenated to produce a hard fat at the same temperature, but on elevation of the temperature a few degrees it will again resume the liquid state. Naturally occurring tung and oiticica oils exist as liquid fats (α-form) but are readily isomerized by the action of light or suitable catalysts into geometrically isomeric solid fats (β-form).[1] By raising the temperature of these solid fats, they again become liquid although the geometrical isomerism is not reversed. The difference, therefore, between a fat and oil is one of physical state which is reversible merely by changing the surrounding environment. Furthermore, as pointed out by Bailey[2] the designation of fats as solids is somewhat misleading since at ordinary temperatures fats are actually plastic solids, and consist of a liquid in intimate mixture with many very small solid particles. At 70°F., for instance, only about one-third of the glycerides of lard are in the solid state.

The term *fat* is now quite generally used to include both *fats and oils* where specification of the physical state is of no importance, and where the constant use of the phrase *fats and oils* becomes monotonous and repeti-

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[1] R. S. Morrell and W. R. Davis, *J. Oil Colour Chem. Assoc.*, **19**, 264–272 (1936).

[2] A. E. Bailey, in *The Chemistry and Technology of Food and Food Products.* Vol. I, M. B. Jacobs, ed., Interscience, New York, 1944, p. 567.

tious. This practice will be followed here for the reasons that have just been mentioned.

3. History

Man has been familiar with fats since prehistoric time. Long before he had any knowledge of the nature of these substances he recognized differences in their properties and employed them in a variety of ways. Their use as foods was probably instinctive but their other applications no doubt resulted from observation of their properties and their behavior under various environmental conditions. When and how man first became familiar with these substances and their manifold uses is lost in antiquity, but certainly fats, as well as waxes, were employed by primitive peoples of all climes as medicinals, in cosmetics, in religious ceremonies, as illuminants and lubricants, and for other purposes.

Klemgard[3] mentions the fact that the Egyptians used olive oil as a lubricant for moving large stones, statues, and building materials and that axle greases consisting of a fat and lime together with other materials were used in lubricating Egyptian chariots as early as 1400 B.C. Friedel[4] analyzed the contents of a number of earthen vases found in the interior of Egyptian tombs believed to predate the First Dynasty. One of these vases contained several kilograms of a pale brown, porous, granular substance which was found to consist of palmitic acid mixed with less than 51% of tripalmitin indicating that the original material was palm oil which had undergone oxidation and partial saponification. Another vase contained a firmer, more granular, paler mass consisting of stearic acid with about 30% tristearin and was probably beef or mutton tallow. A third vase, containing material similar to the first-mentioned, contained palmitic acid and 41% tripalmitin. These materials were probably intended as provisions for the dead. Other smaller vases contained unidentifiable fatty material mixed with galena which was probably used as a cosmetic.

Sarton's[5] *Introduction to the History of Science* contains many references to the use of fats and oils in the arts, technology, and medicine from the dawn of Greek and Hebrew knowledge (9th to the 8th centuries B.C.) to the middle ages. The Homeric poems contain a reference to the use of oil in weaving. Soap, both as a medicinal and as a cleansing agent, was known to Pliny (23–79 A.D.) who mentions both hard and soft soap, and it may be inferred that soaps were known considerably prior to Pliny's time. Candles, made from beeswax and tallow, were known to the Romans and probably were used by others in pre-Roman times.

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[3] E. N. Klemgard, *Lubricating Greases: Their Manufacture and Use.* Reinhold, New York, 1937, p. 14.

[4] C. Friedel, *Compt. rend.*, **124**, 648–653 (1897).

[5] G. Sarton, *Introduction to the History of Science.* 2 vols., Carnegie Inst. Wash. Pub. No. 376, Williams & Wilkins, Baltimore, 1927–31.

Waxes, as well as resins, were used as protection against moisture, especially in shipbuilding and in some forms of wall painting. An early form of painting known as *encaustic*, actual specimens of which are known in the form of portraits on late Egyptian mummy cases and which was certainly used before then on wall decorations, employed a mixture of pigments in natural waxes. Another early form of painting known as *tempera* employed an emulsion of wax or oil, water, pigments, and an emulsifying agent such as a vegetable gum or egg yolk.

Varnishes were certainly used in Egypt on mummy cases of the New Empire. Many of these varnishes are insoluble, but their method of preparation is not known with certainty. The earliest mention of the use of a drying oil in a process connected with painting is given by Aetius, about the 6th century A.D., who stated that nut oils dry and form a protective varnish. From this time on, the use of drying oils and varnishes seems to be well established and recipes dating from the 8th or 9th century A.D. are known for transparent varnishes composed of linseed oil and natural resins.

Theophilus Presbyter, an unknown craftsman, who lived about the end of the 11th and the beginning of the 12th century, devoted many chapters of his *Diversarum artium schedula* to the preparation and use of oil colors. Theophilus used linseed oil together with some kind of resin, probably amber, copal, or sandarac. He gives many recipes for the preparation of paints, varnishes, and dyes. However, the discovery of the effect of driers in linseed oil paints, which is accredited to the brothers van Eyck, was not made until the first half of the 15th century.

The extensibility of oil upon the surface of water appears to have been known by Greek sailors and was applied by them to subduing waves during a storm. This phenomenon of surface tension or extension of oil upon the surface of water, was investigated by the great Hindu mathematician Bhāskara who is presumed to have lived about 1114 to 1178 A.D.

Ample evidence exists which attests the fact that the peoples of all early civilizations were acquainted with numerous uses of fats and waxes and strangely enough, the primary applications of these substances are today much the same as those which prevailed in antiquity. Aside from their uses as foods, they are consumed in the production of protective coatings (paints, varnishes, and finishes of various types), cosmetics and pharmaceuticals, soaps, lubricants, fuels, and illuminants. However, in addition to these uses, fats and oils serve today as the raw materials for the production of such products as textile assistants and synthetic resins, fibers and rubbers, as flotation agents for the separation of the mineral constituents of ores, as de-emulsifiers in the production of petroleum oil, insecticides, weed killers, and in many other products and processes. In fact, the number of products derived from natural fats and oils becomes increasingly larger year by year. This increased and diversified application of natural fats and oils has stemmed primarily from the advances which have been made in the knowledge of the composition, structure, and properties of these substances during the present century.

A number of important discoveries concerning the chemical nature of natural fats were made almost simultaneously with the birth of modern organic chemistry. Scheele obtained glycerol by heating olive oil with litharge in 1779 and about 1815 Chevreul established the fact that the common animal and vegetable fats and oils were composed of glycerol and the higher fatty acids. In 1819 Poutet converted oleic acid to elaidic acid by treatment of the former with the oxides of nitrogen. In 1828 Gusserow differentiated oleic and other unsaturated acids from palmitic and stearic acids on the basis of the differential solubilities of the lead salts of these acids. Following these discoveries little progress was made in the fundamental chemistry of fats and oils until after the beginning of the 20th century, and this despite the fact that during the 19th century the most brilliant and far-reaching discoveries were being made in many fields of organic chemistry.

Various factors appear to have operated to retard the chemists' interest in natural fats. Foremost of these, no doubt, was man's long familiarity with these products, and the fact that over a period of centuries a considerable empirical knowledge concerning them had been acquired, permitting the establishment of numerous industries devoted to the processing of these products for consumption as food, in soapmaking, and in the manufacture of paints, varnishes, and related products. Generally, there were no burdensome surpluses of fats and oils and they did not accumulate as by-products in the manufacture of other products as was the case with coal tar, hence they presented no disposal problem and they were not a source of cheap raw material.

From the academic point of view, fats were not attractive research materials as they were not readily crystallizable and few crystalline derivatives could be prepared from them. Furthermore, they were considered to be very simple substances, or at best, more or less complex mixtures of simple triglycerides of fatty acids. They were assumed to possess few characteristic chemical or physical properties, and they could not be separated into definite chemical entities by any simple method such as crystallization or distillation.

The process of saponification by means of which fats can be broken down to produce fatty acids has been known for about 20 centuries, but the mixtures of fatty acids produced by saponification apparently were no more attractive to the organic chemist than were the original natural fats. Here again, simplicity of structure of the individual acids, the difficulty of isolating them in pure form, and, in the case of the unsaturated acids, the difficulty of converting them to crystalline derivatives appear to have been among the chief reasons for their neglect. The fatty acids were known to consist of a relatively long, saturated or unsaturated, hydrocarbon chain with a terminal carboxyl group. It was assumed that such simplicity of structure afforded little opportunity for applying newly discovered ingenious reactions which were being applied so effectively in other directions in preparing hitherto unknown organic compounds. During this period of development of classical organic reactions, hydrocarbon chemistry, based on petroleum, was in its infancy, and the chemistry of high molecular weight polymers was unknown. However, the development of numerous products from petroleum hydrocarbons, followed by the application of polymerization reactions to many simple organic molecules, undoubtedly stimulated the chemist to turn to the natural fats and their derived fatty acids as a source of raw materials for the production of similar products.

As late as 1924, Armstrong[6] in a Presidential address entitled, *A Neglected Chapter in Chemistry,* presented at the annual meeting of the Society of Chemical Industry, stated: "This account of our knowledge of the fats and of some of the many problems needing study, particularly in the organic branch of chemistry, is mainly written with the hope of reviving interest in them as, apart from physical and analytical investigations, *no other province of chemistry has been so little studied in recent years.*"

Strangely enough, about this time a renaissance in the chemistry of fats had its inception, and at the present time the tempo of research in this field is increasing at a continuously accelerating rate. The increased interest in the chemistry of fats and fatty acids is evident not only in the expansion and diversification of the literature on the subject, but also in the appearance of a number of scientific journals devoted solely to publication of research in this field. Bull[7] has referred to the fact that in 1932, *Chemical Abstracts* contained approximately 800 abstracts on various phases of lipid chemistry compared to approximately 150 in 1917. It should be noted that a very considerable proportion of the recent expansion in the literature relating to fats and fatty acids has had its origin in the multiplication of research laboratories in the United States which are devoted to many phases of research in this field. With the influx of many additional workers in this field there has come a realization that the chemistry of the fats and fatty acids is not as simple as was heretofore supposed and, consequently, many preconceived ideas concerning their nature and reactivity have undergone revision.

It has been found that the glycerides, and/or the fatty acids, are capable of undergoing many types of reactions including condensation and polymerization, halogenation, oxidation, dehydration, isomerization, etc., as well as conversion into numerous derivatives such as amides, amines, ni-

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[6] E. F. Armstrong and J. Allan, *J. Soc. Chem. Ind.*, **43**, 207–218T (1924).

[7] H. B. Bull, *The Biochemistry of the Lipids.* Wiley, New York, 1937.

triles, alcohols, mono- and polyesters, sulfates, sulfonates, etc., and that they otherwise respond to what have been considered the classical reactions of organic chemistry. Furthermore, many of these derived products have been found to possess characteristic properties which adapt them to a variety of special uses including detergents, weed killers, insecticides, wetting agents, flotation agents, cosmetics, pharmaceuticals, plastics, plasticizers, impregnating and finishing agents for textiles and leather, and a host of other uses.

4. Sources

Various lipids, including the glyceride esters or fats, the glycerophosphoric acid esters or phosphatides, and related fatty compounds, occur in almost every type of plant and animal cell and often represent a large part of the total constituents of specialized organs such as seeds, nuts, tubers, animal livers, intermuscular connective tissue, the abdominal cavity, and subcutaneous connective tissue. Hence, whenever any plant or animal material is extracted with certain organic solvents, such as ethyl ether, chloroform, petroleum naphtha, and the like, there is obtained a soluble product generally containing a fat or oil as the principal constituent. Such extractions are made as a matter of course in every proximate analysis of plant or animal tissue but few of these extracts have been examined with respect to their composition and properties. Probably each separate plant or animal organ extracted in this manner yields a fat different in composition from any other fat. In the majority of cases the differences are only of a minor nature, while in others, unusual constituents may be present as has been shown by the investigation of a number of fats elaborated by certain pathogenic microorganisms. Investigations in recent years have established the existence in nature of an appreciable number of fats containing fatty acids having branched aliphatic chains, cyclic substituents, triple bonds, keto groups, and various systems of conjugated double bonds. What other unique structures remain to be discovered cannot be surmised.

Probably less than a thousand fats from all sources have been examined even superficially. Many of these are of academic interest only and many others are of interest primarily because of their biological rather than economic significance. The known fats and oils of economic or industrial significance probably do not exceed a few hundred. However, owing to the widespread distribution of fats and oils, they represent an almost inexhaustible source of long chain aliphatic compounds comparable only with petroleum. They possess an advantage over petroleum in being both more reactive chemically and perennially renewable, whereas petroleum once withdrawn from the earth is nonreplaceable. The greatest advantage enjoyed by petroleum today is its relative cheapness, but with constant shrinkage of supply the price of this raw material may be expected to increase and eventually surpass the cost of crude fats and oils. Thus, it may be expected that eventually perennially renewable fats and oils will supply many of the finished products which are now obtained directly or indirectly from petroleum.

It is generally true for the world as a whole that there are no burdensome surpluses of fats and oils, but at certain times and in certain countries, surpluses have accumulated in sufficient volume to depress market prices of these commodities to a point where they have become attractive industrial raw materials. Potentially, fats and oils are available in enormous volume and await only the application of man's ingenuity to make them available in fact. It is estimated that the jungles of Brazil could supply an amount of oil equivalent to the entire present world demand for these products, whereas at present they contribute but a meager fraction of the world consumption. Other countries of South and Central America likewise possess large potential sources of these products. The exploitation of this vast reservoir of raw material merely awaits the development of adequate transportation facilities, a supply of labor, and the installation of essential processing equipment.[8]

In addition to the vast untapped resources of fats and oils which nature has provided without intervention of man, additional supplies may be produced at will through the application of agricultural methods. The extent to which production can be increased is almost unlimited. The development of the soybean industry in the United States is a good example of these possibilities. The production of soybeans was increased from 4,800,000 bushels in 1925 to 195,000,000 bushels in 1943, and during the same period the production of soybean oil was increased from 2,500,000 to 1,233,000,000 pounds.[9] The production of sunflower seed and oil in the Argentine has undergone a similarly phenomenal increase. The 1925 production of seed is not known but the production of sunflowerseed oil amounted to 694,000 pounds. The 1942 production of seed was 1,400,000,000 pounds and of oil 385,000,000 pounds. By 1944 seed production reached nearly 2,300,000,000 pounds. The world production of linseed and linseed oil in various countries of the world, and especially in the Argentine, has been equally phenomenal but has occurred over a longer period of time. The development of the plantation system of growing the oil palm, *Elaeis guineensis*, in the South Pacific, and the development of the coconut palm and coconut oil industry in the Pacific also testify to the ability of man to produce fats and oils at will and in almost any quantity.

In view of the demonstrated ability of man to expand the production of

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[8] K. S. Markley, *Fat and Oil Resources of Latin America in Plants and Plant Science in Latin America.* F. Verdoorn, ed., Chronica Botanica, Waltham, Mass., 1945, pp. 211–218.

[9] K. S. Markley and W. H. Goss, *Soybean Chemistry and Technology.* Chemical Pub. Co., Brooklyn, 1944.

oil-bearing crops in many parts of the world to supply almost any conceivable demand, and with the approaching exhaustion of irreplaceable raw materials such as fossil resins, petroleum, asphalt, and related products, industry is bound to look more and more to the perennially renewable fats and oils as a source of raw materials. As a matter of fact, so long as the sun shines in the tropics and the fertility of the soil remains, man need not fear the exhaustion of petroleum, coal, and other reserves of organic raw materials as they or their equivalents can be constantly replenished through the production of fats and oils, especially from vegetable sources. They are capable of furnishing a source of long chain carbon compounds, both saturated and unsaturated, which may be broken down by pyrolysis and other reactions to form shorter chain compounds or built up by condensation and polymerization reactions to longer chain compounds. In fact the diversity of products which may be produced from fats and oils, and especially from their component fatty acids, is as great as or greater than those that can be produced from petroleum or coal.

B. CLASSIFICATION AND STRUCTURE OF THE FATTY ACIDS

CHAPTER II

CLASSIFICATION AND NOMENCLATURE

1. Introduction

The fatty acids occur in nature primarily in the form of glycerol or glycerophosphoric acid esters and as the esters of long chain aliphatic alcohols. While the greater portion of the known fatty acids occur naturally in one of these forms, they are also found in small quantities in the form of esters of vitamin A, sterols, and other cyclic compounds. They also occur in small quantities in the uncombined state. In the case of oil seeds, the amount of uncombined fatty acids may be quite large in the early stages of growth but decrease to a low value or disappear entirely by the time complete maturity is attained.

Neglecting the presence of free fatty acids and the fatty acids which are present in the minor constituents, it may be said in general that the characteristics of a given fat or oil are determined primarily by the number and kind of fatty acids which comprise the component glycerides. With few exceptions these fatty acids consist of an even number of carbon atoms arranged in a straight chain with an alkyl group, CH_3—, at one end and a carboxyl group, —COOH, at the opposite end.

Prior to the application of modern methods of identification, and especially the use of x-ray spectroscopy, it was not unusual for workers to report the isolation and identification of various odd-numbered and branched chain acids from natural sources. Of the acids containing an odd number of carbon atoms, margaric acid, $C_{17}H_{34}O_2$, appears to have been most frequently reported from natural sources. Wehmer[1] records ten specific plant sources from which this acid is alleged to have been isolated. The same acid has also been reported from four plant sources under the name daturic acid. The frequency with which margaric acid has presumably been isolated from natural sources results from the fact that stearic and palmitic acids, the two most commonly occurring saturated acids, form a series of solid solutions, as well as a dimeric compound and a eutectic mixture at 50:50 and 30:70 mole per cent of stearic and palmitic acids.[1a] Confusion in identification of margaric acid has arisen from the fact that

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[1] C. Wehmer, *Die Pflanzenstoffe, botanisch–systematisch bearbeitet.* 2nd ed., rev. and enl., Fischer, Jena, 1929–1931. Supplement 1935 (Ergänzungsband zur zweiten Aufl.: Nachträge aus den Jahren 1930–34, unter Mitarbeitung von Magdalena Hadders).

[1a] See Figures 14 and 15, pages 117 and 118.

the properties of various solid solutions and the dimeric compound of stearic and palmitic acids do not differ greatly from those of pure margaric acid.

The property of forming solid solutions and eutectics occurs throughout the homologous series of saturated fatty acids and has led to the misidentification and reporting of a number of nonexistent acids. For example, arachidic acid obtained from peanut oil usually consists of a mixture of C_{20}, C_{22}, and C_{24} acids. Since the melting points of these mixtures are generally lower than the normal C_{20} acid, arachidic acid was for a considerable period assumed to possess a branched chain structure. However, it is now definitely known that pure arachidic acid is *n*-eicosanoic acid, $C_{20}H_{40}O_2$, and whether from peanut oil or any other natural source it possesses a straight chain and an even number of carbon atoms. Many other acids, such as cerotic, montanic, melissic, lacceroic, tachardiacerinic, neocerotic, gossypic, and carnaubic, which have been isolated from natural sources, have been shown by Chibnall *et al.*[2] to consist of mixtures of several acids or of a mixture of acids with alcohols, ketones, or hydrocarbons.

Possibly the only exceptions to the statement that the naturally occurring saturated fatty acids contain only even-numbered, unbranched carbon chains, are isovaleric acid, $(CH_3)_2CHCH_2COOH$, and the recently isolated tubercle bacillus acids. The first-mentioned acid appears to be restricted to the fatty oils of the dolphin and porpoise and the latter to pathogenic microorganisms.

2. Nomenclature

The naturally occurring fatty acids may be divided, on the basis of the absence or presence of double bonds in their hydrocarbon chains, into saturated acids and unsaturated acids. The saturated fatty acids, if they contain no side chains, are also known as normal fatty or aliphatic acids. If they contain substituent atoms or radicals they may bear a prefix such as bromo, hydroxy, keto, etc., to designate the nature of the substituent.

The unsaturated fatty acids can be divided, on the basis of the number of double bonds which are present in the hydrocarbon chain, into monoethenoid, diethenoid, triethenoid, etc., depending on whether they contain one, two, three, etc., double bonds. The polyethenoid acids may also be classified as conjugated or unconjugated depending on the relative positions of the double bonds. If the double bonds are separated by one or more single-bonded carbon atoms, $—C{=}C—C_n—C{=}C—$, the acid is said to be unconjugated. When double-bonded carbon atoms are adjacent to one another, $—C{=}C—C{=}C—$, the acid is referred to as conjugated. If the acid contains one or more triple-bonded carbon atoms, it is referred to as an acetylenic or ethinoid acid.

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[2] A. C. Chibnall, S. H. Piper, A. Pollard, E. F. Williams, and P. N. Sahai, *Biochem. J.*, **28**, 2189–2208 (1934).

If one or more hydrogen atoms of the hydrocarbon chain are substituted with some other atom or radical, such as halogen, hydroxy, or keto, the acid usually retains its specific name which is prefixed by the name and position of the substituent atom or group, such as 2-chlorobutyric acid, 9,10-dihydroxystearic acid, or 10-methylstearic acid. In a few instances the acid may have a distinctive name as well. Thus, 12-hydroxyoleic acid is known as ricinoleic acid after the plant from which it was first obtained. There are still other classes of acids, such as the cyclic acids represented by the chaulmoogra series which are generally referred to by specific names indicating their plant or animal origin.

Much confusion exists in the literature with reference to the nomenclature of the specific fatty acids. Once it was common practice to name each new or supposedly new acid by reference to its specific source without accurate knowledge of its structure. To some extent this practice is still followed. These names provide no clue to the structure of the acid and are generally quite meaningless in this respect. Not infrequently, different names have been assigned to the same acid isolated by different workers, or different names have been assigned to different specimens of the same acid of different degrees of purity.

In 1892, there was adopted at the Geneva Congress[3,4] a system of naming the aliphatic acids which, with certain modifications,[5] is in more or less general use for denoting specific aliphatic acids. By the Geneva rules aliphatic acids are regarded as derivatives of hydrocarbons of the same number of carbon atoms (CH_3— being replaced by —COOH). The name of an acid is formed from the name of the hydrocarbon and a suffix "oic." For the normal saturated fatty acids, the final "e" of the corresponding hydrocarbon is changed to "oic." If the saturated acid contains two carboxyl groups the suffix becomes "dioic," and for three carboxyls, "trioic," etc.

Thus, butyric acid, $CH_3CH_2CH_2COOH$, becomes butanoic acid from butane, $CH_3CH_2CH_2CH_3$, and the suffix "oic." Palmitic acid, $CH_3(CH_2)_{14}COOH$, becomes hexadecanoic acid from hexadecane, $CH_3(CH_2)_{14}CH_3$, and the suffix "oic." In a similar manner the monounsaturated acids are designated by adding "oic" to the Geneva name for the corresponding unsaturated hydrocarbon, thus, the acid $CH_3CH{:}CHCOOH$ is designated as butenoic acid from butene and the suffix "oic." Oleic acid, $CH_3(CH_2)_7CH{:}CH(CH_2)_7COOH$, is octadecenoic acid from octadecene. Triply bonded acids are similarly designated by dropping the final "e" of the corresponding hydrocarbon and adding the suffix "oic." Thus, tariric acid, $CH_3(CH_2)_{10}C{\vdots}C(CH_2)_4COOH$, becomes octadecinoic acid from the triply bonded hydrocarbon octadecine. If multiple numbers of double

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[3] A. Pictet, *Arch. sci. phys. nat.*, **27**, 485–520 (1892).
[4] F. Tiemann, *Ber.*, **26**, 1595–1631 (1893).
[5] A. M. Patterson, *J. Am. Chem. Soc.*, **55**, 3905–3925 (1933).

bonds occur in the carbon chain of the acid the suffix becomes "dienoic," "trienoic," "tetraenoic," etc. Thus, oleic, linoleic, and linolenic acids, containing one, two, and three double bonds are designated octadecenoic, octadecadienoic, and octadecatrienoic acids, respectively.

A modification of this method of nomenclature is the use of the Greek numerical prefix corresponding to the number of carbon atoms in the chain and the generic suffix "oic" to designate a saturated acid, "enic" to designate an acid containing one double bond, and "inic" to designate an acid containing one triple bond. According to this system, the acid having the formula, $C_{10}H_{21}COOH$, is named undecoic acid, and the corresponding double-bond and triple-bond acids, as undecenic and undecinic acids, respectively.

The original Geneva system provided a method of numbering the carbon atoms of the aliphatic saturated acids in which the carbon atom of the terminal carboxyl group was numbered 1 and the adjacent carbon atoms 2, 3, etc. According to this system, the acid corresponding to the formula $CH_3CH_2CHBrCOOH$ would be designated as bromo-2-butanoic acid or 2-bromobutanoic acid, and the acid corresponding to the formula $CH_3(CH_2)_7$-$CHOH(CH_2)_8COOH$ would be designated as 10-hydroxyoctadecanoic or 10-hydroxystearic acid. This system of numbering and nomenclature has also been adopted by *Chemical Abstracts* for indexing purposes.[6]

The Geneva system also provided for numbering the aliphatic acids on the basis of the carboxyl group as a substituent of the corresponding hydrocarbon and, therefore, designates as number 1 the carbon atom adjacent to the terminal carboxyl group.[5] In this system, butyric acid becomes 1-propanecarboxylic acid and 2-bromobutanoic acid becomes 1-bromo-1-propanecarboxylic acid. This system corresponds with the long-practiced method of designating the carbon atoms of the hydrocarbon chain of the acids by the Greek letters α, β, γ, etc., beginning with the carbon atom adjacent to the carboxyl as α. Thus, the acid corresponding to the formula $CH_3CHClCH_2COOH$ would be designated as β-chlorobutanoic or β-chlorobutyric acid.

According to the preferred Geneva system and that used by *Chemical Abstracts*, the bromobutyric acids corresponding to the formulas CH_3CH_2-$CHBrCOOH$, $CH_3CHBrCH_2COOH$, and $CH_2BrCH_2CH_2COOH$ would be designated 2-bromobutanoic, 3-bromobutanoic, and 4-bromobutanoic acids respectively. According to the usage of Greek letters they would be designated α-bromobutyric, β-bromobutyric, and γ-bromobutyric acids, respectively. However, some authors, and especially the *International Critical Tables*,[7] have used the second Geneva system of numbering and designate

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[6] A. M. Patterson and C. E. Curran, *J. Am. Chem. Soc.*, **39**, 1623–1638 (1917); see *Chem. Abstracts*, **39**, 5867–5975 (1945).

[7] *International Critical Tables*, Vol. I, McGraw-Hill, New York, 1926, pp. 176 *et seq.*

these acids as 1-bromobutyric, 2-bromobutyric, and 3-bromobutyric, respectively. The use of this second system of numbering leads to confusion and uncertainty in the absence of the formula for the acid in question. For example, the *International Critical Tables* list without formulas three hydroxystearic acids as 9-hydroxy-, 10-hydroxy-, and 11-hydroxystearic acid. If these acids are named in the same manner as the bromobutyric acids for which formulas are given, they would correspond to the 8-, 9-, and 10-hydroxyoctadecanoic acids of the more generally accepted system of nomenclature. The literature contains many references to 9,10-dihydroxystearic acid by which is generally meant 9,10-dihydroxyoctadecanoic acid indicating that the hydroxyl groups are attached at the ninth and tenth carbon atoms along the chain beginning with the carboxyl carbon atom as 1.

The numbering of the unsaturated acids and substituted unsaturated acids is even more confusing than that of the saturated acids. According to the original Geneva system,[4] the acid corresponding to the formula $CH_2\!:\!CHCH_2COOH$ is named butene-1-carboxylic-4, in which the terminal methylene group is numbered 1. Under the modified system[5] it would be named as 3-butenoic acid or 3-propene-1-carboxylic acid (Rule 64). *Chemical Abstracts* uses the system which would designate this acid as 3-butenoic acid.

The Greek letters α, β, γ, etc., were once used almost universally to designate the position of carbon atoms, or the presence of attached substituents or unsaturation in aliphatic acids. Their use is now generally confined to the shorter chain fatty acids although the Greek letter ω is often used to designate the last carbon atom of the chain irrespective of its length. The use of the system of Greek letters for designating specific carbon atoms finds its greatest vogue in biochemical literature, but even here it is being gradually displaced by the numerical system. However, it is in general use to designate the amino acids, many of which are substituted aliphatic acids.

The Greek letter Δ with a superscript numeral or numerals is commonly used to designate the presence and position of one or more double or triple bonds in the hydrocarbon chain of aliphatic acids. Thus, ordinary oleic acid is designated as $\Delta^{9,10}$-octadecenoic acid, and tariric acid as $\Delta^{6,7}$-octadecinoic acid. Some authors prefer to use only one number to designate the position of a double bond in which case oleic acid would be Δ^{9}-octadecenoic acid, as the double bond is assumed in this case to be between the carbon atom designated and the next higher-numbered carbon atom. *Chemical Abstracts* omits the use of the Δ and also uses only one number to designate the position of the double bond. Thus, linoleic acid is simply designated as 9,12-octadecadienoic acid rather than as $\Delta^{9,10,12,13}$-octadecadienoic acid.

Unfortunately, there is no uniformity in the usage of the various nomenclatures for the fatty acids and it is not uncommon to find the straight chain, saturated acid corresponding to the formula $C_6H_{13}COOH$ referred to as *n*-heptanoic, *n*-heptoic, heptylic, and oenanthic acid, while the acid corresponding to $C_8H_{17}COOH$ is referred to as pelargonic, *n*-nonanoic, *n*-nonoic, and nonylic. Several reasons can be ascribed to the confusion in the nomenclature of the various acids, namely, many common names, such as lauric, palmitic, stearic, etc., are well known, whereas recognition of the systematic names is more restricted, and the application of the systematic nomenclature often results in noneuphonious combinations of syllables which tend to militate against its universal usage. It is not uncommon, therefore, to find an author using one system of nomenclature for one acid and a different system for another acid of the same series. This practice has been followed to some extent in the present work, and although precedence is generally given the Geneva system, or its modification used by *Chemical Abstracts*, long-established common names will also be used wherever they appear preferable. In a few instances the alphabetical system of designating the carbon atoms will be used to avoid confusion in referring to original literature.

It should also be mentioned here that Piper, Chibnall, and Williams[8] examined a considerable number of naturally occurring acids which have been generally designated by such names as lignoceric, cerotic, montanic, and melissic acids. In all cases, these natural acids were shown to consist of variable mixtures of two or more acids of the same homologous series. They, therefore, suggested that the use of these names should be discontinued when reference is made to the pure acids corresponding to the formulas $C_{23}H_{47}COOH$, $C_{25}H_{51}COOH$, etc. Their use is retained here because of the very considerable literature which refers to these acids by their common names. The reader should, however, differentiate between the pure synthetic acids and a mixture of natural acids having the same mean molecular weight as one of the pure acids.

3. Saturated Fatty Acids

The empirical formula for all of the members of the saturated fatty acid series is $C_nH_{2n}O_2$ where n may be any even or odd integer. Since all the acids of the series, except formic, consist of an alkyl chain and terminal carboxyl group, they may be conveniently represented by the formula RCOOH and all members above acetic by the formula $CH_3(CH_2)_nCOOH$. The lower members of the series are liquids at ordinary temperatures, but as the series is ascended the individual members become increasingly more viscous and ultimately pass to crystalline solids. The lower members are

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[8] S. H. Piper, A. C. Chibnall, and E. F. Williams, *Biochem. J.*, **28**, 2175–2188 (1934).

TABLE 1

SATURATED FATTY ACIDS, $C_nH_{2n}O_2$

Systematic name	Common name	Formula	Molecular weight[a]	Neutralization value[b]
n-Methanoic, methoic	Formic	$HCOOH$	46.03	1218.96
n-Ethanoic, ethoic	Acetic	CH_3COOH	60.05	934.26
n-Propanoic, propoic	Propionic	C_2H_5COOH	74.08	757.36
n-Butanoic, butoic	Butyric	C_3H_7COOH	88.10	636.79
n-Pentanoic, pentoic	Valeric	C_4H_9COOH	102.13	549.34
n-Hexanoic, hexoic	Caproic	$C_5H_{11}COOH$	116.15	483.00
n-Heptanoic, heptoic	Heptylic[c]	$C_6H_{13}COOH$	130.18	430.96
n-Octanoic, octoic	Caprylic	$C_7H_{15}COOH$	144.21	389.05
n-Nonanoic, nonoic	Nonylic[d]	$C_8H_{17}COOH$	158.23	354.56
n-Decanoic, decoic	Capric	$C_9H_{19}COOH$	172.26	325.69
n-Undecanoic, undecoic	Undecylic	$C_{10}H_{21}COOH$	186.29	301.17
n-Dodecanoic, dodecoic	Lauric	$C_{11}H_{23}COOH$	200.31	280.08
n-Tridecanoic, tridecoic	Tridecylic	$C_{12}H_{25}COOH$	214.34	261.75
n-Tetradecanoic, tetradecoic	Myristic	$C_{13}H_{27}COOH$	228.36	245.68
n-Pentadecanoic, pentadecoic	Pentadecylic	$C_{14}H_{29}COOH$	242.39	231.46
n-Hexadecanoic, hexadecoic	Palmitic	$C_{15}H_{31}COOH$	256.42	218.80
n-Heptadecanoic, heptadecoic	Margaric	$C_{16}H_{33}COOH$	270.44	207.45
n-Octadecanoic, octadecoic	Stearic	$C_{17}H_{35}COOH$	284.47	197.23
n-Nonadecanoic, nonadecoic	Nonadecylic	$C_{18}H_{37}COOH$	298.49	187.96
n-Eicosanoic, eicosoic	Arachidic	$C_{19}H_{39}COOH$	312.52	179.52
n-Heneicosanoic, heneicosoic	. . .	$C_{20}H_{41}COOH$	326.55	171.81
n-Docosanoic, docosoic	Behenic	$C_{21}H_{43}COOH$	340.57	164.73
n-Tricosanoic, tricosoic	. . .	$C_{22}H_{45}COOH$	354.60	158.22
n-Tetracosanoic, tetracosoic	Lignoceric	$C_{23}H_{47}COOH$	368.62	152.20
n-Pentacosanoic, pentacosoic	. . .	$C_{24}H_{49}COOH$	382.65	146.62
n-Hexacosanoic, hexacosoic	Cerotic	$C_{25}H_{51}COOH$	396.68	141.44
n-Heptacosanoic, heptacosoic	. . .	$C_{26}H_{53}COOH$	410.70	136.60
n-Octacosanoic, octacosoic	Montanic	$C_{27}H_{55}COOH$	424.73	132.09
n-Nonacosanoic, nonacosoic	. . .	$C_{28}H_{57}COOH$	438.75	127.87
n-Triacontanoic, triacontoic	Melissic	$C_{29}H_{59}COOH$	452.78	123.91
n-Hentriacontanoic, hentriacontoic	. . .	$C_{30}H_{61}COOH$	466.80	120.19
n-Dotriacontanoic, dotriacontoic	. . .	$C_{31}H_{63}COOH$	480.83	116.68
n-Tritriacontanoic, tritriacontoic	. . .	$C_{32}H_{65}COOH$	494.86	113.37
n-Tetratriacontanoic, tetratriacontoic	. . .	$C_{33}H_{67}COOH$	508.88	110.24
n-Pentatriacontanoic, pentatriacontoic	. . .	$C_{34}H_{69}COOH$	522.91	107.29
n-Hexatriacontanoic, hexatriacontoic	. . .	$C_{35}H_{71}COOH$	536.94	104.49
n-Heptatriacontanoic, heptatriacontoic	. . .	$C_{36}H_{73}COOH$	550.96	101.83
n-Octatriacontanoic, octatriacontoic	. . .	$C_{37}H_{75}COOH$	564.99	99.30

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[a] Calculated on basis of the International Atomic Weights for 1940.

[b] The neutralization value of a monobasic fatty acid is equal to the number of milligrams of potassium hydroxide required to neutralize one gram of the acid, or 56.104 × 1000/M.W. acid.

[c] Also known as oenanthylic acid. *Chemical Abstracts*, **39**, 5892 (1945), recommends the adoption of *enanthic* as the common name for this acid.

[d] Also known as pelargonic acid.

soluble in water and exhibit weakly acidic properties compared to the strongly dissociated inorganic acids. As will be discussed more fully elsewhere, the boiling and melting points increase, and the specific gravity decreases with increased molecular weight, whereas the dissociation constant varies only slightly from member to member.

The systematic and common names, formulas, molecular weights, and calculated neutralization values of all members of the saturated acid series from formic to octatriacontanoic are given in Table 1. The odd-numbered acids shown in Table 1 do not occur in natural fats. With but two or three exceptions, all of the odd-numbered acids have been prepared synthetically. All of the even-numbered acids from acetic to octatriacontanoic occur either in the free or combined state in nature, and all of them from butyric to octatriacontanoic are present either as glycerides or as monoesters in fats or waxes.

Formic Acid.—The lowest member of the series of saturated acids does not occur as a constituent of fats but is obtained by pyrolysis of many organic substances. It was first obtained by distillation of the red ant, *Formica rufa*, from which it derived its name. It has been reported to occur in the stinging nettle, pine needles, various fruits and other plants and plant organs, as well as in muscle and blood, and in caterpillars.

Acetic Acid.—Acetic acid has not been demonstrated as a constituent of fats but occurs both free and combined in the form of esters of various alcohols in many plants. It is produced by fermentation through the action of various microorganisms and has been detected in animal secretions.

***n*-Propionic Acid.**—This acid does not occur in nature but is produced in small quantities in various fermentation processes.

***n*-Butyric Acid.**—Butyric acid is likewise a product of fermentation, especially by the action of bacteria on starches and sugars. It occurs in the form of monoesters in various ethereal oils and has been shown to be present in the free state in the juice of muscle, in perspiration, and in the feces of animals. It occurs in small proportions (2% to 4%) as a component of the milk fat of various mammals.

***n*-Valeric Acid.**—*n*-Valeric acid contains an odd number of carbon atoms and probably does not occur in fats or possibly elsewhere in nature. Isovaleric acid, $(CH_3)_2CHCH_2COOH$, occurs free in valerian root and as an ester in various ethereal oils. It is also reported to occur as a constituent of dolphin and porpoise oils.

***n*-Caproic Acid.**—This acid is found in milk fats to the extent of about 2% and, in very small amounts ($<1\%$), in coconut oil. At one time it was produced in relatively large quantities from butyl alcohol by the acetoacetic acid synthesis and used as an intermediate in the manufacture of hexylresorcinol.

n-Caprylic Acid.—Caprylic acid occurs in milk fats in small proportions and to the extent of 6% to 8% in coconut oil and in certain other kernel fats of the *Palmae*.

n-Capric Acid.—Capric acid is found in the same fats which contain caprylic acid, and in small quantities in the head oil of the sperm whale.

Lauric Acid.—Lauric acid is one of the three most widely distributed saturated acids found in nature, the other two being palmitic and stearic acids. It is found in practically all of the seed fats of the laurel family from which it derives its name. It occurs in varying and, oftentimes, in large proportions, in these seed fats and also in the seed fats of the *Palmae* or *Palmaceae* where it usually comprises 45% to 50% of the total fatty acids. It is found in cow's butter to the extent of 4% to 8% and also in the milk fats of other mammals.

Myristic Acid.—Myristic acid is found in varying proportions in most animal and vegetable fats. Generally, it comprises only 1% to 5% of the total fatty acids but in milk fats it normally comprises 8% to 12% of the total acids. The head oil of the sperm whale has been found to contain as much as 15% of myristic acid and in some palm seed fats it may comprise 20% of the total fatty acids. Myristic acid predominates in practically all of the fats of the *Myristicaceae.* It occurs to the extent of 70% to 80% in nutmeg (*Myristica fragrans*) butter, from which it derives its name.

Palmitic Acid.—Palmitic acid has been reported to be present in practically every vegetable and animal fat examined to date. On the basis of the frequency of its occurrence it may be considered as the characteristic saturated acid of natural fats. However, the predominance of this acid in nature may be more apparent than real. Despite its wide distribution, it is generally not present in fats in very great proportions. It is a minor component, usually forming less than 5% in the majority of fats but in many of the common vegetable oils of commerce, such as peanut, soybean, and corn oils, and many fish and marine oils, it may comprise as much as 10% of the total fatty acids. Cottonseed and kapok oils may contain up to 20% or more of palmitic acid, while palm oil contains 35% to 40% and Chinese vegetable (*stillingia*) tallow contains 60% to 70% of this acid. It is the most common saturated acid in aquatic animal fats and generally comprises about 15% of the total fatty acids.

Stearic Acid.—Stearic acid, although reported from fewer species of plants and animals and often in smaller amounts than palmitic acid where the two occur together, is of prime importance in commercial fats. It occurs in small amounts in most fruit-flesh and seed fats and in marine oils, and to the extent of 5% to 15% in milk fats. It is the predominant component of the body fats of practically all animals, and comprises 10% to 30% of the fatty acids of lard and tallows.

Arachidic Acid.—Arachidic acid, although fairly widely distributed, constitutes a minor component in most fats. It is found principally in peanut oil and in the oil of related species of plants. The quantity of arachidic acid in peanut oil is apparently influenced by variety and by climatic and soil conditions. The analytical separation of arachidic and lignoceric acids is extremely difficult, and consequently the relative proportions of this pair of acids is not known exactly. However, in certain species of *Sapindaceae* (rambutan tallow, kusum oil, etc.), arachidic acid is reported to exceed 20%.

Behenic Acid.—Behenic acid is a minor component of a few oils such as peanut, rapeseed, and some of the other mustard oils. It was first isolated from ben (behen) oil from which it derives its name. Traces have been reported in the fats of some sharks and a few other species of marine animals.

Lignoceric Acid.—Lignoceric acid is widely distributed in natural fats, but occurs in very small amounts. It is found principally in the seed oils of the legume family. It is a minor constituent of peanut oil but occurs to the extent of 25% in the seed oil of *Adenanthera pavonina* of India.

The remaining acids from C_{26} to C_{38} of Table 1 are found principally in waxes, especially those of insect and plant origin. The difficulties of quantitatively determining the relative percentages of these acids in a mixture of higher fatty acids, or even of isolating pure components from such mixtures, are almost insuperable. Except in the case of the plant waxes examined by Chibnall and co-workers, few rigorously purified, higher fatty acid homologs have been isolated from plant and animal organisms.

4. Unsaturated Fatty Acids

In addition to the saturated acids, there are found in nature a considerable number of unsaturated acids. The known natural acids of this group are characterized by an even number of carbon atoms, and by the fact that they contain one or more double or triple bonds. This series of acids is more heterogeneous than the corresponding saturated acid series, and it can, therefore, be divided into several subgroups on the basis of the number of double bonds which characterize the individual members. As has been previously mentioned, the members of the various subgroups are designated as monoethenoid, diethenoid, triethenoid, etc., acids depending on the number of double bonds present in the carbon chain.

(a) *Monoethenoid Acids*, $C_nH_{2n-2}O_2$

The monoethenoid acids contain two less hydrogen atoms than the corresponding saturated acids and can, therefore, be represented by the empirical formula $C_nH_{2n-2}O_2$. Except for crotonic acid, $CH_3CH:CHCOOH$, which occurs in croton oil, no naturally occurring monoethenoid with a chain length below C_{10} is known. The more important monoethenoid acids which have been identified as components of natural fats are given in Table 2 together with some of their characteristics and sources. These acids differ from one another in chain length, position of the double bond, or both.

TABLE 2

MONOETHENOID FATTY ACIDS, $C_nH_{2n-2}O_2$

Systematic name	Common name	Formula	Molecular weight[a]	Neutralization value[a,b]	Iodine value[a]	Principal source
$\Delta^{4,5}$-Decenoic	Obtusilic	$C_{10}H_{18}O_2$	170.24	329.55	149.10	*Lindera obtusiloba* butter
$\Delta^{9,10}$-Decenoic	Caproleic	$C_{10}H_{18}O_2$	170.24	329.55	149.10	Milk fat
$\Delta^{9,10}$-Dodecenoic	Lauroleic	$C_{12}H_{22}O_2$	198.30	282.93	128.01	*Lauraceae*, sperm whale
$\Delta^{5,6}$-Tetradecenoic	......	$C_{14}H_{26}O_2$	226.35	247.87	112.15	Sperm whale
$\Delta^{9,10}$-Tetradecenoic	Myristoleic	$C_{14}H_{26}O_2$	226.35	247.87	112.15	Milk fats, sperm whale
$\Delta^{9,10}$-Hexadecenoic	Palmitoleic	$C_{16}H_{30}O_2$	254.40	220.53	99.78	Milk fats, marine animals, seed fats
$\Delta^{6,7}$-Octadecenoic	Petroselinic	$C_{18}H_{34}O_2$	282.45	198.63	89.87	*Umbelliferae*
$\Delta^{9,10}$-Octadecenoic	Oleic	$C_{18}H_{34}O_2$	282.45	198.63	89.87	Generally in plants and animals
$\Delta^{11,12}$-Octadecenoic	Vaccenic	$C_{18}H_{34}O_2$	282.45	198.63	89.87	Butter, tallow
$\Delta^{9,10}$-Eicosenoic	Gadoleic	$C_{20}H_{38}O_2$	310.50	180.69	81.75	Fish and marine oils
$\Delta^{11,12}$-Eicosenoic	......	$C_{20}H_{38}O_2$	310.50	180.69	81.75	Jojoba wax
$\Delta^{11,12}$-Docosenoic	Cetoleic	$C_{22}H_{42}O_2$	338.56	165.72	74.98	Marine animals
$\Delta^{13,14}$-Docosenoic	Erucic	$C_{22}H_{42}O_2$	338.56	165.72	74.98	*Cruciferae*
$\Delta^{15,16}$-Tetracosenoic	Sclacholcic	$C_{24}H_{46}O_2$	366.61	153.04	69.24	Fish oils
$\Delta^{17,18}$-Hexacosenoic	......	$C_{26}H_{50}O_2$	394.66	142.16	64.32	*Ximenia americana*
$\Delta^{21,22}$-Tricosenoic	......	$C_{30}H_{58}O_2$	450.76	124.46	56.31	*Ximenia americana*

[a] Calculated on the basis of International Atomic Weights for 1940.

[b] Neutralization or acid value equals the number of milligrams of potassium hydroxide required to neutralize one gram of acid.

In addition to the naturally occurring monoethenoid acids isolated from natural sources, many have been prepared synthetically. The monounsaturated acids which have been synthesized include both odd and even members of the series. Among the synthetic acids, especially those having relatively long carbon chains, the double bond has been confined primarily, although not exclusively, to the α and ω carbon atoms of the methylene chain, *i. e.*, to the carbon atom adjacent to the carboxyl and to the terminal methylene group. However, all of the various possible positional isomers of the lower members of the series have been synthesized. For example, the four hexenic acids corresponding to caproic or hexanoic acid of the saturated series, have been synthesized and many of their properties and reactions investigated.

The majority of unsaturated fatty acids, whether mono- or polyethenoid, which have been isolated from plants and animals, contain a double bond between the ninth and tenth carbon atoms. Of these acids, oleic, $C_{18}H_{34}O_2$, and palmitoleic, $C_{16}H_{30}O_2$, are by far the most important. Both are widely distributed in nature and, in frequency of occurrence, constitute the predominant natural acids of the monoethenoid series just as stearic and palmitic acids constitute the predominant natural acids of the saturated series. A number of the naturally occurring monoethenoid acids have their double bond at other than the 9,10-position. These acids represent minor components of the fats in which they are found and are limited to a few families, and generally to a few species of plants and animals. The principal exceptions are the occurrence of petroselinic, $C_{18}H_{34}O_2$, and erucic, $C_{22}H_{42}O_2$, acids. These acids, which have double bonds between the 6,7- and 13,14-carbon atoms, respectively, have been found to comprise 70% to 80% of the total fatty acids of a few seed fats.

Decenoic Acid.—With the exception of crotonic acid, $C_4H_6O_2$, decenoic acid, $C_{10}H_{18}O_2$, appears to be the lowest molecular weight, monoethenoid fatty acid isolated from natural sources. Two isomers are known, one containing a double bond in the 9,10-position and the other in the 4,5-position. The former has been detected in milk fat to the extent of about 0.2%. Traces of $\Delta^{9,10}$-decenoic acid have also been reported to occur in the head oil of the sperm whale. Komori and Ueno[9] and Toyama[10] reported the isolation of the second isomer from the seed oil of *Lindera obtusiloba* grown in Korea. The acid, which was obtained in very small quantity (2.9 g. from 5 kg. of oil), was named obtusilic acid after its source.

Dodecenoic Acid.— 3 isomeric dodecenoic acids, $C_{12}H_{22}O_2$, have been found to occur in nature. Lauroleic acid, the $\Delta^{9,10}$-isomer, has been found in butter in very small proportions and the $\Delta^{4,5}$-isomer in the seed oil of *Lindera obtusiloba.* Hilditch and Lovern[11] reported the presence in sperm head oil of about 4% of $\Delta^{3,4}$-dodecenoic acid. Because of its occurrence in denticete whales it has been referred to as denticetic acid.

Tetradecenoic Acid.—Myristoleic acid has been frequently used in the literature to refer to $\Delta^{9,10}$-tetradecenoic acid because of its constitutional analogy to oleic and myristic acids. However, at least three isomeric tetradecenoic acids have been isolated from various sources. The $\Delta^{9,10}$-isomer has been found in traces in the depot fats of some land animals (beef and pork), and in butter, and to the extent of about 1% in most marine animal oils. According to Atherton and Meara,[12] this acid constitutes over 20% of the total fatty acids of kombo fat from *Pycnanthus kombo.* The $\Delta^{4,5}$-isomer, tsuzuic acid, has been found to be a minor component of the seed fat of *Lindera obtusiloba,* and the $\Delta^{5,6}$-isomer, which is also known as physteric acid, has been reported as a constituent of sperm head oil to the extent of about 14%. With the exception of the $\Delta^{9,10}$- and $\Delta^{5,6}$-tetradecenoic acids in kombo fat and sperm head oil, respectively, none of the monoethenoid acids referred to thus far have been found in any appreciable quantity, and they have seldom been isolated from a given source in quantities exceeding a few grams.

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[9] S. Komori and S. Ueno, *Bull. Chem. Soc. Japan,* 12, 226 (1937).
[10] Y. Toyama, *J. Soc. Chem. Ind. Japan,* 40, 285–289B (1937).
[11] T. P. Hilditch and J. A. Lovern, *J. Soc. Chem. Ind.,* 47, 105–111T (1928).
[12] D. Atherton and M. L. Meara, *J. Soc. Chem. Ind.,* 58, 353–357 (1939).

Hexadecenoic Acid.—Palmitoleic or $\Delta^{9,10}$-hexadecenoic acid, like myristoleic acid, has been named from its analogy to palmitic and oleic acids. It has been found to occur quite widely throughout the plant and animal kingdoms. It has also been reported under the name zoömaric and physetoleic acid. Palmitoleic acid appears to be the characteristic acid of cold-blooded animals (fish, amphibia, and reptiles); as oleic acid is of warm-blooded animals. It is also associated with the fats of lower orders of both plants and animals, and has been isolated in varying amounts from the head oil and blubber of whales, from porpoise blubber, seal oil, cod liver oil, and from fish oils in general, including the oils of various rays and sharks. It has also been found in algae, diatoms, plankton, bacteria, yeast, and crytogamous spores, and in the depot fats of amphibia and reptiles.

Marine animal oils usually contain 15% to 20% of palmitoleic acid; the depot fats of amphibia and reptiles from 8% to 15%; the depot fats of birds and mammalian liver fats from 6% to 8%; mammalian depot fats 2% to 3%; and milk fats, 3% to 4%. The seed fats usually contain only small proportions of palmitoleic acid. Cottonseed, peanut, soybean, palm, olive, and teaseed oils have been shown to contain this acid in small amounts usually less than 1% of the total fatty acids.

Octadecenoic Acid.—Oleic or *cis*-$\Delta^{9,10}$-octadecenoic acid, $C_{18}H_{34}O_2$, is generally considered to be the predominant fatty acid of natural fats. It has been found in practically every plant and animal fat in some proportion and frequently comprises 50% or more of the total fatty acids. Relatively few fats contain so little as 10% of this acid.

Of the 16 positionally isomeric *cis*-octadecenoic acids only three authentic natural isomerides have been isolated and characterized, namely, ordinary oleic or $\Delta^{9,10}$-octadecenoic acid, petroselinic or $\Delta^{6,7}$-octadecenoic acid, and vaccenic or $\Delta^{11,12}$-octadecenoic acid. *Petroselinic acid* has been observed to occur in many members of the *Umbelliferae* and it has also been isolated from ivy seed oil. In parsley seed oil and other umbelliferous oils, it comprises 20% to 75% of the total fatty acids and it is also the chief unsaturated fatty acid of nigaki oil. *Vaccenic acid* has been reported by various workers as a minor constituent of butter, beef, and mutton fats, lard, and whale oil.

Millican and Brown[13] systematically investigated the oleic acid fraction of a variety of animal and vegetable fats and concluded that the octadecenoic acids of chicken fat, peanut, cottonseed, corn, and linseed oils appear to be identical with the oleic acid of olive oil. On the other hand, the octadecenoic acids of lard, beef tallow, beef adrenal phosphatides, pork liver lipids, human fat, and to a somewhat lesser degree, soybean and rapeseed oils appear to be mixtures of oleic acid with other isomeric octadecenoic

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[13] R. C. Millican and J. B. Brown, *J. Biol. Chem.*, 154, 437–450 (1944).

TABLE 3

POLYETHENOID FATTY ACIDS

Systematic name	Common name	Formula	Molecular weight[a]	Neutralization value[a, b]	Theoretical iodine value[a]	M.p., °C.	Principal source
$\Delta^{9,10,12,13}$-Octadecadienoic	Linoleic	$C_{18}H_{32}O_2$	280.44	200.06	181.03	−5.0 to −5.2[c]	Most seed fats
$\Delta^{6,7,10,11,14,15}$-Hexadecatrienoic	Hiragonic	$C_{16}H_{26}O_2$	250.37	224.08	304.16	.....	Japanese sardine oil
$\Delta^{9,10,12,13,15,16}$-Octadecatrienoic	Linolenic	$C_{18}H_{30}O_2$	278.42	201.51	273.51	−11.0 to −11.3[c]	Linseed, perilla, chia, soybean
$\Delta^{9,10,11,12,13,14}$-Octadecatrienoic	Elaeostearic	$C_{18}H_{30}O_2$	278.42	201.51	273.51	α-form 48–49 β-form 71.5–71.8	Tung, po-yoak, neou, essang, loofah
$\Delta^{9,10,11,12,13,14,15,16}$-Octadecatetraenoic	Parinaric	$C_{18}H_{28}O_2$	276.40	202.98	367.35	α-form 85–86 β-form 95–96	*Parinarium laurium*
$\Delta^{5,6,8,9,11,12,14,15}$-Eicosatetraenoic	Arachidonic	$C_{20}H_{32}O_2$	304.46	184.28	333.50	−49.5	Liver, brain, and depot fats of animals, especially in phosphatides
$\Delta^{4,5,8,9,12,13,15,16,19,20}$-Docosapentaenoic	Clupanodonic	$C_{22}H_{34}O_2$	330.49	169.76	384.03	.....	Marine animal oils
$\Delta^{4,5,8,9,12,13,15,16,18,19,21,22}$-Tetracosahexaenoic	Nisinic	$C_{24}H_{36}O_2$	356.53	157.36	427.19	.....	Japanese sardine oil

[a] Calculated on the basis of International Atomic Weights for 1940.

[b] Neutralization or acid value equals the number of milligrams of potassium hydroxide required to neutralize one gram of acid.

[c] Values according to Matthews, Brode, and Brown.[19] Melting of linoleic acid has also been reported as −6.0° to −6.5°C., and linolenic as −14° to −15°C.

acids. Beef fat and lard appear to contain vaccenic acid as had been previously reported. The authors conclude that octadecenoic acids, other than oleic acid, are of general occurrence in lipids of animal origin. In this connection, it might be mentioned that Channon, Irving, and Smith[14] suggested the presence of $\Delta^{10,11}$-octadecenoic acid in pork liver lipids.

Until recently, oleic acid has probably never been obtained in anything approaching a high degree of purity, consequently nearly all of the older data relative to the physical constants and, in some instances, chemical behavior of this acid are, except in fortuitous cases, probably reliable only as approximations.

Eicosenoic Acid.—Gadoleic or $\Delta^{9,10}$-eicosenoic acid, $C_{20}H_{38}O_2$, and the isomeric $\Delta^{11,12}$-acid represent the only authentic C_{20} monoethenoid acids thus far identified from natural sources. The former has been found in cod liver oil, sardine, herring, whale, and other fish and marine animal oils in varying proportions but usually less than 5% to 10% of the total fatty acids. The $\Delta^{11,12}$-isomer has been reported from only one source, namely, jojoba wax.

Docosenoic Acid.—Erucic or $\Delta^{13,14}$-docosenoic acid, $C_{22}H_{42}O_2$, and cetoleic or $\Delta^{11,12}$-docosenoic acid appear to be the only authentic C_{22} monoethenoid acids thus far identified from natural sources. The absence in natural fats of the corresponding $\Delta^{9,10}$-acid is difficult to understand.

Cetoleic acid has been reported only from marine animal oils, usually in small proportions. Erucic acid has been found only in the seed fats of the *Cruciferae* and *Tropaeolaceae* and in these fats it is the characteristic acid. It constitutes 40% to 50% of the total fatty acids of rapeseed, mustard- and wallflowerseed, and it represents up to 80% of fatty acids of nasturtium seeds. The isolation of pure erucic acid has been even more difficult than the isolation of oleic acid. Dorée and Pepper[15] systematically investigated various methods of obtaining this acid from rapeseed and reported a procedure which gives what they consider to be a relatively pure product.

Tetracosenoic Acid.—Selacholeic or $\Delta^{15,16}$-tetracosenoic acid, $C_{24}H_{46}O_2$ also known as nervonic acid, has been reported to occur in small proportion in the elasmobranch fish oils, but not in the fats and oils of teleostid fish and other marine animals. It has also been shown to be a constituent of the cerebrosides of the brain, hence the name, nervonic acid.

Hexacosenoic Acid.—Traces of a hexacosenoic acid have been reported in the body oil of the castor oil fish.

(*b*) *Diethenoid Acids*, $C_nH_{2n-4}O_2$

In addition to the monoethenoid fatty acids of Table 2, there are known a number of polyethenoid acids which possess unbranched hydrocarbon

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[14] N. J. Channon, E. Irving, and J. A. B. Smith, *Biochem. J.*, **28**, 840–852 (1934).

[15] C. Dorée and A. C. Pepper, *J. Chem. Soc.*, **1942**, 477–483.

chains and two or more double bonds. The principal acids of this class are listed in Table 3 together with some of their properties. Only two of these acids, namely, linoleic and linolenic acids, containing two and three double bonds, respectively, can be considered to occur in nature with appreciable frequency. No acyclic, polyethenoid fatty acids containing less than eighteen carbon atoms are known with certainty to occur in plant fats. Lovern,[16] in a critical review of the occurrence of polyethenoid fatty acids in aquatic animals, mentions the occurrence of C_{14} and C_{16} acids of this type. Hiragonic acid, $C_{16}H_{26}O_2$, which has been found in Japanese sardine oil appears to be the principal representative of these acids.

Although the introduction of two or more double bonds in the carbon chain provides increased opportunity for the formation of positional isomers, actually fewer isomeric polyethenoid than monoethenoid acids have been detected in natural fats. For example, only one diethenoid fatty acid, namely, ordinary linoleic acid, has been unequivocally identified as being present in plant or animal fats, whereas sixteen monoethenoid acids have been identified from these sources.

Linoleic Acid.—Linoleic or $\Delta^{9,10,12,13}$-octadecadienoic acid, $C_{18}H_{32}O_2$, is widely distributed in the plant kingdom, and by frequency, as well as proportionality, it is the most important polyethenoid acid found in fats and oils. It is a characteristic, and oftentimes major component of many of the important fats of commerce, including cottonseed, soybean, peanut, corn, sunflowerseed, poppyseed, linseed, and perilla oils. This acid almost invariably accompanies oleic acid in vegetable fats and is generally thought to be the characteristic acid of drying oils. However, unless modified in some manner to improve their drying characteristics, oils containing fatty acids no more unsaturated than linoleic, find only limited employment in the drying oil industry. Oils, such as peanut, palm, olive, teaseed, kapok, etc., having less than 25% linoleic acid, have practically no value as drying oils. Oils such as corn germ, cottonseed, sunflowerseed, poppyseed, sesame, etc., which contain 40% to 65% of linoleic acid but no linolenic acid, are sometimes classed as semidrying oils, but actually they find little employment in the drying oil industry. Linoleic and other diethenoid fatty acids appear to be absent in all but a very few marine animal oils.

Evidence that linoleic acid from whatever natural source is invariant as regards its chemical configuration is conflicting. Although long the subject of investigation and discussion, the structure of the linoleic acid obtained from the great majority of plant sources is now firmly established as *cis*-$\Delta^{9,10}$-*cis*-$\Delta^{12,13}$-octadecadienoic acid. The evidence on which this structure rests is very voluminous and has been ably summarized by Hil-

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[16] J. A. Lovern, *The Composition of the Depot Fats of Aquatic Animals.* Food Investigation Board, Special Report No. 51, H. M. Stationery Office, London, 1942.

ditch.[17] Although no positional or geometric isomer of ordinary linoleic acid has been isolated from plant fats and unequivocally identified, the existence of such isomers has been inferred. The principal basis for assuming the existence of isomeric linoleic acids has been the failure to obtain insoluble tetrabromo derivatives corresponding to known amounts of linoleic acid used in bromination experiments even though the yield of α-tetrabromostearic acid has been corrected as proposed by Brown and co-workers[18–21] by multiplying the yield of petroleum ether-insoluble tetrabromides by a factor of 100/90.6 or 1.1037.

For example, Inoue and Suzuki[21a] isolated a linoleic acid from the oil of the silk worm pupa which gave no solid tetrabromide. On partial hydrogenation with one mole of hydrogen this isolinoleic acid gave oleic acid which on oxidative cleavage gave pelargonic and azelaic acids. The velocity of the hydrogenation of ordinary linoleic acid was found to be more rapid than that of the new isolinoleic acid. The authors claimed the original iso acid possessed a structure corresponding to $\Delta^{9,10,12,13}$-octadecadienoic acid, thus indicating it was a geometrical rather than a positional isomer of linoleic acid.

Frankel, Stoneburner, and Brown[20] isolated from olive oil by low temperature crystallization, various fractions of linoleic acid which, on the basis of corrected tetrabromide and thiocyanogen values, apparently contained only 52% to 78% of the normal linoleic acid, whereas, on the basis of iodine numbers, they contained 81% to 96% of this acid. Linoleic acid prepared by the same method from corn, sesame, cottonseed, grapeseed, and poppyseed oils gave corrected tetrabromide and thiocyanogen values corresponding to 95% to 100% of the normal acid. These authors concluded, therefore, that the various linoleic acid fractions from olive oil contained 19% to 40% of an octadecadienoic acid which was not identical with *cis*-$\Delta^{9,10}$-*cis*-$\Delta^{12,13}$-octadecadienoic acid.

Ambiguity also exists concerning the nature of the linoleic acid obtained from sources other than the seed fats. Wherever the normal linoleic acid of the seed fats has been identified from animal sources, it has been presumed to have been present as a result of ingestion and storage by the animal of the fat *per se.* The linoleic acid which is present in fish and marine animal oils, milk fat, liver and depot fats of beef and sheep, etc., is generally presumed to possess a configuration different from that of the

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[17] T. P. Hilditch, *The Chemical Constitution of Natural Fats.* Chapman & Hall, London, 1940, pp. 331–336.

[18] J. B. Brown and J. Frankel, *J. Am. Chem. Soc.*, **60**, 54–56 (1938).

[19] N. L. Matthews, W. R. Brode, and J. B. Brown, *J. Am. Chem. Soc.*, **63**, 1064–1067 (1941).

[20] J. S. Frankel, W. Stoneburner, and J. B. Brown, *J. Am. Chem. Soc.*, **65**, 259–262 (1943).

[21] J. S. Frankel and J. B. Brown, *J. Am. Chem. Soc.*, **65**, 415–418 (1943).

[21a] Y. Inoue and B. Suzuki, *Proc. Imp. Acad. Tokyo*, **7**, 15–18 (1931).

acid present in plant fats. Considerable evidence is available to the effect that linoleic acid, as well as linolenic and arachidonic acids, are not only essential to the maintenance of health and normal reproduction of animals, but also that at least some species of animals are incapable of synthesizing these acids and must obtain them by ingestion from other sources. If this is actually the case, the linoleic acid found in these animals must be the same as that contained in the ingested vegetable matter unless it undergoes rearrangement in the animal organism. Spectroscopic and other evidence indicates that the fatty acids which are stored in various fat depots of experimental animals correspond to those which the animal has ingested. If, indeed, this is the case, and also that different linoleic acids actually occur in animal organisms, then it may be assumed that they also occur in plants. On the other hand, it may be possible that the apparent dissimilarities in the linoleic acids derived from plants and animals may result from limitations in analytical techniques, and especially in the bromination and oxidation procedures, when applied to small amounts of linoleic acid in the presence of complex mixtures of other unsaturated fatty acids.

(c) *Triethenoid Acids,* $C_nH_{2n-6}O_2$

Unlike the diethenoic acid series, which is represented by only one well-known member, namely, linoleic acid, the triethenoic series is represented by the equally well-known linolenic acid and several isomers. These acids, with one exception, contain C_{18} carbon chains and three double bonds either in isolated or in conjugated positions.

Hiragonic Acid.—Hiragonic or $\Delta^{6,7,10,11,14,15}$-hexadecatrienoic acid, $C_{16}H_{26}O_2$, is the only member of the triethenoid acid series which contains less than eighteen carbon atoms. Its presence was reported by Toyama and Tsuchiya[22] as a minor component of the oil of the Japanese sardine, *Clupanodon melanostica.*

Linolenic Acid.—Linolenic or $\Delta^{9,10,12,13,15,16}$-octadecatrienoic acid $C_{18}H_{30}O_2$, is of frequent occurrence in many seed fats, although oftentimes in very small quantities. The presence of linolenic acid in oils markedly increases their drying properties. However, it must be present in appreciable proportion to produce effective drying and film formation. Oils containing relatively large proportions of linoleic acid, but less than 15% linolenic acid, *e. g.,* soybean, safflower and walnut seed, find only limited direct use in the drying oil industry. Their principal use is in the preparation of synthetic resins or in admixture with faster drying oils in the manufacture of paints, varnishes, printing inks, linoleum, etc. When the proportion of linolenic acid exceeds 25%, the drying and film-forming properties become quite pronounced. Only a few oils of commerce, *e. g.,* linseed, pe-

[22] Y. Toyama and T. Tsuchiya, *Bull. Chem. Soc. Japan,* **10,** 192–199 (1935).

rilla, and hempseed, possess a linolenic acid content of 25% to 50%, together with an appreciable content of linoleic acid. Therefore, only such oils find direct employment in the manufacture of the majority of house paints and related products.

An isomer of linolenic acid, namely, $\Delta^{6,7,9,10,12,13}$-octadecatrienoic acid, has been isolated from the seed fat of the evening primrose, *Oenothera biennis.*

Elaeostearic Acid.—Another isomer of linolenic acid, elaeostearic or $\Delta^{9,10,11,12,13,14}$-octadecatrienoic acid is the principal acid occurring in tung or China wood oil. It occurs to the extent of 85% to 90% of the total fatty acids of this oil and has been reported to be present in small proportions in the seed fats of a few other plants. Unlike the other fatty acids mentioned thus far, its double bonds are arranged in conjugated instead of isolated positions.

Arrangement of the double bonds of a fatty acid in conjugated positions, $-\mathrm{C{=}C{-}C{=}C{-}C{=}C}-$, as contrasted with a similar number of double bonds in the isolated or nonconjugated positions, $-\mathrm{C{=}C{-}C{-}C{=}C{-}C{-}C{=}C}-$, results in marked differences in chemical and physical properties of the two types of acids. The most apparent differences resulting from this difference in arrangement of double bonds are observed in the refractive indices, absorption spectra, addition of halogens, rates of absorption of oxygen, and polymerization. A striking effect resulting from the presence of double bonds in the conjugated position is noted in the melting points of such acids. All of the C_{18} unsaturated acids considered thus far are liquids at ordinary temperatures. It is generally assumed that the effect of shifting double bonds toward the carboxyl end of the molecule tends to raise the melting point, and shifting them away from the carboxyl tends to lower it. However, nearly all of the polyethenoid acids contain a double bond in the 9,10-position with additional bonds farther removed from the carboxyl. When additional double bonds are introduced, the normal tendency is to depress the melting point (oleic 13–16°C., linoleic acid −5°C. linolenic acid −11°C.). The same number of double bonds in conjugated positions, however, appear to result in an increase in the melting point, *e. g.*, α-elaeostearic acid, 48–49°C.; β-elaeostearic acid, 71°C.; punicic acid, 44°C.; trichosanic acid, 35–35.5°C.

Fats and fatty acids containing conjugated double bonds do not add halogens to complete saturation in the same manner as those containing nonconjugated bonds and, therefore, they give lower than the theoretical iodine values under standard conditions. On the other hand, they absorb oxygen and polymerize more readily to form alkali- and water-resistant films than is the case with nonconjugated fats and fatty acids, and they are, therefore, used extensively in the manufacture of rapid drying varnishes and enamels, insulation and waterproofing compounds, and similar products. The introduction of double bonds in conjugated positions likewise results in a tendency of these acids to form crystalline isomerides which can be differentiated primarily on the basis of melting points. The naturally occurring elaeostearic acid melting at 48–49°C. has been designated as α-elaeostearic. It is readily converted by the action of light and other agents to a higher melting form which has been designated β-elaeostearic acid, m.p. 71°C.

To date, no conclusive evidence has been adduced to indicate that conjugated double bond acids occur in animal fats and oils of either land or marine origin. In fact, Miller and co-workers[23,24] have shown spectroscopically that when conjugated fatty acids are ingested by animals they are stored as such in the various fat depots and their disappearance from these depots is accompanied by the appearance of absorption maxima unrelated to any known fatty acid.

Punicic and Trichosanic Acids.—Two additional isomers of elaeostearic acid have been reported, namely, punicic acid, m.p. 44°C., from pomegranate oil and trichosanic acid, m.p. 35°C., from *Trichosanthes cucumeroides.* Both are $\Delta^{9,10,11,12,13,14}$-octadecatrienoic acids and both can be converted by the action of light to β-elaeostearic acid. They appear, therefore, to be crystalline isomerides of α-elaeostearic acid.

(*d*) *Tetraethenoid Acids,* $C_nH_{2n-8}O_2$

The tetraethenoic acid series is represented by at least two members, namely, parinaric acid containing a C_{18} carbon chain, and arachidonic acid containing a C_{20} carbon chain. It is not improbable, however, that other tetraethenoid acids occur in nature. The difficulties involved in isolating these acids in pure form and of determining their structures increase with increasing degree of unsaturation and corresponding instability.

Parinaric Acid.—Parinaric or $\Delta^{9,10,11,12,13,14,15,16}$-octadecatetraenoic acid is the only authentic acid containing four double bonds which has thus far been isolated from seed fats. The positions of the double bonds are not exactly known, but probably are as represented above. The naturally occurring modification, or α-form, melts at 85–86°C. but is readily converted to another modification, or β-form, melting at 95–96°C. Farmer and Sunderland[25] have shown that the acid contained four double bonds in a conjugated position. The high melting point and existence of two crystalline isomers are in accord with the conjugated position of its double bonds.

Arachidonic Acid.—Arachidonic or $\Delta^{5,6,8,9,11,12,14,15}$-eicosatetraenoic

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[23] E. S. Miller and G. O. Burr, *Proc. Soc. Exptl. Biol. Med.*, **36,** 726–729 (1937).

[24] E. S. Miller, R. H. Barnes, J. P. Kass, and G. O. Burr, *Proc. Soc. Exptl. Biol. Med.*, **41,** 485–489 (1939).

[25] E. H. Farmer and E. Sunderland, *J. Chem. Soc.*, **1935,** 759–761.

acid, $C_{20}H_{32}O_2$, is an unsaturated acid containing four double bonds, none of which are in a conjugated position. The exact locations of the double bonds in this acid was a matter of controversy for a time but the positions assigned to them now appear to be firmly established. This structure was first proposed by Dolby, Nunn, and Smedley-Maclean[26] and definitely proved by Mowry, Brode, and Brown[27] on the basis of ozonolysis at dry ice temperatures and acetone-potassium permanganate oxidation of methyl arachidonate. Subsequently, this structure was also confirmed by Arcus and Smedley-Maclean.[28]

Arachidonic acid has been found to occur in small quantities in the brain, liver, blood, and depot fats of cattle and pigs. It appears to be present in various amounts in the phosphatides of animals, especially the suprarenal phosphatides in which it has been found to comprise 20% of the total fatty acids. According to Turpeinen,[29] Smedley-Maclean and co-workers,[30,31] Burr and co-workers,[32] Sinclair,[33] Quackenbush and co-workers,[34] and others, arachidonic, like linoleic acid, is an essential fatty acid which must be supplied in the diet for the maintenance of normal health and reproduction. However, arachidonic acid does not occur in plants, consequently it must be synthesized by herbivorous animals and there is some evidence which indicates that this is possible provided the animal organism is supplied with linoleic or linolenic acid. The presence of isomeric eicosatetraenoic acids has been reported to occur in marine animal oils but the structures of these acids have not been determined with certainty.

(*e*) *Other Polyethenoid Acids*

A number of other polyethenoid acids, primarily, if not entirely, of marine animal origin, are known. They contain twenty or more carbon atoms and five to six double bonds. Those of most frequent occurrence and in largest proportion contain C_{20} and C_{22} skeletons. Considerable uncertainty exists with respect to the number and location of the double bonds in these acids.

Clupanodonic Acid.—Clupanodonic or $\Delta^{4,5,8,9,12,13,15,16,19,20}$-docosapentaenoic acid, $C_{22}H_{34}O_2$, contains five double bonds probably arranged as indicated above. It occurs in practically all marine animal oils from which

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[26] D. E. Dolby, L. C. A. Nunn, and I. Smedley-Maclean, *Biochem. J.*, **34**, 1422–1426 (1940).

[27] D. T. Mowry, W. R. Brode, and J. B. Brown, *J. Biol. Chem.*, **142**, 679–91 (1942).

[28] C. L. Arcus and I. Smedley-Maclean, *Biochem. J.*, **37**, 1–6 (1943).

[29] O. Turpeinen, *Proc. Soc. Exptl. Biol. Med.*, **37**, 37–40 (1937); *J. Nutrition*, **15**, 351–366 (1938).

[30] L. C. A. Nunn and I. Smedley-Maclean, *Biochem. J.*, **32**, 2178–2184 (1938).

[31] I. Smedley-Maclean and L. C. A. Nunn, *Biochem. J.*, **34**, 884–902 (1940).

[32] G. O. Burr, J. B. Brown, J. P. Kass, and W. O. Lundberg, *Proc. Soc. Exptl. Biol. Med.*, **44**, 242–244 (1940).

[33] R. G. Sinclair, *J. Nutrition*, **19**, 131–140 (1940).

[34] F. W. Quackenbush, F. A. Kummerow, and H. Steenbock, *J. Nutrition*, **24**, 213–224 (1942).

source it was first isolated by Tsujimoto. It has been shown to contain an aliphatic chain containing twenty-two carbon atoms and five double bonds,[35,36] whose positions were established by Toyama and Tsuchiya[37] to be as indicated in the formula above. The exact location of the double bonds of clupanodonic acid has been a matter of controversy for years, and on the basis of Lovern's[16] review of the subject it cannot be considered entirely settled.

A docosahexaenoic acid, $C_{22}H_{32}O_2$, containing six double bonds has been isolated from Japanese sardine oil by Toyama and Tsuchiya[38] and from cod liver oil by Farmer and van den Heuvel.[39] According to the latter authors it is the predominant unsaturated acid in cod liver oil. The exact location of the six double bonds in this acid has been the subject of controversy and at least five different structures have been assigned to it. The two structures which have received most general acceptance correspond to $\Delta^{4,5,8,9,12,13,15,16,18,19,21,22}$- and $\Delta^{4,5,8,9,11,12,14,15,17,18,20,21}$-docosahexaenoic acids.

Scoliodonic Acid.—Scoliodonic is one of a number of C_{24} unsaturated acids which have been reported to occur in very small proportions in marine animal oils. Ozonolysis indicates the presence of five double bonds.

Nisinic Acid.—A tetracosahexaenoic acid, $C_{24}H_{36}O_2$, containing six double bonds has been reported to occur in Japanese sardine oil. The acid is assumed to have a structure corresponding to $\Delta^{4,5,8,9,12,13,15,16,18,19,21,22}$-tetracosahexaenoic acid.

Other polyethylenic acids including a tetracosaheptaenoic, hexacosapentaneoic, octacosapentaenoic, and octacosaheptaenoic acids have been reported to occur in various marine animal oils.[16,17]

(*f*) *Ethinoic Acids*

Although many aliphatic triply bonded or ethinoic acids are known, only two have been identified with certainty as components of natural fats. However, many acids of this series have been prepared in the laboratory. The majority of them have a triple bond at either the α or ω position in the hydrocarbon chain, *e. g.*, propiolic or α-propinoic acid, $HC{:}C{\cdot}COOH$, m.p. 9°C., b.p. 144°C.; tetrolic or α-butinoic acid, $CH_3C{:}C{\cdot}COOH$, m.p. 76°C., b.p. 203°C.; ω-pentinoic acid, $HC{:}C{\cdot}CH_2CH_2COOH$, dehydroundecylenic or ω-undecinoic acid, $HC{:}C(CH_2)_8COOH$, m.p. 43°C., b.p.

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[35] M. Tsujimoto, *J. Soc. Chem. Ind. Japan*, **23**, 1007–1010 (1920); *Bull. Chem. Soc. Japan*, **3**, 299–307 (1928).

[36] M. Tsujimoto and K. Kimura, *J. Soc. Chem. Ind. Japan*, **26**, 1162 (1923).

[37] Y. Toyama and T. Tsuchiya, *Bull. Chem. Soc. Japan*, **10**, 411–453 (1935); **11**, 745–750, 751–753 (1936).

[38] Y. Toyama and T. Tsuchiya, *Bull. Chem. Soc. Japan*, **10**, 539–543 (1935).

[39] E. H. Farmer and F. A. van den Heuvel, *J. Chem. Soc.*, **1938**, 427–430; *J. Soc. Chem. Ind.*, **57**, 24–31T (1938).

at 15 mm. 175°C. Some of the synthetic ethinoic acids have a triple bond elsewhere in the chain, *e. g.*, stearolic or $\Delta^{9,10}$-octadecinoic acid, $CH_3(CH_2)_7$-$C{\vdots}C(CH_2)_7COOH$. Stearolic acid is isomeric with naturally occurring tariric acid.

Tariric Acid.—Tariric or $\Delta^{6,7}$-octadecinoic acid, which is also designated as 6,7-stearolic acid, constitutes 90% of the glycerides of the seed fat of *Picramnia Sow*[40] found in Guatemala. It is known to occur in the seed oils of a few other species of the *Picramnia* genus but in relatively small proportions. A related acid, $\Delta^{6,7,9,10}$-octadeceninoic acid, which contains one double bond and one triple bond, has been isolated from the fatty acids of the seeds of *Ongokea klaineana* (*Onguekoa Gore Engler*).[41] It is not known with certainty which position contains the double bond and which the triple bond.

TABLE 4

MELTING POINTS (IN DEGREES C.) OF THE STEAROLIC ACIDS, $C_{18}H_{32}O_2$, AND THEIR OXIDATION AND REDUCTION PRODUCTS[a]

Position of triple bond	RC≡CR′	RCI=CIR′	RCO—COR′	RCH=CHR′	RCOH—COHR′
$\Delta^{5,6}$	52.5	52	94	47.5	94
$\Delta^{6,7}$ (Tariric)	51.5	48	98	54	117.5
$\Delta^{7,8}$	49.25	68.25	86.5	45.5	96.5
$\Delta^{8,9}$	47.5	67	...	53	98.5
$\Delta^{9,10}$	48	51	86	45	95.5
$\Delta^{10,11}$	47	45	...	52	97

[a] M. S. Posternak, *Compt. rend.*, **162**, 944–946 (1916).

In addition to the naturally occurring stearolic or tariric acid, several isomers of it have been prepared by adding hydriodic acid to tariric acid and treating the dihydroidide with alcoholic potassium hydroxide which results in a displacement of the triple bond to either the right or left of the position it originally occupied. By repeating the operation with the new isomer, a series of stearolic acids can be prepared. Corresponding elaidic acids can be obtained by treating the isomeric stearolic acids with hydriodic acid and reducing the reaction product with zinc in acetic acid solution. The melting points of a series of stearolic acids and corresponding oxidation and reduction products prepared by Posternak[42] are given in Table 4.

Behenolic acid, $CH_3(CH_2)_7C{\vdots}C(CH_2)_{11}COOH$, m.p. 57°C., has been prepared from the dibromides of erucic and brassidic acids. Mild reduction of behenolic acid produces erucic acid while more vigorous reduction gives brassidic acid.

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[40] A. Steger and J. van Loon, *Rec. trav. chim.*, **52**, 593–600 (1933).
[41] A. Steger and J. van Loon, *Fette u. Seifen*, **44**, 243–246 (1937).
[42] M. S. Posternak, *Compt. rend.*, **162**, 944–946 (1916).

5. Substituted Fatty Acids

All of the fatty acids listed in Tables 1 to 3, and discussed in the preceding pages, contain only unsubstituted, saturated or unsaturated hydrocarbon chains, and a terminal carboxyl group. There are also known a number of naturally occurring fatty acids which are differentiated from those previously mentioned by the substitution of various atoms and radicals for one or more of the hydrogen atoms of the hydrocarbon chain. The substituting groups may be alkyl, hydroxyl, keto, or pentacarbocyclic rings. The replacement of a hydrogen atom by an alkyl group produces branching in the hydrocarbon chain. The substituted acids may belong to the saturated or the unsaturated fatty acid series.

(*a*) *Substituted Saturated Acids*

Among the few known, naturally occurring, saturated acids in which a methyl group has been substituted for hydrogen are isovaleric, tuberculostearic, phthioic, phytomonic, and others of uncertain structure.

Isovaleric Acid.—Although *n*-valeric acid has never been identified as a constituent of fats, its isomer, 3-methylbutanoic or isovaleric acid, $CH_3CH(CH_3)CH_2COOH$, has been reported as a constituent of dolphin and porpoise oils. Two things are noticeable regarding the structure of this acid, namely, that its longest straight chain contains four carbon atoms, the fifth being in a side chain, thus conforming, with respect to its long chain to the general rule that only even-numbered carbon atoms are found as constituents of natural fats; also, that the whole carbon skeleton is the same as that which occurs in isoprene, the monomeric unit of various natural polymers and condensation products, such as rubber, terpenes, hydrocarbon pigments, etc.

Chevreul[43] first reported the presence of isovaleric acid in the oil of the dolphin and porpoise and named it *acide phocenique.* The accuracy of the identification of this acid has been questioned at various times, but few serious efforts have been made to determine its exact identity by rigorous and irrefutable means. Perhaps the most thorough examination of the natural acid has been made by André[44] who compared the product obtained from dolphin and from porpoise oil with a specimen of isovaleric acid from valerian root and one prepared synthetically from isobutylmagnesium bromide and carbon dioxide. The boiling points of the acids from each of the four sources were compared, also the melting and mixed melting points of the amides, and the refractive indices of the liquid acids. These properties were also compared with those of a 50:50 mixture of *n*-butyric and *n*-caproic acids. On the basis of the latter comparison, it was concluded that

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[43] M. E. Chevreul, *Recherches chimiques sur les corps gras d'origine animale.* Levrault, Paris, 1823, p. 115.

[44] E. André, *Bull. soc. chim.*, **35**, 857–868 (1924); *Compt. rend.*, **178**, 1188–1191 (1924).

phocenic acid is not an equimolar mixture of butyric and caproic acids. Although the agreement in values for the acids and their derivatives from the four sources mentioned above were not in every case the best possible, it appears likely that the acid isolated by Chevreul and others from the head oil of the dolphin and from porpoise oil is indeed isovaleric or 3-methylbutanoic acid.

Subsequent to the work of André, Gill and Tucker[45] examined a sample of porpoise jaw oil which they claimed contained 26.7% isovaleric acid. The evidence for the presence of this acid was based on the observation that 89.6% of the mixed fatty acids of porpoise jaw oil distilled at 170–171°C., and that this distillate fraction had a zero iodine value and a neutralization equivalent of 104 compared to 102 for valeric acid. The ethyl esters of the same fraction distilled over a range of 133–145°C., and since the boiling points of the ethyl esters of the four isomeric valeric acids vary from 133.5–144.6°C., the authors concluded their acid was isovaleric although they also state that the amount available did not permit them to determine which of the four isomers they had isolated.

Klein and Stigol[46] also reported the presence of isovaleric acid from the oil of the Black Sea dolphin. On distillation of the mixed fatty acid esters, a fraction distilling between 133° and 135°C. was obtained which had a characteristic fruity odor. They concluded that since the ethyl ester of isovaleric acid boiled at 134.3°C. and that of valeric acid at 145°C., the fatty acid they isolated was, therefore, isovaleric acid. Confirmation of the identity of the isovaleric acid consisted in the detection of a valerian odor of a specimen of the regenerated acid after treatment with sulfuric acid, and of a ferric chloride and copper acetate test for isovaleric acid.

Tuberculostearic Acid.—Anderson and Chargaff[47] isolated an acid from tubercle wax which was reported by Spielman[48] to have the formula $C_{19}H_{38}O_2$ and corresponded to 10-methylstearic acid. This acid also constitutes an exception to the rule that natural fatty acids consist solely of straight chains containing only even numbers of carbon atoms. It is isomeric with *n*-nonadecanoic acid which has never been isolated from natural sources. The acid which was optically inactive, was not identical with synthetic *dl*-10-methylstearic acid. It melted at 10–11°C. while the synthetic acid melted at 20–21°C. However, the amides and tribromoanilides of the natural and synthetic acids had the same melting points, namely, 76–77°C. and 93–94°C., respectively. Velick[49] examined natural tuberculostearic acid and its amides by x-rays and concluded from the observed spacing values that it probably possessed a structure corresponding

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[45] A. H. Gill and C. M. Tucker, *Oil & Fat Industries*, 7, 101–102 (1930).
[46] A. Klein and M. Stigol, *Pharm. Zentralhalle*, 71, 497–500 (1930).
[47] R. J. Anderson and E. Chargaff, *J. Biol. Chem.*, 85, 77–88 (1929).
[48] M. A. Spielman, *J. Biol. Chem.*, 106, 87–96 (1934).
[49] S. F. Velick, *J. Biol. Chem.*, 154, 497–502 (1944).

to *d*- or *l*-10-methylstearic acid previously assumed for it on the basis of chemical evidence.

Phthioic Acid.—Anderson and co-workers[50,51] reported the isolation from tubercle bacillus of an acid which they designated as phthioic acid which melted at 20–21°C. and was optically active, $[\alpha]_D = +12.56°$. Ultimate analysis of the acid and its amide indicated that it had the formula $C_{26}H_{52}O_2$. On the basis of its melting point, optical activity, and ultimate analysis it was assumed to be a polymethylated acid although no direct evidence was obtained of the number and position of the attached methyl groups. This acid would be isomeric with cerotic or *n*-hexacosanoic acid which is found in beeswax and in plant waxes. At least three other branched chain, optically active homologs, corresponding to $C_{24}H_{48}O_2$, $C_{25}H_{50}O_2$, and $C_{27}H_{54}O_2$, were found to accompany phthioic acid from the acetone-soluble fat of an unidentified strain of tubercle bacillus.[51]

Phytomonic Acid.—Velick and Anderson[52] and Velick[53] isolated a liquid saturated fatty acid from the acetone-soluble fat and from the phosphatide of the crown-gall bacillus, *Phytomonas tumefaciens*, which had an empirical formula corresponding to $C_{20}H_{40}O_2$. Insufficient physical and chemical data were obtained to permit determination of its structure, but it appeared to contain one or more branched chains.

Saturated Hydroxy Acids.—Small amounts of various saturated hydroxy acids are known to be present in fats. Dihydroxystearic acid is known to occur in castor oil.[54–56] Brain lipids contain at least three α-hydroxylated saturated fatty acids in the form of phrenosins. They have been shown by Chibnall *et al.*[57] to be α-hydroxy-*n*-docosanoic, α-hydroxy-*n*-tetracosanoic, and α-hydroxy-*n*-hexacosanoic acids.

(*b*) *Substituted Unsaturated Acids*

The substituted fatty acids of the unsaturated series are more numerous and constitutionally more variable than those encountered in the saturated series. Also, a number of the substituted acids of the unsaturated series are of considerable economic value while those of the saturated series possess little or no such value. Among the former are ricinoleic, licanic, and chaulmoogric acids. The more important substituted, unsaturated fatty acids are listed in Table 5 together with some of their properties.

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[50] M. A. Spielman and R. J. Anderson, *J. Biol. Chem.*, **112**, 759–767 (1936).

[51] L. G. Ginger and R. J. Anderson, *J. Biol. Chem.*, **156**, 443–451 (1944).

[52] S. F. Velick and R. J. Anderson, *J. Biol. Chem.*, **152**, 523–531 (1944).

[53] S. F. Velick, *J. Biol. Chem.*, **152**, 533–538 (1944).

[54] A. Eibner and E. Münzing, *Chem. Umschau Fette Öle Wachse Harze*, **32**, 153–162 (1925).

[55] P. Panjutin and M. Rapoport, *Chem. Umschau Fette Öle Wachse Harze*, **37**, 130–135 (1930).

[56] H. P. Kaufmann and H. Bornhardt, *Fette u. Seifen*, **46**, 444–446 (1939).

[57] A. C. Chibnall, S. H. Piper, and E. F. Williams, *Biochem. J.*, **30**, 100–114 (1936).

TABLE 5

SUBSTITUTED AND TRIPLE BOND UNSATURATED ACIDS

Systematic name	Common name	Formula	Molecular weight[a]	Neutralization value[a, b]	Theoretical iodine value[a]	M.p., °C.	Optical rotation, $[\alpha]_D$
12-Hydroxy-$\Delta^{9,10}$-octadecenoic	Ricinoleic	$C_{18}H_{34}O_3$	298.45	187.98	85.05	5	+6.7
4-Keto-$\Delta^{9,10,11,12,13,14}$-octadecatrienoic	Licanic	$C_{18}H_{28}O_3$	292.40	191.87	260.43	α-form 74–75 β-form 99.5	....
11-$\Delta^{2,3}$-Cyclopentenyl-*n*-undecanoic	Hydnocarpic	$C_{16}H_{28}O_2$	252.38	222.30	100.58	59–60	+68
13-$\Delta^{2,3}$-Cyclopentenyl-*n*-tridecanoic	Chaulmoogric	$C_{18}H_{32}O_2$	280.44	200.06	90.52	71	+56
13-Δ-^{2,3}-Cyclopentenyl-$\Delta^{6,7}$ tridecenoic	Gorlic	$C_{18}H_{30}O_2$	278 42	201.51	182.34	liq.	+60
$\Delta^{6,7}$-Octadecinoic	Tariric	$C_{18}H_{32}O_2$	280.44	200.06	181.03	liq.	....

[a] Calculated on the basis of International Atomic Weights for 1940.

[b] Neutralization or acid value equals the number of milligrams of potassium hydroxide required to neutralize one gram of acid.

Ricinoleic Acid.—Ricinoleic or 12-hydroxy-$\Delta^{9,10}$-octadecenoic acid, $C_{18}H_{34}O_3$, is found primarily in castor oil in which it comprises 80% or more of the total fatty acids. It has been reported in appreciable quantities from only a few other sources, for example, ivory wood oil. Small quantities of hydroxy acids have been reported to occur in various fats and oils but little work has been done on them and their constitutions and identities are uncertain. Ricinoleic acid is optically active, $[\alpha]_D = +6.7$, owing to the molecular asymmetry which results from substitution of a hydroxyl for a hydrogen at the twelfth carbon atom in the chain. Its melting point has been reported as 5° and 17°C., probably indicating its existence in two polymorphic forms. The presence of the hydroxyl group imparts to this acid, which is otherwise similar to oleic acid, a number of properties which enhance its utility. Formerly, the most important of its derivatives resulted from sulfonation, but the discovery by Fokin[58] that ricinoleic acid can be dehydrated to form unsaturated, conjugated, and nonconjugated linoleic acids has led to its use in the drying oil industry as a replacement for elaeostearic acid. Other derivatives are of importance as plasticizers for resins and it serves as a source of sebacic acid which has a number of industrial uses.

Licanic Acid.—Licanic or 4-keto-$\Delta^{9,10,11,12,13,14}$-octadecatrienoic acid, $C_{18}H_{28}O_3$, is the only known naturally occurring fatty acid which contains a keto group. Besides the keto group attached at the fourth carbon atom, it contains three conjugated double bonds in the same positions as in elaeostearic acid. The naturally occurring acid is a solid at room temperature

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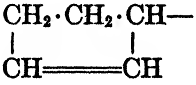
[58] S. Fokin, *J. Russ. Phys. Chem. Soc.*, **46**, 224–226, 1027–1042 (1914).

and melts at 74–75°C. It is readily converted to a crystalline, isomeric, or β-form, melting at 99.5°C.[59,60] The acid was first isolated from oiticica oil, *Licania rigida*,[61] obtained from Brazil, but is now known to be present in a number of other oils, including cacahuananche or Mexican oiticica oil, *Licania arborea*, and po-yoak oil, *Parinarium sherbroense*, from Sierra Leone. Oiticica oil contains 75–80% of this acid, and po-yoak oil 45–50% together with about 30% of elaeostearic acid. Owing to the presence of three double bonds in conjugated positions, licanic acid readily undergoes polymerization and film formation in a manner similar to elaeostearic acid. The resulting films are alkali- and water-resistant, consequently the oils containing this acid are used in the drying oil industry much the same as tung oil is used.

Chaulmoogra Acids.—Six acids containing cyclopentenyl rings have been isolated from the seed fats of various species of the *Flacourtiaceae* and especially from the genus *Hydnocarpus*. Chaulmoogric acid, $C_{18}H_{32}O_2$, and hydnocarpic acid, $C_{16}H_{28}O_2$, contain a cyclopentenyl ring:



and a saturated side chain containing thirteen and eleven carbon atoms, respectively. The acids are strongly dextrorotatory and are solids at room temperature. They are used primarily as medicinal agents especially in the treatment of leprosy.

Four homologs of chaulmoogric acid have recently been isolated by Cole and Cardoso[62] from the oil of *Hydnocarpus wightianus*. These unsaturated acids, differing primarily in the length of the side chain, were designated as *alepric*, *aleprylic*, *aleprestic*, and *aleprolic*. Since all of them, as well as their ethyl esters, are optically active, they will be discussed further under the section on optical activity.

Gorlic Acid.—Gorlic acid, $C_{18}H_{30}O_2$, like the chaulmoogra acids, contains a cyclopentenyl ring, but in addition it contains a double bond in the side chain between the sixth and seventh carbon atoms. Gorlic acid occurs principally in gorli seed oil obtained from *Oncoba echinata* of Africa. It forms about 10% of the total fatty acids of gorli seed oil. It is optically active and owing to the presence of a second double bond in the side chain it is a liquid at room temperature.

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[59] W. B. Brown and E. H. Farmer, *Biochem. J.*, 29, 631–639 (1935).

[60] R. S. Morrell and W. R. Davis, *J. Chem. Soc.*, 1936, 1481–1484; *J. Oil Colour Chem. Assoc.*, 19, 359–362 (1936).

[61] H. A. Gardner, *Natl. Paint Varnish Lacquer Assoc.*, Circ. No. 654, 28–34 (1943).

[62] H. I. Cole and H. T. Cardoso, *J. Am. Chem. Soc.*, 61, 2349–2351, 2351–2353, 3442–3445 (1939); 60, 614–619 (1938).

Other Substituted Acids.—Hilditch, Meara, and Zaky[63] reported the presence of an unusual unsaturated acid containing an odd number of carbon atoms and a methyl side chain in so-called Java "olive" oil, *Sterculia foetida.* The acid comprised more than 70% of the total acids present in the oil. Considerable difficulty was encountered in isolating the acid and determining its structure owing to its tendency to undergo polymerization. By indirect methods its constitution was determined to be 12-methyl-$\Delta^{9,10,11,12}$-octadecadienoic acid:

$$CH_3 \cdot [CH_2]_5 \cdot C \cdot Me{:}CH \cdot CH{:}CH \cdot [CH_2]_7 \cdot COOH$$

Many substituted acids, both of the saturated and unsaturated series, have been prepared synthetically or by chemical treatment of natural acids. A number of them will be considered in subsequent sections.

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[63] T. P. Hilditch, M. L. Meara, and Y. A. H. Zaky, *J. Soc. Chem. Ind.*, **60**, 198–203T (1941).

CHAPTER III

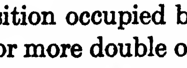
ISOMERISM

1. Introduction

Many chemical, as well as physical, properties of the fatty acids like those of other compounds, depend upon molecular configuration, *i. e.*, upon the mode of arrangement of the component atoms within the molecule. Many compounds are known which have the same empirical formula but differ in chemical and physical properties and therefore in molecular configuration. Such compounds are said to be isomeric. Isomerism is frequently encountered among the fatty acids, monoesters, glycerides, and other lipids (alcohols, hydrocarbons, ketones, etc.), which are found in various proportions in natural fats and waxes.

Since the molecular structure or arrangement of atoms within the molecule may be of several different types, correspondingly different forms of isomerism may occur. The principal types of isomerism are as follows:[1]

(*1*) Simple structural isomerism
  (*a*) Nucleus or chain isomerism
  (*b*) Positional isomerism
  (*c*) Functional group isomerism
(*2*) Stereoisomerism or space isomerism
  (*a*) Optical isomerism
  (*b*) Geometrical or *cis-trans*-isomerism

The differences between isomers included under *structural isomerism* can be adequately expressed by simple structural formulas. For example, *nucleus* or *chain isomerism* results from differences in the arrangement of carbon atoms, as exemplified by butyric acid, $CH_3CH_2CH_2COOH$, and isobutyric acid,  $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}HCOOH$. *Positional isomerism* results from differences in the position occupied by substituent atoms or radicals, or in the position of one or more double or triple bonds, in the carbon nucleus. This form of isomerism may be illustrated by the three isomeric hydroxybutyric acids — namely: 2-hydroxybutyric acid, $CH_3CH_2CHOHCOOH$; 3-

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[1] R. L. Shriner, R. Adams, and C. S. Marvel, in H. Gilman, *Organic Chemistry*. 2nd ed., Vol. I, Wiley, New York, 1943, pp. 214–488.

hydroxybutyric acid, $CH_3CHOHCH_2COOH$; and 4-hydroxybutyric acid, $CH_2OHCH_2CH_2COOH$ — or by oleic acid, $CH_3(CH_2)_7CH{:}CH(CH_2)_7COOH$, and petroselinic acid, $CH_3(CH_2)_{10}CH{:}CH(CH_2)_4COOH$. *Functional group isomerism* is represented by compounds which possess the same molecular formulas but have different functional groups, *i. e.*, they belong to different homologous series. This type of isomerism may be illustrated by methyl-*n*-octyl ketone, $CH_3CO(CH_2)_7CH_3$, and *n*-capryl aldehyde, $CH_3(CH_2)_8CHO$, which have the same empirical formula, namely, $C_{10}H_{20}O$, but different functional groups. *Tautomerism* is a special case of functional group isomerism and is best known in the form of *keto-enol isomerism.*

Stereoisomerism or *space isomerism* occurs in compounds which have the same molecular formulas and the same functional groups, but which differ in the three-dimensional space arrangement of the atoms or groups within the molecule. One of the two types of stereoisomerism, namely, *optical isomerism,* results when the molecules of two compounds possess spatial structures which are mirror images and are not superimposable, one on the other. Such isomers, regardless of their physical state, rotate a plane of polarized light passed through them. They are said to be *asymmetric* because their structure is without complete asymmetry from a geometrical point of view.

The second type of stereoisomerism, namely, *geometric* or *cis-trans-isomerism,* occurs in organic molecules which contain two unsymmetrically substituted atoms attached to each other by a double bond. This type of isomerism results from the restricted rotation in the molecule resulting from the double bonding of two atoms in a chain. Although double bonding may occur between various types of atoms, only the carbon to carbon double bonds are involved in *cis-trans*-isomerism of the fatty acids and their derivatives. The phenomenon of *cis-trans*-isomerism in fats has been known since 1819 when Poutet[2] converted triolein into trielaidin by treatment of the former with the oxides of nitrogen. This transformation was, however, not recognized as *cis-trans*-isomerism until many years later.

2. Structural Isomerism

(*a*) *Nuclear Isomerism*

The naturally occurring saturated fatty acids, with few exceptions, do not exhibit isomerism of any form. The normal fatty acids consist of zigzag chains of methylene groups with a terminal carboxyl group at one end of the chain and a terminal methyl group at the opposite end. The number of theoretically possible *nucleus* or *structural isomers* of the saturated fatty acids increases with increasing length of the carbon chain, but actually extremely few of them occur in nature. Such isomers have been reported

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[2] J. J. E. Poutet, *Ann. chim. phys.*, **12,** 58–62 (1819).

from natural sources, but except in a few instances their apparent identification has been a result of inadequate analytical technique or failure to apply critical methods of identification.

Valeric acid, and a few other methyl-substituted acids, may be exceptions to this statement and also to the general rule that only fatty acids containing even numbers of carbon atoms are found in natural fats. *n*-Valeric acid, $CH_3CH_2CH_2CH_2COOH$, does not appear to occur naturally in fats and oils, but isovaleric acid, $(CH_3)_2CHCH_2COOH$, has been reported to occur in dolphin and porpoise oils. It contains a branched chain consisting of a single methyl group. Tuberculostearic or 10-methylstearic acid, $C_{19}H_{38}O_2$, is isomeric with *n*-nonadecanoic acid. It, too, is an exception to the rule of nonoccurrence in natural fats of branched chain and odd-numbered carbon acids. Phthioic acid, $C_{26}H_{52}O_2$, has been reported from a natural fat. It is isomeric with cerotic or *n*-hexacosanoic acid and is presumed to contain several branched chains consisting of one or more methyl groups. Three other branched chain homologs of phthioic acid, namely, $C_{24}H_{48}O_2$, $C_{25}H_{50}O_2$, and $C_{27}H_{54}O_2$, have been reported from the same source. Phytomonic acid, $C_{20}H_{40}O_2$, a homolog of tuberculostearic acid, contains a single branched chain. It has been reported from the phosphatides of crown-gall bacillus. All of these methyl-substituted saturated acids from natural sources are liquids at room temperature, whereas the isomeric normal fatty acids, except valeric, are solids melting above 70°C.

Many branched chain isomers of the normal aliphatic series have been synthesized in recent years for comparison with the natural acids. Chargaff[3] synthesized a series of α-substituted hexacosanoic acids. Birch and Robinson[4] prepared a number of long chain substituted acetic and propionic acids. Schneider and Spielman[5] synthesized a series of 2-methyl- and 10-methyl-substituted fatty acids containing from nineteen to twenty-seven carbon atoms. Buu-Hoï and Cagniant[6] synthesized 2,2-dimethylmyristic, 2,2-dimethylpalmitic, and 2,2-dimethylstearic acids. Polgar and Robinson[7] synthesized a series of trisubstituted acetic and other branched chain acids. None of the synthetic acids possessed the properties of the natural acids.

Nucleus isomerism, which is generally accompanied by positional isomerism, occurs in a number of unsaturated acids. For example, linoleic and chaulmoogric acids have the same empirical formula, $C_{18}H_{32}O_2$, but have a different arrangement of methylene groups and double bonds. Linoleic acid contains a straight chain of eighteen carbon atoms and chaulmoogric acid contains a cyclopentenyl ring and a straight chain containing

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[3] E. Chargaff, *Ber.*, **65**, 745–754 (1932).

[4] A. J. Birch and R. Robinson, *J. Chem. Soc.*, **1942**, 488–497.

[5] A. K. Schneider and M. A. Spielman, *J. Biol. Chem.*, **142**, 345–354 (1942).

[6] N. P. Buu-Hoï and P. Cagniant, *Z. physiol. Chem.*, **279**, 76–86 (1943); *Ber.*, **76**, 689–693 (1943).

[7] N. Polgar and R. Robinson, *J. Chem. Soc.*, **1943**, 615–619.

thirteen carbon atoms. Nucleus isomerism of the same type is exhibited by linolenic and gorlic acids.

(b) *Positional Isomerism*

Positional isomerism, resulting from differences in the point of attachment of atoms or radicals, is observed in only a few natural fatty acids but it occurs in many derivatives of such acids, as well as in many synthetic acids, *e. g.*, hydroxy and keto acids which have been prepared in considerable number. Positional isomerism, due to differences in location of the double bonds in the unsaturated fatty acids, is not only of frequent occurrence, but it is responsible for marked differences in the chemical and physical properties of several commercially important acids, *e. g.*, linolenic and elaeostearic.

Isomeric Monoethenoid Acids.—Fatty acids which contain only one double bond may exhibit two types of isomerism, namely, positional and geometrical isomerism. The first type is represented by the variation in the position of the double bond, and the second by the spatial arrangement of the component parts of the molecule with respect to the double bond.

Octadecenoic acid, $C_{18}H_{34}O_2$, occurs naturally in at least three positionally isomeric forms, namely, oleic or $\Delta^{9,10}$-octadecenoic, petroselinic or $\Delta^{6,7}$-octadecenoic, and vaccenic or $\Delta^{11,12}$-octadecenoic acid. In addition to these isomers, various other positionally isomeric octadecenoic acids have been prepared artificially. For example, when stearic acid is brominated it forms 2-bromostearic acid which, upon treatment with alcoholic potassium hydroxide, splits out hydrobromic acid and forms $\Delta^{2,3}$-octadecenoic acid. When this acid is treated with hydriodic acid and heated with alcoholic potash, $\Delta^{3,4}$-octadecenoic acid is produced. By a repetition of the process of treating the monoethenoid acid with hydriodic acid and then with alcoholic potash, an extensive series of octadecenoic acids has been prepared.

The melting points of both the natural and synthetic octadecenoic acids from $\Delta^{2,3}$ to $\Delta^{12,13}$ are given in Table 6. Both positional and geometric isomers are included in the table and the stereo configuration is indicated where known. It has been observed that the melting points of a series of positional isomers having the same geometrical configuration are inversely proportional to the distance of the double bond from the carboxyl group. In general this is true for the octadecenoic acids of Table 6. It might be assumed, therefore, that if the melting points given in Table 6 were plotted against the position of the double bond, two smooth parallel curves could be drawn through the points connecting all of the *cis*-isomers on the one hand, and all of the *trans*-isomers on the other. Actually this is not the case and it would appear that, either there is no regularity between the melting point and the position of the double bond, or the melting point and/or the stereo configuration of a number of the individual acids is questionable.[7a]

Table 6

MELTING POINTS OF ISOMERIC OCTADECENOIC ACIDS, $C_{18}H_{34}O_2$

Position of double bond	Isomeric form and reference number	M.p., °C.	Position of double bond	Isomeric form and reference number	M.p., °C.
$\Delta^{2,3}$	*cis*[8,9]	59	$\Delta^{8,9}$	*trans*[15]	53
$\Delta^{3,4}$	*cis*[10]	56–57	$\Delta^{9,10}$	*trans*[15,16]	43.7(45)[c]
$\Delta^{4,5}$	*cis*[10]	52–53	$\Delta^{9,10}$	*cis*[16]	13.4 α-form[d] 16.3 β-form[d]
$\Delta^{5,6}$	*trans*[11]	47.5	$\Delta^{10,11}$	*trans*[17]	42
$\Delta^{6,7}$	*trans*[12,12a,13]	53[a]	$\Delta^{11,12}$	*trans*[18]	39[e]
$\Delta^{6,7}$	*cis*[14]	30[b]	$\Delta^{12,13}$	*trans*[19]	39.7–40.1
$\Delta^{7,8}$	*trans*[11]	45.5	$\Delta^{12,13}$	*cis*[19]	9.8–10.4

[a] Petroselaidic acid.
[b] Petroselinic acid.
[c] Elaidic acid.
[d] Oleic acid.
[e] Vaccenic acid.

During the process of hydrogenation of linolenic and linoleic acids, and more particularly of glycerides containing these acids, there are produced various positional, as well as stereoisomers of *cis*-$\Delta^{9,10}$-oleic acid. The exact mechanism of hydrogen addition to double bonds of polyethenoid acids during catalytic hydrogenation is a matter of considerable controversy. According to Suzuki and Inoue,[20] addition of hydrogen to linolenic and linoleic acids occurs preferentially at the double bond farthest removed from the carboxyl group, whereas, according to van der Veen[21] and Lemon[22] preferential hydrogen addition occurs at the middle double bond of linolenic acid. If hydrogen addition occurred in a completely preferential manner as assumed by Suzuki and Inoue, only one oleic acid would be produced by hydrogenation of linolenic and linoleic acids to the oleic acid stage. This acid would be identical with the naturally occurring *cis*-$\Delta^{9,10}$-oleic acid or its geometric isomer.

[7a] W. Koczy and F. Griengl, *Monatsh.*, **57**, 253–290 (1931).
[8] H. R. LeSueur, *J. Chem. Soc.*, **85**, 1708–1713 (1904).
[9] G. Ponzio, *Atti accad. sci. Torino*, **39**, 552–560 (1903-04); *Gazz. chim. ital.*, **34**, 77–85 (1904).
[10] A. Eckert and O. Halla, *Monatsh.*, **34**, 1815–1824 (1913).
[11] S. Posternak, *Compt. rend.*, **162**, 944–946 (1916).
[12] H. N. Griffiths and T. P. Hilditch, *J. Chem. Soc.*, **1932**, 2315–2324.
[12a] L. Mascarelli and G. Sanna, *Atti accad. Lincei*, **24**, II, 91–97 (1915).
[13] A. Arnaud and S. Posternak, *Compt. rend.*, **150**, 1130-1132 (1910).
[14] T. P. Hilditch and E. E. Jones, *J. Soc. Chem. Ind.*, **46**, 174–177T (1927).
[15] A. Arnaud and S. Posternak, *Compt. rend.*, **150**, 1525–1528 (1910).
[16] J. C. Smith, *J. Chem. Soc.*, **1939**, 974–980.
[17] J. Böeseken and R. Hoevers, *Rec. trav. chim.*, **49**, 1161–1164 (1930).
[18] S. H. Bertram, *Biochem. Z.*, **197**, 433–441 (1928).
[19] A. Grün and W. Czerny, *Ber.*, **59**, 54–63 (1926).
[20] B. Suzuki and Y. Inoue, *Proc. Imp. Acad. Tokyo*, **6**, 266–268 (1930); **7**, 15–18 (1931).
[21] H. van der Veen, *Chem. Umschau Fette Öle Wachse Harze*, **38**, 89–96 (1931).
[22] H. W. Lemon, *Can. J. Research*, **F22**, 191–198 (1944).

On the other hand, if linolenic acid is preferentially hydrogenated at the 12,13-double bond to form 9,10,15,16-linoleic acid, as shown by van der Veen on the basis of ozonization of partially hydrogenated linolenic acid, and spectroscopically by Lemon in the case of partially hydrogenated linseed oil, then it is possible that a different oleic acid, namely, 15,16-oleic could result on further hydrogenation. In fact, van der Veen concludes that during the first stage of hydrogenation a portion of the new isomer, 9,10,15,16-linoleic acid, undergoes rearrangement to form some 10,11,14,15-linoleic acid. In the second stage of the hydrogenation, employing two moles of hydrogen per mole of linolenic acid, van der Veen assumes that the 14,15-double bond of the 10,11,14,15-linoleic acid is saturated to produce 10,11-elaidic acid, and that the 15,16-double bond of the 9,10,15,16-linoleic acid is saturated to produce normal 9,10-oleic acid which undergoes partial rearrangement to form 8,9-oleic acid and possibly some 10,11-oleic acid.

As a matter of fact, Hilditch and Vidyarthi[23] have shown that hydrogenation of oleic acid and its esters leads to formation of 8,9- and 10,11-oleic and elaidic acids and that during the partial hydrogenation of palmitoleic or $\Delta^{9,10}$-hexadecenoic acid and of erucic or $\Delta^{13,14}$-docosenoic acid, the same migration of ethylenic linkages occurs. Thus, a partially hydrogenated fat, which originally contained linoleic acid, or linoleic and linolenic acids, may contain a variety of positional and stereoisomers of *cis*-$\Delta^{9,10}$-octadecenoic acid, depending on the nature of the original fat and the conditions of hydrogenation. Up to the present there has been a considerable accumulation of experimental evidence bearing on the existence of both positional and stereoisomers of normal oleic acid but, except for elaidic acid, none of these isomers has been isolated from hydrogenated fats in sufficiently pure form to determine its exact structure.

Isomeric Polyethenoid Acids.—When two or more double bonds are present in the same unsaturated fatty acid the opportunity for the occurrence of positional isomers is increased. However, only a few such isomers have been observed in natural fats, and most of these belong to the trienoic acid series. The probable occurrence in nature of isomeric octadecadienoic acids and the known occurrence of isomeric octadecatrienoic acids have been discussed under linoleic and linolenic acids.

There is considerable evidence that, in addition to the natural isomers, other positional isomers of linoleic acid are produced by a variety of chemical reactions, several of which are of industrial importance. These artificial linoleic or octadecadienoic acids have their origin in three natural sources, namely: (*1*) fatty acids more highly unsaturated than linoleic acid, which on partial hydrogenation form isomeric acids, (*2*) normal linoleic

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[23] T. P. Hilditch and N. L. Vidyarthi *Proc. Roy. Soc. London*, **A122**, 552–563, 563–570 (1929).

acid whose double bonds may be shifted by isomerization catalysts, and (*3*) monoethenoid hydroxy acids, such as ricinoleic acid, which on dehydration form an additional double bond.

The processes by which these isomeric acids may be produced include: (*1*) hydrogenation of conjugated and nonconjugated polyethenoid acids, (*2*) action of heat and isomerization catalysts, (*3*) debromination of tetrabromostearic acids, and (*4*) action of heat and catalytic dehydration catalysts on partially oxidized unsaturated acids or on naturally occurring hydroxy acids.

Two general methods are available for the determination of the position of the double bonds in polyunsaturated acids, namely, oxidative fission at the double bond and isolation of the oxidation fragments, and the application of spectroscopy (see sections on oxidation and spectroscopy). The first method is of limited application because it requires, first, that the unsaturated acid be isolated in reasonably pure form, and second, that oxidation and recovery of the fragments be accomplished quantitatively. The second method, namely, spectroscopy, is also limited in its application because although it provides information concerning the relative amounts of conjugated and unconjugated double bonds, it provides no information concerning their location in the aliphatic chain and it does not distinguish with certainty between *cis*- and *trans*-isomers. A third method, namely the reaction of conjugated acids with maleic anhydride, has been used to measure the presence and relative amounts of conjugation in fatty acids or esters but its application is more limited and less reliable than the spectroscopic method.

It is a well-established fact that naturally occurring linoleic acid possesses the structure $CH_3(CH_2)_4CH{=}CH{-}CH_2{-}CH{=}CH(CH_2)_7COOH$ in which the double bonds are located at the $\Delta^{9,10}$- and $\Delta^{12,13}$-positions. It is evident that a shift of either double bond can lead to the formation of a new isomer. If either bond is shifted toward its neighbor a conjugated system of double bonds, $-CH{=}CH{-}CH{=}CH-$, corresponding to $\Delta^{9,10,11,12}$- or $\Delta^{10,11,12,13}$-octadecadienoic acid will be formed. Spectroscopic examination will reveal the presence of these conjugated isomers but will not differentiate between them. If either double bond is shifted away from its neighbor, new positional isomers will be formed corresponding to $\Delta^{8,9,12,13}$- or $\Delta^{9,10,13,14}$-octadecadienoic acid. These acids cannot be differentiated spectroscopically but if available in relatively pure form the position of the double bond can be established by oxidation experiments.

Ricinoleic acid is known to possess a structure corresponding to $CH_3(CH_2)_5CHOHCH_2CH{=}CH(CH_2)_7COOH$ in which a double bond is present at the $\Delta^{9,10}$-position and a hydroxyl group at the twelfth carbon atom. By removal of the elements of water in the form of the hydroxyl group and an adjacent hydrogen, two isomeric linoleic acids may be formed. If the hydrogen removed with the hydroxyl group is removed from the eleventh carbon atom a conjugated $\Delta^{9,10,11,12}$-octadecadienoic acid is obtained, and if from the thirteenth carbon atom an unconjugated $\Delta^{9,10,12,13}$-octadecadienoic acid identical with naturally occurring linoleic acid is obtained. If ricinoleic acid is dehydrated and then halogenated and dehalogenated by removal of hydrogen halide, various isomeric unsaturated acids are formed.

Other polyethenoid acids containing isolated double bonds are subject to the same types of rearrangement as occur with linoleic acid. However, when three or more double bonds are present, rearrangement may occur involving only one double bond or more than one double bond, either in the direction of conjugation or to a more isolated position, and it is conceivable that both types of rearrangement could occur in the same molecule.

Linolenic acid possesses the structure $CH_3CH_2CH{=}CHCH_2CH{=}CH$-$CH_2CH{=}CH(CH_2)_7COOH$, in which unconjugated double bonds occur at the $\Delta^{9,10,12,13,15,16}$-positions. Preferential saturation with hydrogen of one of the double bonds of linolenic acid can lead to the formation of three isomeric linoleic acids, namely, $\Delta^{9,10,12,13}$-octadecadienoic acid, identical with naturally occurring linoleic acid, and $\Delta^{12,13,15,16}$- and $\Delta^{9,10,15,16}$-octadecadienoic acids.

Elaeostearic acid possesses the structure $CH_3(CH_2)_3CH{=}CH{-}CH{=}CH{-}CH{=}CH{-}(CH_2)_7COOH$, in which the double bonds are located at the $\Delta^{9,10,11,12,13,14}$-positions. Preferential hydrogenation of one double bond of elaeostearic acid can theoretically lead to the formation of a number of isomers of linoleic acid containing either an isolated double bond system, $\Delta^{9,10,13,14}$, or conjugated double bond systems, $\Delta^{9,10,11,12}$ and $\Delta^{11,12,13,14}$.

Evidence is available to substantiate the fact that the various reactions described above do occur and that at least certain of the isomers mentioned are actually formed. For example, Moore[24] found that the controlled catalytic reduction of tung oil caused a shift in the position of the absorption maximum of the mixed acids from 2700 to 2300 Å. The saturation of one double bond of elaeostearic acid with hydrogen results in the formation of an octadecadienoic acid containing two double bonds in conjugated positions. However, which of the two possible conjugated acids were formed could not be ascertained from the measurement of the absorption maximum.

In the commercial production of dehydrated castor oil, which is accomplished by heating the oil, or the separated fatty acids in the presence of a dehydrating catalyst, a molecule of water is split out of each molecule of ricinoleic acid. As previously mentioned, this acid contains a hydroxyl

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[24] T. Moore, *Biochem. J.*, **33**, 1635–1638 (1939).

group on the twelfth carbon atom which can combine, under the influence of high temperature and a dehydrating catalyst, with a hydrogen attached at either the eleventh or thirteenth carbon atom to form water. Since ricinoleic acid already contains a double bond at the $\Delta^{9,10}$-position, the introduction of a second double bond at the $\Delta^{12,13}$- or $\Delta^{11,12}$-position will produce either ordinary linoleic acid or a conjugated linoleic acid. All available evidence to date indicates that both reactions occur and at approximately the same rates under conditions of commercial dehydration. However, this is not the only reaction which occurs as is evident by the fact that Von Mikusch[25] was able to isolate from the alkali-isomerized dehydration mixture, a solid isomer corresponding to $\Delta^{10,11,12,13}$-octadecadienoic acid. This acid, which melted at 57°C., is presumed to have been formed by the isomerization of $\Delta^{9,10,12,13}$-linoleic acid which was produced by dehydration. Since other oils containing $\Delta^{9,10,12,13}$-linoleic acid, such as soybean and walnut, do not yield a solid fatty acid under similar treatment, it may be concluded that the linoleic acid present in dehydrated castor oil, or at least a portion of it, is not identical with ordinary linoleic acid but a stereoisomer thereof. Thus, at least three isomeric linoleic acids are known to be produced on dehydration or dehydration and isomerization of ricinoleic acid and the formation of other positional and geometric isomers is possible.

Mitchell and Kraybill[26] observed that the absorption spectra of linseed, soybean, corn, and cottonseed oils, and the esters of linoleic and linolenic acids, were quite dissimilar before and after bleaching with fuller's earth. Linoleic acid and the oils containing these acids, when subjected to the action of bleaching earths, were found to have developed a specific absorption maximum at 2680 Å. which is characteristic of triene conjugation. Ordinary commercial bleaching of the acid or oil with activated fuller's earth resulted in the formation of 0.1% to 0.2% of conjugated triethenoid acids or glycerides which were not present prior to bleaching. The proportion of conjugated product could not be increased by repeated or more drastic bleaching. However, it was found that if the acid or oil was first oxidized by blowing it with air at 100°C., and then bleached with fuller's earth, the concentration of triene conjugation was increased. These authors conclude, therefore, that the action of bleaching earths results in dehydration of pre-existing oxygenated acids or of similar acids which may be produced by blowing the oil with air, in a manner analogous to the formation of the conjugated isomer of linoleic acid by dehydration of ricinoleic acid and castor oil.

It was also observed that similar treatment of linolenic acid or of glyceride oils of linolenic acid led to the production of absorption bands at

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[25] J. D. Von Mikusch, *J. Am. Chem. Soc.*, **64**, 1580–1582 (1942).
[26] J. H. Mitchell, Jr., and H. R. Kraybill. *J. Am. Chem. Soc.*, **64**, 988–994 (1942).

2860, 3000, and 3160 Å. which are characteristic of tetraene conjugation. The formation of tetraene conjugated double bond systems from triene unconjugated double bond systems was attributed to the same mechanism as described in the case of linoleic acid.

Moore[27] observed that the fatty acids produced by prolonged saponification with potassium hydroxide of fats containing ordinary linoleic acid exhibited absorption maximum at 2300 Å. which is characteristic of the presence of conjugated double bonds. It was later established by Kass and Burr[28] that when equal weights of linolenic acid and potassium hydroxide were heated for two hours with four volumes of ethylene glycol, the linolenic acid was converted into a new crystalline acid melting at 79°C. The acid gave a methyl ester which melted at 41°C. and a hexabromostearic acid which melted at 152.5°C. On the basis of the results of disruptive oxidation, the acid was identified as $\Delta^{10,11,12,13,14,15}$-octadecatrienoic acid and hence a positional isomer of naturally occurring elaeostearic acid. The acid was designated as pseudo-elaeostearic acid.

Mowry, Brode, and Brown[28a] subjected the methyl ester of arachidonic acid, $\Delta^{5,6,8,9,11,12,14,15}$-eicosatetraenoic acid to alkali isomerization in ethylene glycol obtaining a product which exhibited an absorption spectra characteristic of a tetraene conjugated system of double bonds. The recovered acid melted at 95–98°C. and probably consisted of a mixture of conjugated acids, since the isolated double bonds may shift in several ways to produce conjugation.

It was originally thought that relatively anhydrous conditions were essential for successful alkali isomerization, but it is now known that similar reactions occur when concentrated aqueous soaps of linoleic and linolenic acids are heated to high temperatures under pressure. In fact, isomerization of polyunsaturated fatty acids and oils can be effected, in the presence or absence of solvent, by heat and the action of alkalies,[29,30] siliceous earths,[31] metallic oxides,[32] and various other catalysts.

It has been known since the classical work of Rollett[33] in 1909 that the bromination of linoleic acid leads to the formation of two tetrabromostearic acids, one a solid melting at 115.5°C. and the other a liquid at room temperature. Much argument has been waged concerning the nature of these bromination products and the acids which are regenerated from them on debromination. It was first believed that the bromo derivatives represented geometric isomers of the *cis-trans*-type but more recently they have

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[27] T. Moore, *Biochem. J.*, **31**, 141–148, 148–154 (1937).

[28] J. P. Kass and G. O. Burr, *J. Am. Chem. Soc.*, **61**, 3292–3294 (1939).

[28a] D. T. Mowry, W. R. Brode, and J. B. Brown, *J. Biol. Chem.*, **142**, 671–678 (1942).

[29] G. O. Burr (to Regents of the Univ. of Minn.), U. S. Pat. 2,242,230 (May 20, 1941).

[30] T. F. Bradley and D. Richardson, *Ind. Eng. Chem.*, **34**, 237–242 (1942).

[31] A. Turk and J. Feldman, *Paint Oil Chem. Rev.*, **106** [13], 10–11 (1943).

[32] A. Turk and P. D. Boone, *Oil & Soap*, **21**, 321–322 (1944).

[33] A. Rollett, *Z. physiol. Chem.*, **62**, 410–421 (1909).

been held to represent racemic mixtures of optical isomers.[34,35] It was also believed that both tetrabromostearic acids produced the same linoleic acid on debromination. Brode *et al.*[36] have, however, shown that the nature of the linoleic acid produced on debromination is a function of both the structure of the original tetrabromostearic acid and the method of debromination, but principally the former. On the basis of melting point, iodine value, tetrabromide value, and absorption spectra analysis, the regenerated acids were generally found to consist of mixtures of conjugated and unconjugated linoleic acids, and in some cases of triene and tetraene conjugated acids. The percentages of isomeric acids from the high melting tetrabromostearic acid ranged from 0 to 12, while those from the low melting bromide varied from 34 to 70. The formation of conjugated acids on debromination was attributed by the authors to the catalytic isomerization action of zinc bromide formed during debromination, and to the variation of the proportions of different stereoisomers in the original tetrabromides.

A number of the methods which have just been discussed have found commercial application in the manufacture of substitutes for tung oil from various oils possessing no conjugated double bond systems and none of the drying characteristics of tung and other oils which do possess conjugated double bonds. The first industrial products of this type were produced by catalytic dehydration of the fatty acids separated from castor oil followed by their re-esterification with glycerol or other alcohols. Later, it was found that castor oil could be dehydrated directly and the saponification, distillation, and re-esterification steps could be avoided. Subsequently, other processes were developed by means of which the double bonds of linoleic and linolenic acids could be shifted to conjugated positions. Generally, this is accomplished by saponification of fats and oils, *e. g.*, linseed and soybean, fractionally distilling the acids to obtain the desired unsaturated fraction, isomerizing the acids by treatment with alkalies, alkaline earths, siliceous earths, or metallic oxides at high temperature, and re-esterifying the isomerized acids with glycerol or other polyhydric alcohols. Similar types of synthetic or modified drying oils are produced from soybean and linseed oils by blowing them with air, or treatment with other oxidizing agents, followed by catalytic dehydration. The dehydration reaction leads to the formation of additional double bonds in both the linoleic and linolenic acids which are present in these oils. At least a portion of the newly introduced double bonds are conjugated and, therefore, represent positional isomers of the acids containing the same number of bonds in isolated posi-

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[34] J. W. McCutcheon, *Can. J. Research*, **B16**, 158–175 (1938).

[35] R. W. Riemenschneider, D. H. Wheeler, and C. E. Sando, *J. Biol. Chem.*, **127**, 391–402 (1939).

[36] W. R. Brode, J. W. Patterson, J. B. Brown, and J. Frankel, *Ind. Eng. Chem., Anal. Ed.*, **16**, 77–80 (1944).

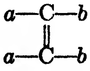
tions. These isomerized acids and esters have distinct advantages for use in the production of various types of polymerized products such as alkyd resins. The polymerization speed of these acids reduces the time necessary for cooking compared with the natural acids, gives faster baking speed, better water resistance, and in the case of isomerized linoleic acid, better color retention in the finished product.

It should be mentioned that in the case of these commercial products it is not possible to determine quantitatively the complete extent of the conjugation produced by the dehydration or isomerization reactions owing to the fact that the production of conjugated double bonds under the conditions essential to induce conjugation also results in a variable amount of polymerization which destroys some of the bonds. It is, however, possible to determine spectroscopically with relatively good accuracy the amount of conjugation existing in the dehydrated or isomerized product at any given time. It is not improbable that geometric as well as positional isomerides are formed in these reactions and that the final product is an even more complex mixture than is generally assumed. None of the available chemical or spectroscopic methods differentiate with certainty between the various possible geometric isomerides containing the same number of double bonds.

3. Stereoisomerism

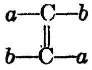
(*a*) *Geometric Isomerism*

Of the two forms of stereoisomerism, geometrical or *cis-trans*-isomerism is a property common to all unsaturated fatty acids. The structural relationships of this type of isomerism when of the simplest form, *i. e.*, involving only a single carbon to carbon double bond, may be illustrated as follows:



$$\begin{array}{c} a\text{—}C\text{—}b \\ \| \\ a\text{—}C\text{—}b \end{array}$$

(I) *cis*

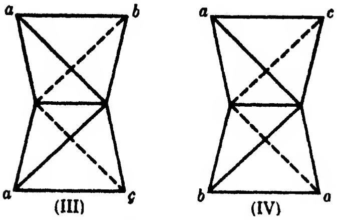


$$\begin{array}{c} a\text{—}C\text{—}b \\ \| \\ b\text{—}C\text{—}a \end{array}$$

(II) *trans*

In the hypothetical compounds illustrated above, the one with two similar groups on the same side of the double bond is referred to as the *cis*-isomer (I) and the other as the *trans*-isomer (II). The spatial arrangements of the *cis*- and *trans*-isomers become more plainly evident when they are considered from the geometric point of view. The carbon atom is known to have a tetrahedral structure and when a double bond is shared between two carbon atoms it can be represented as occurring at the common edge as shown in (III) and (IV). The double bond is therefore a fairly rigid structure around which no rotation can occur in contrast to the free rotation at the single bond which is situated at the common apex of a pair of tetrahedrons.

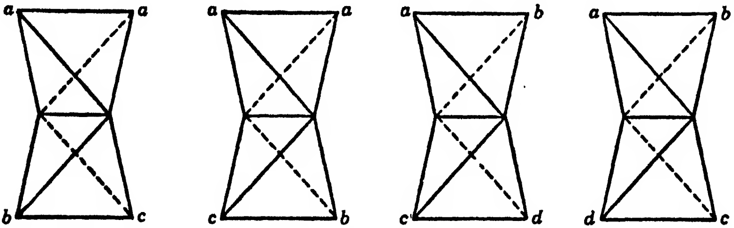
In one of these structures it is evident that the two *a* groups are closer together (III) than they are in the other (IV). If a plane is passed through that edge of the tetrahedrons which is shared between them and continued in each direction so as to bisect the lines joining the *a* and the *b* or *c* groups, the similar groups are either on the same side of the plane, *i. e.*, in the *cis*-position (III), or they fall on opposite sides of this plane and are in the *trans*-positions (IV). The four groups (*aabc*) fall in one plane, hence the mirror image of each form is identical with the object, and no *optical* isomers can exist in this series.



(III) (IV)

Carbon-carbon double bonds.

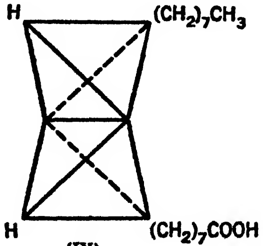
It can also be seen that each of the atoms joined by the double bond must be unsymmetrically substituted. When one of the atoms carries two *a* groups, and is thus symmetrical (V and VI), the two molecules are superimposable, and hence do not represent isomers. Even though all four attached groups are different (VII and VIII), only one pair of isomers is possible.



(V) (VI) (VII) (VIII)

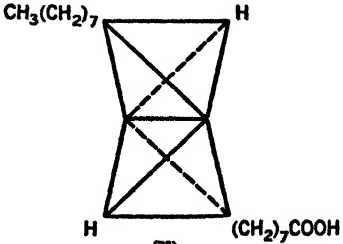
Carbon-carbon double bonds.[36a]

The two forms of $\Delta^{9,10}$-octadecenoic acid would be represented by the tetrahedral arrangement shown in IX and X:



(IX)

cis-Oleic acid.

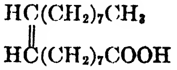


(X)

trans-Oleic or elaidic acid.

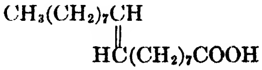
[36a] H. Gilman, *Organic Chemistry*. Vol. I, Wiley, New York, 1938, p. 369.

For convenience, instead of using tetrahedrons, the structural relationships of *cis-trans*-isomers are usually represented by condensed formulas, for example:



$$\begin{array}{l} HC(CH_2)_7CH_3 \\ \| \\ HC(CH_2)_7COOH \end{array}$$

(XI) *cis*-Oleic acid



$$\begin{array}{r} CH_3(CH_2)_7CH \\ \| \\ HC(CH_2)_7COOH \end{array}$$

(XII) *trans*-Oleic or elaidic acid

It has been observed from a study of various *cis-trans*-isomers whose configurations have been established that there is a surprising regularity in the difference in physical properties between the *cis*- and *trans*-forms. The *cis*-form usually has the lower melting point (Table 7), the greater solubility in inert solvents, the higher heat of combustion, and in the case of acids, the higher ionization constant. The unsymmetrical *cis*-form exhibits a considerably higher dipole moment than the more symmetrical *trans*-form. The x-ray spacing of the *cis*-form is shorter than that of the *trans*-form. The *cis*-form is almost always found in nature whereas the *trans*-form is generally produced by treatment of the *cis*-form by chemical and physical agents. In most cases the *cis*-form is labile and the *trans*-form stable, but, if the two forms are of the same approximate stability, equilibrium inversion will occur by proper treatment of either form.

TABLE 7

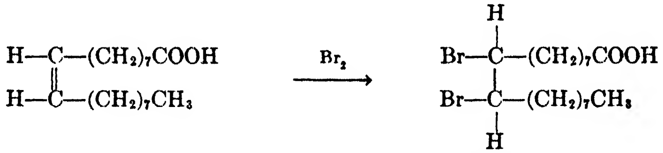
MELTING POINTS OF *cis*- AND *trans*-ISOMERS OF MONOETHENOID ACIDS AND DIHYDROXY DERIVATIVES

Acid	Number of C atoms	Position of double bond	Unsaturated acids, m.p., °C.		Dihydroxy acids, m.p., °C.	
			cis-acid	*trans*-acid	*cis*-addition	*trans*-addition
Myristoleic	14	9,10	. . .	. . .	. . .	. . .
Palmitoleic	16	9,10	−0.5 to 0.5	. . .	87 (84)	124–5
Petroselinic	18	6,7	30	53	114–5	122
Oleic	18	9,10	α-form, 13.4 β-form, 16.3	43.7	95	132
Vaccenic	18	11,12	. . .	38.5–39	. . .	. . .
Gadoleic	20	9,10	. . .	. . .	. . .	. . .
Erucic	22	13,14	33.5	60	100	133[a]
Selacholeic	24	15,16	39	69 (61)	. . .	. . .
Ricinoleic	18	9,10	5.5 (17)	53	110–11[b]	140–2[b]

[a] Melting points in literature vary from 129° to 133°C.
[b] Trihydroxystearic acid.

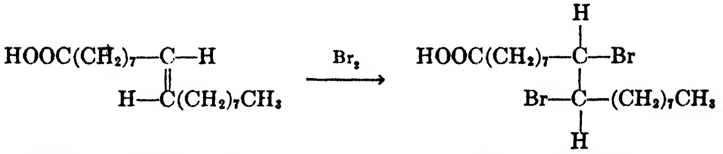
Monoethenoid Acids.—All of the known monoethenoid fatty acids are capable of existing in the two geometric forms illustrated by oleic and elaidic acids but generally only the *cis*-form occurs naturally. Any of the naturally occurring *cis*-acids can be converted into the *trans*-form by treatment with appropriate reagents such as the oxides of nitrogen (mercury and nitric acid), sulfur, selenium, etc. Griffiths and Hilditch[37,38] established the fact that the *cis-trans*-transformation is an equilibrium reaction which is completely reversible so that the same equilibrium mixture is attained regardless of the nature of the isomer used. For the oleic-elaidic transformation, equilibrium is attained at 66% of elaidic acid.

When the double bonds of *cis*-oleic acid and *trans*-elaidic acid are saturated with hydrogen, the same stearic acid is obtained, whereas the addition of halogens results in the formation of different dihalogenated stearic acids. Treatment of oleic and elaidic acids with bromine produces two isomeric dibromostearic acids melting at 28.5–29°C. and 29–30°C., respectively. On debromination with zinc and alcoholic hydrogen chloride each dibromo compound reverts exclusively to the acid from which it was prepared. It is, therefore, evident that the bromine has entered the molecules of oleic and elaidic acids at the same position on the carbon tetrahedrons which were previously united in a double bond, and so-called *cis*-addition has occurred. These stereochemical relationships may be represented as follows:



cis-Oleic acid
m.p. 13.4°C.

Dibromostearic acid
m.p. 28.5–29°C.



trans-Oleic (elaidic) acid
m.p. 44°C.

Dibromostearic acid
m.p. 29–30°C.

It has long been recognized that oxidation of maleic acid with alkaline potassium permanganate leads to the formation of mesotartaric acid, while similar treatment of fumaric acid produces *dl*-tartaric acid. The hydroxyl group enters the molecule at the same positions on the carbon tetrahedrons which were previously united in a double bond and *cis*-addition occurs in a manner analogous to the bromine addition to oleic and elaidic acids.

When the dibromostearic acids produced by the addition of bromine to oleic and elaidic acids are treated with aqueous or alcoholic potash, two isomeric dihydroxystearic acids are formed which melt at 95° and 132°C.,

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[37] H. N. Griffiths and T. P. Hilditch, *J. Chem. Soc.*, **1932**, **2315–2324**.
[38] H. N. Griffiths and T. P. Hilditch, *J. Soc. Chem. Ind.*, **53**, **75–81T (1934)**.

respectively. The structures of the hydroxy acids correspond to those of the original *cis*- and *trans*-oleic acids. Oxidation of oleic and elaidic acids with peracetic or other per acids results in the formation of the same two dihydroxy stearic acids melting at 95° and 132°C., respectively. All of these reactions represent *cis*-additions, but *cis*-addition does not always occur, especially under certain conditions of oxidation. For example, when oleic and elaidic acids are oxidized in alkaline media, especially with ice-cold aqueous alkaline potassium permanganate, the products of oxidation are exactly the reverse of those produced by per-acid oxidation, oleic acid yields dihydroxystearic acid melting at 132°C. and elaidic acid yields a dihydroxystearic acid melting at 95°C.[39,40] Alkaline permanganate oxidation of oleic and elaidic acids, therefore, represents *trans*-addition. The mechanism by which these *trans*-additions are produced is not completely understood but Hilditch[40] has advanced the theory that alkali produces an inversion at the double bond similar to a Walden inversion at the instant that addition occurs. Any inversion or similar transformation must occur in the actual formation of the dihydroxystearic acids since both of them are perfectly stable even in boiling alkaline solution (see oxidation and hydroxylation).

Although all of the naturally occurring and synthetic monoethenoid *cis*-acids can be converted to the corresponding *trans*-isomers, only a few of the latter have been specifically investigated. Detailed knowledge of the physical and chemical properties of the *trans*-isomers is much to be desired because various, and sometimes considerable, proportions of these acids are produced in the hydrogenation of fats containing polyethenoid fatty acids. For example, Bailey, Feuge, and Smith[41] found in a series of cottonseed and peanut oils which had been moderately hardened by hydrogenation (I.V., 55 to 71) that iso-oleic acids were produced to the extent of 5.0% to 22%. These iso-oleic acids probably comprise a mixture of positional and geometric isomers in unknown proportions. Other hydrogenated oils such as fish oils and vegetable oils containing unsaturated acids, other than linoleic and linolenic, yield a variety of isomerides on hydrogenation.

Diethenoid Acids.—When more than one unsymmetrically substituted double bond is present in a molecule, the number of geometric or *cis-trans*-isomers can be readily determined by writing out the possible structures. If the groups attached to the doubly bonded carbon atoms are such as to make all of the ethenoid units unlike, the number of isomers possible is 2^n, where n is the number of ethenoid linkages. Thus, the compound *ab*—C═CR—CR═C—*cd* can exist in four *cis-trans*-forms.

The only naturally occurring unsaturated fatty acids containing two

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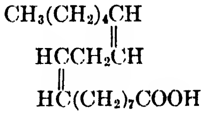
[39] A. Lapworth and E. N. Mottram, *J. Chem. Soc.*, **127**, 1628–1631 (1925).
[40] T. P. Hilditch, *J. Chem. Soc.*, **1926**, 1828–1836.
[41] A. E. Bailey, R. O. Feuge, and B. A. Smith, *Oil & Soap*, **19**, 169–176 (1942).

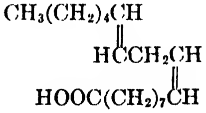
double bonds which have been isolated in pure form belong to the C_{18} series. The principal, and perhaps the only authentic acid of this group is $\Delta^{9,10,12,13}$-octadecadienoic or linoleic acid. Relatively recent investigations have indicated the probable existence of other linoleic acids but whether they are geometric or positional isomers is not certain. If the rule referred to above is applied to the naturally occurring $\Delta^{9,10,12,13}$-linoleic acid, it is evident that the number of theoretically possible isomers is 2^2 or 4. The configuration of these four acids may be represented as follows:

9-*cis*-12-*cis*



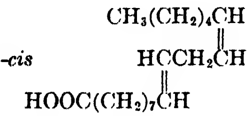
$$\begin{array}{r} CH_3(CH_2)_4CH \\ \| \\ HCCH_2CH \\ \| \qquad\qquad \\ HC(CH_2)_7COOH \end{array}$$

9-*cis*-12-*trans*



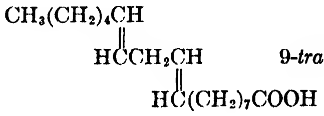
$$\begin{array}{l} CH_3(CH_2)_4CH \\ \qquad\quad \| \\ \qquad\quad HCCH_2CH \\ \qquad\qquad\qquad\quad \| \\ HOOC(CH_2)_7CH \end{array}$$

9-*trans*-12-*cis*



$$\begin{array}{r} CH_3(CH_2)_4CH \\ \| \\ HCCH_2CH \\ \| \\ HOOC(CH_2)_7CH \end{array}$$

9-*trans*-12-*trans*



$$\begin{array}{l} CH_3(CH_2)_4CH \\ \qquad\quad \| \\ \qquad\quad HCCH_2CH \\ \qquad\qquad\quad \| \\ \qquad\qquad\quad HC(CH_2)_7COOH \end{array}$$

The fact that four $\Delta^{9,10,12,13}$-linoleic acids are possible of existence and that each of these four geometric isomers are theoretically capable of producing four tetrabromo or tetrahydroxy acids has resulted in general confusion concerning the nature of the known linoleic acids. However, on the basis of theoretical considerations, Riemenschneider, Wheeler, and Sando[35] concluded that the number of tetrabromo- or tetrahydroxystearic acids which would actually be obtained by bromination or oxidation of a given geometric isomer of linoleic acid would be two instead of four. They illustrate their basis for this conclusion by formulas XIII to XVIII.

The addition of bromine to *cis*-$\Delta^{9,10}$-*cis*-$\Delta^{12,13}$-octadecadienoic or α-linoleic acid is assumed to occur in two steps which gives rise to two intermediate bromination products (XV) and (XVI) which undergo further bromination to produce products (XIII), (XIV), (XVII), and (XVIII). Since products (XIII) and (XVIII) and products (XIV) and (XVII) represent optical isomers, each pair of these isomers would produce one racemic acid and, therefore, but two tetrabromo- or tetrahydroxystearic acids would result from bromination or oxidation of the original linoleic acid. Actually only two such products are known. If the same reasoning is applied to the *trans*-$\Delta^{9,10}$-*trans*-$\Delta^{12,13}$-octadecadienoic or linolelaidic acid, there would likewise result but two end products of bromination or oxidation. In this case they would represent the racemates of the optical isomeric pairs of acids represented by formulas (XIII) and (XIV), and (XVII) and (XVIII), respectively. The same conclusions concerning the identity of these isomers were arrived at independently by McCutcheon.[42,43]

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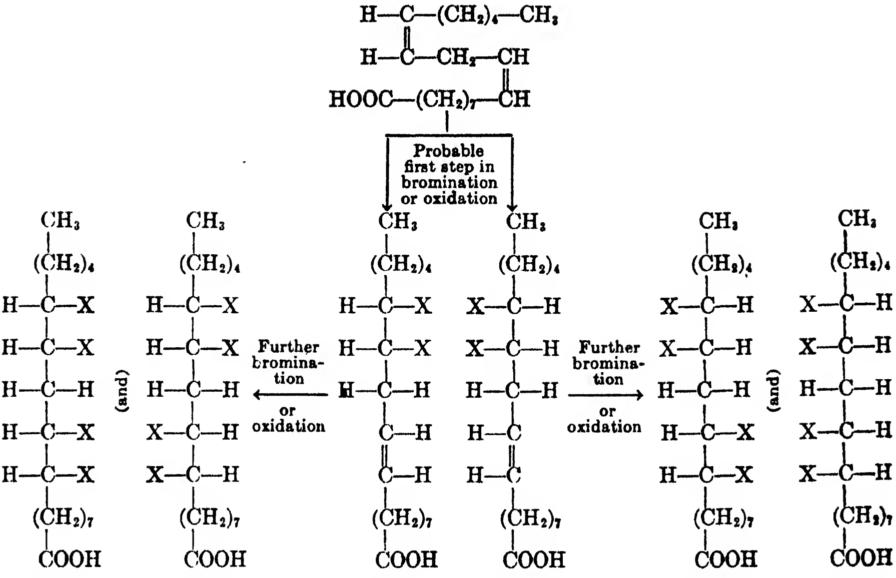
[42] J. W. McCutcheon, *Can. J. Research*, **B18**, 231–239 (1940).

[43] J. W. McCutcheon, M. F. Crawford, and H. L. Welsh, *Oil & Soap*, **18**, 9–11 (1941).



(XIII) (XIV) (XV) (XVI) (XVII) (XVIII)

The first known and most familiar linoleic acid is that found in linseed, cottonseed, peanut, soybean, corn, and many other commercial vegetable oils and it has been designated α-linoleic acid. The designations α and β which are applied to linoleic acids have no geometric significance but have been generally used to differentiate the high melting and low melting forms of a pair of isomers of these acids. Much experimental work and even more controversy has been carried on with regard to the geometric configurations of α- and β-linoleic acids. The work and conclusions concerning the configuration of α-linoleic acid has been well summarized by Hilditch,[44] McCutcheon,[34,43] Riemenschneider *et al.*,[35] and others. It is sufficient to state here that there is little doubt that the naturally occurring α-linoleic acid is the *cis*-$\Delta^{9,10}$-*cis*-$\Delta^{12,13}$-octadecadienoic acid.

When α-linoleic acid is treated with oxides of nitrogen or with selenium, it undergoes elaidinization in a manner similar to oleic acid. The resulting linolelaidic acid (m.p. 28–29°C.) corresponds to the *trans*-$\Delta^{9,10}$-*trans*-$\Delta^{12,13}$-octadedienoic acid. Kass and Burr[45] found that, on isomerization, linoleic acid produced 16% of linolelaidic acid. The isomerization product was characterized by its melting point, the formation of an insoluble salt, and the fact that on bromination it gave equal parts of a crystalline tetrabromostearic acid melting at 78°C. and a liquid tetrabromostearic acid.

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[44] T. P. Hilditch, *The Chemical Constitution of Natural Fats.* Chapman & Hall, London; Wiley, New York; 1940, pp. 331 *et seq.*

[45] J. P. Kass and G. O. Burr, *J. Am. Chem. Soc.*, 61, 1062–1066 (1939).

It also yields two tetrahydroxy acids melting at 146°C. and 122°C., respectively. These authors also reported the isolation of a liquid linolelaidic acid from the isomerization mixture which gave no solid tetrabromide and on oxidation yielded two tetrahydroxy acids melting at 156–158°C. and 126–127°C., respectively. They concluded that this liquid acid is a third geometric isomer of naturally occurring α-linoleic acid and it would, therefore, have to possess a *cis-trans-* or a *trans-cis-*configuration or possibly a mixture of the two.

Both the naturally occurring α-linoleic acid and the corresponding isomerized linolelaidic acid are reasonably well known but relatively little is known concerning the properties of the other two geometric isomers. α-Linoleic acid is chiefly characterized by the fact that on bromination it forms a tetrabromostearic acid melting at 115.5°C. (generally reported as 114–115°C.) and a liquid tetrabromostearic acid in an approximate ratio of 1:1. On oxidation of α-linoleic acid with alkaline potassium permanganate it forms two tetrahydroxystearic or α- and β-sativic acids which melt at 173° and 163.5°C., respectively. According to Riemenschneider *et al.*,[35] the tetrahydroxystearic acid melting at 157–159°C., which has been generally reported to be present in the products of oxidation of α-linoleic acid, is a eutectic mixture of the α- and β-sativic acids melting at 173° and 163.5°. On the basis of the analogy with the oxidation of oleic acid, these sativic acids would represent *trans-*addition products. Oxidation of α-linoleic acid in an acid medium, *e. g.*, peracetic or other per acid, produces two additional tetrahydroxystearic acids, designated as γ- and δ-sativic acids, melting at 145°C. and 134°C., respectively. In this case, which is also analogous to oleic acid, the sativic acids represent *cis-*addition products of α-linoleic acid.

The geometrically isomeric linolelaidic acid also produces a solid tetrabromostearic acid which melts at 78°C. and a liquid tetrabromostearic acid, in a 1:1 ratio. It yields the same sativic acids on oxidation as does α-linoleic acid. However, addition is the reverse of that occurring with α-linoleic acid, *i. e.*, oxidation in alkaline medium produces γ- and δ-sativic acids (m.p. 145° and 134°C.) and in acid medium, α- and β-sativic acids (m.p. 173° and 163.5°C.).

The isolation of linoleic acids which are not characterized by the above-mentioned bromination and oxidation products has been frequently reported. Suzuki and Inoue[20] isolated a linoleic acid from the fat of silkworm pupae which failed to yield an insoluble tetrabromide and it was, therefore, designated as isolinoleic acid. When oxidized with alkaline potassium permanganate in acetone, the isolinoleic acid yielded caproic and azelaic acids in the same manner as α-linoleic acid. When reduced with one mole of hydrogen it apparently yielded normal oleic acid, since the latter acid on oxidation gave the same dihydroxy acids as are produced by the oxidation of oleic acid under the same conditions. The oleic acid formed by hydrogenation of the isolinoleic acid gave elaidic acid when subjected to isomerization. α-Linoleic acid and the isolinoleic acid were hydrogenated in two stages and the velocity of the hydrogenation of the α-acid was observed to be greater than that of the iso-acid in both stages.

Smith and Chibnall[46] reported the isolation of a linoleic acid from cocksfoot and perennial ryegrass which gave no crystalline tetrabromide. The oily bromination product which they obtained contained 52.6% of bromine compared to 53.3% required by theory for $C_{18}H_{32}O_2Br_4$. The product was considered to be a mixture of isomeric linoleic acids including α-linoleic acid since a small amount of sativic acid was produced on oxidation. Hilditch[46a] states that cod liver oil and whale oil contain about 10% of octadecadienoic acids but no α-linoleic acid and that the latter acid is absent in butterfat but that there is present in this fat other octadecadienoic acids. Also, according to Hilditch, liver and depot fats of oxen and sheep contain octadecadienoic acids which do not give insoluble tetrabromides.

Kass, Lundberg, and Burr[47] examined corn, cottonseed, peanut, poppyseed, sunflowerseed, coconut, olive, and almond oils, and cocao butter with respect to their content of linoleic acid and concluded that only one octadecadienoic acid was present in these oils although the yield of tetrabromostearic acid varied from 27% to 51% of the amount calculated to be present on the basis of the iodine–thiocyanogen determination. These authors concluded that the variation in the recovery of tetrabromostearic acid was due to the unreliability of the "insoluble bromide" method rather than to the presence of isomeric linoleic acids which failed to give insoluble derivatives on bromination. Frankel, Stoneburner, and Brown[48] prepared linoleic acid from corn, sesame, cottonseed, grapeseed, and poppyseed oils by low temperature crystallization and concluded that in each case the acid was identical with α-linoleic acid prepared by debromination of α-tetrabromostearic acid. When the crystallization procedure was applied to olive oil, the linoleic isolated gave abnormally low yields of the high melting or α-tetrabromostearic acid, and the acid itself had an appreciably lower melting point than the corresponding acid isolated from other vegetable oils. They, therefore, concluded that olive oil contains a mixture of isomeric linoleic acids in which α-linoleic acid predominates. No definite experimental evidence has been adduced by any of these investigators, with the exception of Suzuki and Inoue, which would distinguish between positional and geometric isomers.

Much of the confusion concerning the existence of the natural isomers

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[46] J. A. B. Smith and A. C. Chibnall, *Biochem. J.*, **26**, 218–234 (1932).

[46a] T. P. Hilditch, *loc. cit.*, pp. 336–337.

[47] J. P. Kass, W. O. Lundberg, and G. O. Burr, *Oil & Soap*, **17**, 50–53 (1940).

[48] J. S. Frankel, W. Stoneburner, and J. B. Brown, *J. Am. Chem. Soc.*, **65**, 259–262 (1943).

of linoleic acid has resulted from numerous investigations of the nature of the bromination and debromination products of ordinary linoleic acid. Prior to the development of the low temperature crystallization procedure for the isolation of natural linoleic acid, the only known method of obtaining this acid was by debromination of the high melting or α-isomer of tetrabromostearic acid obtained by brominating the mixed unsaturated acids of natural fats and oils. The recent application of spectroscopic methods has shown that debromination of α-tetrabromostearic acid may or may not yield pure α-linoleic acid.[36] Various proportions of di-, tri-, and tetraene conjugated acids are present in the debrominated acid (see the section on spectroscopy). Despite the considerable amount of work which has been reported on the subject, the exact nature of the debromination products of the solid and liquid α-tetrabromostearic acids has not been determined with certainty.

Hilditch and Jasperson[49] and Green and Hilditch[50] concluded that the debromination of α-tetrabromostearic acid produced only α-linoleic acid but that β-tetrabromostearic acid produced a mixture of equal parts of α- and β-linoleic acids. On the other hand, McCutcheon,[34] Riemenschneider *et al.*,[35] and Kass and co-workers[45,47] claim that the linoleic acids obtained by debromination of the solid, α-, and the liquid, β-tetrabromostearic acids are identical with each other and with the naturally occurring linoleic acid.

Frankel and Brown[51] and Brode *et al.*[36] debrominated both α- and β-tetrabromostearic acids in a variety of solvents and concluded from an examination of the debromination products that both tetrabromostearic acids produce a mixture of isomeric acids whose composition depends on the nature of the solvent and other conditions obtaining during debromination. They further concluded that the predominant acid in the product obtained by debrominating the α-tetrabromostearic acid is identical with the naturally occurring linoleic acid, while the product obtained by debrominating β-tetrabromostearic acid contains but 15% to 53% of this linoleic acid together with a mixture of other isomeric linoleic acids. They also claim that the isomeric acids are *cis-trans-* and/or *trans-cis*-modifications and that they are definitely not the *trans-trans*-isomer. In the later publication[36] they demonstrated the presence of considerable proportions of conjugated acids in the debromination products.

Two conclusions may be drawn from the foregoing discussion, namely: (*1*) the exact nature of the debromination products of the solid, α-, and liquid, β-tetrabromostearic acids has not been established with certainty, and (*2*) the existence of any natural linoleic acid other than *cis*-$\Delta^{9,10}$-*cis*-

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[49] T. P. Hilditch and H. Jasperson, *J. Soc. Chem. Ind.*, **58**, 233-241 (1939).
[50] T. G. Green and T. P. Hilditch, *Biochem. J.*, **29**, 1552-1563 (1935).
[51] J. S. Frankel and J. B. Brown, *J. Am. Chem. Soc.*, **65**, 415-418 (1943).

$\Delta^{12,13}$-octadecadienoic acid is, to say the least, debatable. The possibility that the natural linoleic acids which failed to give normal yields of tetrabromo and tetrahydroxy acids are positional isomers is ruled out, at least in some cases, by the fact that on disruptive oxidation they yield caproic and azelaic acids which is possible only if the double bonds are located at the $\Delta^{9,10}$- and $\Delta^{12,13}$-positions. It may be significant that the linoleic acids, isolated from natural sources, which fail to respond to the tetrabromide test are always present as minor components and oftentimes represent an insignificant portion of the total mixed fatty acids or of the total unsaturated fatty acid fraction.

It is now realized that at every step in the isolation and purification of polyethenoid acids from natural sources, alteration of their structure can occur unless meticulous care is observed to avoid such changes. These alterations include oxidative changes, shifting of the double bond, especially to form conjugated systems, polymerization, cyclization, etc. It is also recognized that the yield of insoluble tetrabromostearic acid which is obtained on bromination of the mixed unsaturated fatty acids may be markedly affected by the nature and amount of other acids and bromo derivatives which are present in the mixture. It is possible, therefore, that some of the anomalous behavior, which has been recorded with respect to certain naturally occurring linoleic acids, may be explained by limitations of the preparative and analytical methods rather than on the basis of the existence of isomeric, and especially geometrically isomeric, linoleic acids.

At least it can be stated that no geometric isomer of linoleic acid has been isolated from natural sources by unequivocal methods and its identity established by rigid standards of chemical and physical homogeneity. All that can be stated with certainty is that two of the four theoretically possible geometric isomers of linoleic acid, namely, the *cis*-$\Delta^{9,10}$-*cis*-$\Delta^{12,13}$- and the *trans*-$\Delta^{9,10}$-*trans*-$\Delta^{12,13}$-octadecadienoic acids are relatively well known and their constitutions established unequivocally. The first of these two acids is of common occurrence in vegetable oils and the second can be produced by the well-known elaidinization reaction. It is not at all improbable that one or both of the other two geometric isomers of linoleic acid are present in the products of debromination of β-tetrabromostearic acid and possibly also to some extent of α-tetrabromostearic acid. It is also probable that they occur to some extent in the elaidinization products of α-linoleic acid. There is also good reason to believe that geometric isomers of linoleic acid are also produced on hydrogenation of linolenic acid or of oils containing these acids.

Triethenoid Acids.—Since the number of geometric isomers of the polyethenoid acids which are possible of existence increases exponentially with the number of double bonds, each positional isomer of the triethenoid series can exist in 2^3 or 8 different forms. Two of these forms would be represented by *cis-cis-cis-* and *trans-trans-trans*-configurations and the other six forms by various *cis-trans*-configurations.

Of the eight possible geometric isomers of linolenic acid, only two are known with certainty, namely, ordinary or α-linolenic acid, and elaidolinolenic or linolenelaidic acid obtained by treatment of the natural acid with oxides of nitrogen. The configurations of these two forms are not exactly known, but it has been assumed that they possess *cis-cis-cis-* and *trans-trans-trans*-structures. However, it is possible that not all of the double bonds are elaidinized by treatment with oxides of nitrogen, in which case the known elaidolinolenic acid would be expected to possess one of the six possible *cis-trans*-configurations or a mixture of these geometric isomers.

The efforts which have been made to determine the geometric structures of the two forms of linolenic acid have paralleled those of linoleic acid, but the results have been more difficult to interpret. These difficulties have been increased owing to the fact that it has not been possible to obtain the natural acid in a high degree of purity by low temperature crystallization methods. Shinowara and Brown[52] prepared linolenic acid from linseed and perilla oils which, on the basis of analytical data, represented a maximum purity of 88% on the assumption that the impurity was linoleic acid. The nature of the naturally occurring acid has, therefore, generally been inferred on the basis of knowledge derived from the linolenic acid obtained by debrominating α-hexabromostearic acid obtained by bromination of the mixed unsaturated fatty acids of linseed, perilla, and similar oils.

The naturally occurring linolenic acid produces, on bromination, a solid, or α-hexabromostearic acid, melting at 185°C.[52a] and a liquid, or β-hexabromostearic acid. On oxidation with alkaline potassium permanganate, α-linolenic acid produces two hexahydroxystearic acids which are designated as linusic (m.p. 203°C.) and isolinusic acid (m.p. 173–175°C.). Erdmann and Bedford[53] obtained a 25% yield of the solid, or α-hexabromostearic acid, and 75% of the liquid, or β-hexabromostearic acid, when they brominated linolenic acid, originally obtained by debrominating the solid hexabromide. They therefore considered the original debrominated acid to be a 1:3 mixture of α- and β-linolenic acids. Rollett[54] disputed this view and assumed that the linolenic acid obtained by debromination of the solid hexabromide was a homogeneous substance identical with the naturally occurring acid, and that on rebromination four pairs of racemic hexabromostearic acids were produced, only one of which was an ether-insoluble crystalline product. Rollett, and also McCutcheon,[42] claimed that both the

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[52] G. Y. Shinowara and J. B. Brown, *J. Am. Chem. Soc.*, **60**, 2734–2738 (1938).

[52a] T. R. Wood, F. L. Jackson, A. R. Baldwin, and H. E. Longenecker, *J. Am. Chem. Soc.*, **66**, 287–289 (1944).

[53] E. Erdmann and F. Bedford, *Ber.*, **42**, 1324–1333 (1909); *Z. physiol. Chem.*, **69**, 76–84 (1910).

[54] A Rollett, *Z. physiol. Chem.*, **70**, 404–407 (1911); **62**, 422–431 (1909).

solid, α-, and the liquid, β-hexabromostearic acids produced the same linolenic acid on debromination, and that the regenerated acid formed the same hexabromo- and hexahydroxystearic (linusic) acids as did the natural acid.

On the other hand, Shinowara and Brown[52] found that linolenic acid prepared from linseed and perilla oils by low temperature crystallization yielded 30% to 36% of hexabromostearic acid, rather than 25% claimed by most workers.

These workers, as well as Matthews, Brode, and Brown,[55] concluded from a comparative investigation of the properties of the natural acid, prepared by low temperature crystallization, and the acid recovered by debrominating α-hexabromostearic acid, that the two were not identical, and that the debrominated acid consists of a mixture of isomeric linolenic acids. They further concluded that the linolenic acid produced by debrominating α-hexabromostearic acid contains 12% to 15% of a *cis-trans*-isomer which yields no petroleum ether-insoluble or ethyl ether-insoluble hexabromide. Furthermore, Matthews *et al.* found that while the properties (melting point, refractive index, hexabromide number, etc.) of various specimens of linolenic acid obtained by debromination of the solid hexabromide were similar, those of the acids produced from linseed oil and perilla oil by low temperature crystallization varied, and depended on the oil from which the acid was derived. For these reasons, they concluded that the linolenic acids from these two oils were not identical and represented mixtures of isomeric acids and in both cases differed from the linolenic acid produced by debromination of α-hexabromostearic acid.

In contrast to the attention given linolenic acid, little work has been done on the solid geometric isomer, elaidolinolenic acid. This isomer has been prepared by Kass, Nichols, and Burr[56] by heating the ethyl ester of the naturally occurring acid with selenium for seventeen hours at 205–215°C. The regenerated and purified elaidolinolenic acid melted at 29–30°C. and gave a hexabromostearic acid melting at 169–170°C. The ethyl ester of the hexabromide melted at 114–115°C. On the basis of a 31% yield of solid hexabromostearic acid (m.p. 169–170°C.) from elaidolinolenic acid and similar yields of hexabromostearic acid (m.p. 181.0–181.5°C.) from natural linolenic acid, Kass and co-workers concluded that bromination of linolenic acid resulted in the formation of three pairs of racemic hexabromostearic acids instead of four, as was postulated by Rollett[54] and which would be expected for a triethenoid acid. Formation of the fourth pair was assumed to be impossible owing to stearic hindrance. They further concluded, from the nature of liquid bromides in the bromination products of

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[55] N. L. Matthews, W. R. Brode, and J. B. Brown, *J. Am. Chem. Soc.*, **63**, 1064–1067 (1941).

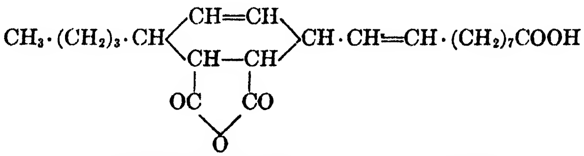
[56] J. P. Kass, J. Nichols, and G. O. Burr, *J. Am. Chem. Soc.*, **63**, 1060–1063 (1941).

their elaidolinolenic acid, that there remained no demonstrable proof for the existence of β or isolinolenic acids in drying oils.

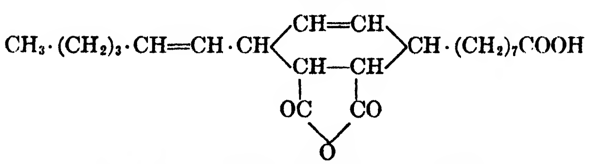
In view of the foregoing summary of the present knowledge of linolenic acid, it can only be said that the exact geometric configuration of naturally occurring linolenic acid is not known. It cannot even be stated with assurance whether this acid is a single geometric isomer or a mixture of isomers, and, if the latter, in what proportions. It is equally difficult to say whether the linolenic acids regenerated from the solid, α-, and the liquid, β-hexabromostearic acids are identical with one another and whether they are definite entities or mixtures of geometrical isomers.

Conjugated Triethenoid Acids.—Elaeostearic or $\Delta^{9,10,11,12,13,14}$-octadecatrienoic acid is a doubly-conjugated, positional isomer of linolenic acid and is capable of existing in eight *cis-trans-* or geometric modifications, only two of which are known with certainty, namely, α-elaeostearic acid melting at 48–49°C. and β-elaeostearic acid melting at 71°C. The existence of two other isomers, namely, punicic and trichosanic acids has been reported. α-Elaeostearic acid is present in the form of glycerides in tung and related oils. On exposure to light α-elaeostearic acid, as well as punicic and trichosanic acids, are transformed into the higher melting β-elaeostearic acid.

Morrell and co-workers[57,58] found that the α- and β-forms of elaeostearic acid react with maleic anhydride to produce two different diene addition products, melting at 62.5° and 77°C., respectively. According to these workers, the maleic anhydride condensation products of the α- and β-acids have the following structures:



α-Elaeostearic diene product, m.p. 62.5°C.



β-Elaeostearic diene product, m.p. 77°C.

On the basis of the maleic anhydride reaction products it is presumed that the original acids possessed *cis-* and *trans-*configurations in the portions of the molecules which were involved in the Diels-Alder condensation. If

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[57] R. S. Morrell and H. Samuels, *J. Chem. Soc.*, **1932**, 2251–2254.

[58] R. S. Morrell and W. R. Davis, *J. Soc. Chem. Ind.*, **55**, 237–246T, 261–267T (1936)

this is indeed the case, it may be presumed that the natural or α-form possesses the *cis*-configuration and the β-form, the *trans*-configuration.

Toyama and Tsuchiya[59] isolated two octadecatrienoic acids from common pomegranate, *Punica granatum* L., and Japanese snakegourd (karasu-uri), *Trichosanthes cucumeroides* Maxim., seed oils. Both acids were believed to be isomeric with elaeostearic acid, but since they differed from each other and from elaeostearic acid in various physical properties they were designated as punicic acid (m.p. 43.5–44°C.) and trichosanic acid (m.p. 35–35.5°C.). Punicic and trichosanic acids were shown to be identical with elaeostearic in having a conjugated system of double bonds at the $\Delta^{9,10,11,12,13,14}$-positions and like α-elaeostearic acid they are converted by the action of light into β-elaeostearic acid. When the two acids were mixed with each other, or with α-elaeostearic acid, a marked depression was observed in the melting point of the pure acid. On the other hand, when the light-inverted forms were mixed with β-elaeostearic acid no depression in the melting point was observed. On the basis of these observations the authors concluded that punicic and trichosanic acids were natural geometric isomers of α-elaeostearic acid. Later, Farmer and van den Heuvel[60] re-examined punicic acid and confirmed the results of Toyama and Tsuchiya. X-ray powder photographs of α- and β-elaeostearic and of punicic acids showed that they were distinct entities. Unlike α- and β-elaeostearic acids, punicic acid does not give a maleic anhydride derivative. To date no attempt has been made to determine the geometric configuration of these two natural isomers of elaeostearic acid, and since the geometric configurations of α- and β-elaeostearic acids are themselves not known with certainty, the exact identity of all four acids remains a problem for future solution.

Licanic acid or 4-keto-$\Delta^{9,10,11,12,13,14}$-octadecatrienoic acid is, like all other triethenoid fatty acids, capable of existing in eight geometrically isomeric forms. Two such forms are known, namely, α-licanic acid (m.p. 74–75°C.) and β-licanic acid (m.p. 99.5°C.). The α-form which occurs naturally in oiticica and po-yoak oils passes to the β-form on the action of light in the presence of traces of iodine or sulfur. The two forms of licanic acid are also distinguished by differences in their derivatives. α-Licanic acid yields a semicarbazone, melting at 110–111°C., and a maleic anhydride addition product, melting at 79°C., whereas β-licanic acid gives a semicarbazone, melting at 138°C., and a maleic anhydride adduct, melting at 97°C.[61]

Parinaric acid or $\Delta^{9,10,11,12,13,14,15,16}$-octadecatetraenoic acid contains four double bonds and hence is capable of existing in 2^4 or 16 geometrically

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[59] Y. Toyama and T. Tsuchiya, *J. Soc. Chem. Ind. Japan*, Suppl. bind., **38**, 182–185, 185–187 (1935).

[60] E. H. Farmer and F. A. van den Heuvel, *J. Chem. Soc.*, **1936**, 1809–1811

[61] R. S. Morrell and W. R. Davis, *J. Chem. Soc.*, **1936**, 1481–1484.

isomeric forms. Actually only two forms are known, namely, α-parinaric acid (m.p. 85–86°C.) which occurs naturally in the seed fat of *Parinarium laurinum* and β-parinaric acid (m.p. 95–96°C.) which is produced by the action of light on the α-form in the presence of a trace of iodine.

Other natural polyethenoid acids containing four to six double bonds are known and each of these acids is capable of existing in various geometric modifications. However, so little is known concerning the properties of these acids it is scarcely worth discussing them. The melting points of the various polyethenoid acids which are known to occur in two or more geometric forms are collected in Table 8.

TABLE 8

MELTING POINTS OF THE GEOMETRICALLY ISOMERIC POLYETHENOID FATTY ACIDS

Acid	Position of double bonds	M.p., °C.
Linoleic	9,10,12,13	−5.0 to −5.2
Linolelaidic	9,10,12,13	28–29
Linolenic	9,10,12,13,15,16	−11.0 to −11.3
Elaidolinolenic	9,10,12,13,15,16	29–30
α-Elaeostearic	9,10,11,12,13,14	48–49
β-Elaeostearic	9,10,11,12,13,14	71–72
Psuedo-elaeostearic	10,11,12,13,14,15	79
Punicic	9,10,11,12,13,14	43.5–44
Trichosanic	9,10,11,12,13,14	35–35.5
α-Parinaric	9,10,11,12,13,14,15,16	85–86
β-Parinaric	9,10,11,12,13,14,15,16	95–96
α-Licanic	4-Keto-9,10,11,12,13,14	74–75
β-Licanic	4-Keto-9,10,11,12,13,14	99.5

(*b*) *Optical Isomerism*

Optical isomerism, which is detected by measuring the degree to which a given substance is capable of rotating a plane of polarized light, occurs in compounds having no complete symmetry from a geometric standpoint. The structural configurations of *asymmetric* molecules are such that one molecule is not identical with its mirror image. Such molecules and their mirror images are identical in all respects in their chemical and physical properties except in their ability to rotate a plane of polarized light. Optical activity occurs in: (*1*) compounds containing one or more asymmetric atoms, and (*2*) compounds which contain no individual asymmetric atoms but in which asymmetry is due to the absence of any of the necessary elements of symmetry which permit the mirror image of the molecule to be superimposable.

The isomer which rotates a plane of polarized light to the right is designated as *dextrorotatory* and the one which rotates it to the left is designated as *levorotatory*. The optical activity of both isomers is the same in degree but opposite in sign. The two forms are often referred to as *enantiomorphs*.

When equal amounts of the *dextro-* and *levo-*isomers are mixed, the resulting product will show no activity owing to the fact that the optical effect of one form is neutralized by that of the other. Such a product is known as a *racemic* modification and is designated as a *dl*-form. Most synthetic preparations are *dl*-modifications, since the reactions by which they are formed result in the production of equal amounts of each isomer. Generally, *racemates* differ in many respects from their optically active isomers and in many cases they can be resolved into their component *d*- and *l*-forms.

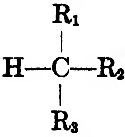
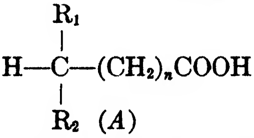
A compound which would otherwise exhibit optical activity may be optically inactive owing to internal compensation. If the compound contains two asymmetric carbon atoms, one of which is dextrorotatory and the other levorotatory by exactly the same amount, the net rotation will be zero and the compound is inactive. Such compounds are designated as *meso*-forms. The *meso*-form of a compound differs from its *dl*-form in physical properties, and both the *meso-* and the *dl*-forms differ from the individual *d*- and *l*-forms.

If a compound contains several asymmetric carbon atoms the optical rotation of the compound as a whole will be the algebraic sum of the individual rotations. The resultant sum of these rotations, which may individually be relatively large, may be an immeasurably small value. Unfortunately, there is no known method whereby the absolute rotation of a single asymmetric carbon atom can be determined in a compound containing two or more asymmetric carbon atoms.

The optical activity of a compound may be expressed as specific rotation, $[\alpha]$, or molecular rotation, $[M]$. The specific rotation of an optically active liquid was originally defined as the rotation produced by a layer of active substance one decimeter in length, or if a solution, of one gram of active substance in a volume of one cubic centimeter. However, the density of the liquid must be taken into account, therefore, the specific rotation, $[\alpha]$, at a temperature, t, and definite wave length of light is expressed as $[\alpha]_\lambda^t = r/ld$, where r equals the observed polarimetric rotation in degrees, l, the length of the column, and d, the density; or in the case of a solution, $[\alpha] = rv/lp$, where v equals the volume in cubic centimeters and p the grams of substance contained in v volume of the solution.

In order to intercompare the optical rotations of various substances, it is necessary to convert specific rotations to molecular rotations. The molecular rotation calculated on the basis of gram-molecular weights may be a very large value, and for convenience this value divided by 100 is used in expressing the molecular rotation $[M]$. The molecular rotation is, therefore, expressed as $[M]_\lambda^t = m/100 \cdot rv/lp$, where m is the molecular weight of the substance and the other symbols have the same significance as in the case of specific rotation.

All of the known optically active natural or synthetic fatty acids are, as would be expected, substituted aliphatic acids. The natural acids are generally dextrorotatory, whereas both levo- and dextrorotatory synthetic acids have been prepared. Substituted acids, such as bromo and hydroxy acids, produced by bromination or oxidation of natural unsaturated acids, are racemic mixtures and, therefore, inactive.

Synthetic Acids.—The most extensive investigation of the optical activity in the fatty acid series has been carried out by Levene and coworkers,[62,63] who prepared and determined the optical activity of alkyl-, hydroxy-, and halogen-substituted aliphatic acids as well as their related esters, alcohols, and hydrocarbons. They concluded from these investigations that the optical rotation of each molecular species may be regarded as the resultant of two major contributions. In the case of acyclic hydrocarbons of the trisubstituted methane type, the two heavier groups should furnish contributions of opposite sign. In the series represented by  $H—\overset{R_1}{\underset{R_3}{C}}—R_2$, an increase in the weight of R_3 should bring about an increase of the molecular rotation toward the right, whereas an increase in the weight of R_2 should have the opposite effect. When R_2 and R_3 are not simple alkyl radicals, as, for example, in  $H—\overset{R_1}{\underset{R_2}{C}}—(CH_2)_nCOOH$ (*B*), (*A*) a prediction is impossible since the contribution of any group depends upon its structure and consequently it may function as a lighter or heavier group than an alkyl group of the same weight.

Thus, if $[M] = A + B$ and if A has a higher value than B, the direction of the rotation is determined by that of the contribution A. Then the values of the rotations of the consecutive members of the series, homologous with respect to A, should progressively increase. If the value of B is greater than A, the direction of rotation is determined by that of the contribution B. In this case, if a series is formed homologous to A, the changes in the rotations of the members of the homologous series should be in the direction of A, although the values may progressively diminish. Thus, if A is positive, and B is negative and of a higher value than A, the substance should rotate to the left, but as A progressively increases in weight, B remaining approximately constant, the values of the negative rotations of the successive members of the homologous series should progressively decrease, thus indicating a change toward the right.

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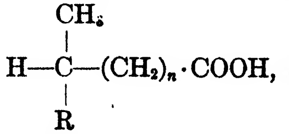
[62] P. A. Levene and L. A. Mikeska, *J. Biol. Chem.*, **84**, 571–599 (1929).

[63] P. A. Levene and R. E. Marker, *J. Biol. Chem.*, **91**, 77–103 (1931); **92**, 455–460 (1931); **93**, 749–774 (1931); **95**, 153–164 (1932).

The theoretical implications here described are illustrated in Table 9. The values of the rotations given in Table 9 for the members of the first vertical series are not the maximum values, whereas those of all other members are maximum values. A comparative analysis of the second vertical series may serve as a key to the character of each of the two contributions in all the substances listed in Table 9. The rotation of the first member is negative and that of all successive members is increasingly positive, indicating that the contribution of the heavier alkyl radical is positive, and that of the group containing the carboxyl is negative. In the first member the direction of rotation is determined by the group $—(CH_2)COOH$; in the remaining members by that of the heavier alkyl radical. Assuming then that the direction of the contribution A remains constant for all these configurationally related substances, the conclusion is reached that in all the substances enumerated in Table 9 the contribution B is levorotatory. In the substances of column *1*, the value of B is higher than that of A, hence all the members rotate to the left. In column *2* the negative value of B is smaller than in column *1*, so that it determines the direction of rotation of the first member only. In column *3* the value of B is higher than A, so that all members rotate to the left, but the rotations progressively change toward the right because of the increase in the dextrorotation of the contribution A. Finally, in column *4* the value of B is still higher than that of A, but not to the same extent as for the members of column *3*; hence the values of rotation of the individual members are lower than those of the corresponding members of column *3* and again, the change of rotation of the individual members is progressively toward the right.

Comparing the members of any horizontal row, one observes an alternating change in the values of the rotations of individual members. Thus, it seems as if the carboxyl group attached directly to the asymmetric carbon atom furnishes a higher negative contribution than the corresponding group of the second horizontal member. The third member furnishes a higher contribution than the second member and lower than the fourth, thus the contributions are *1* > *2* < *3* > *4*. Thus, the effect of distance upon the contribution of a polar group is to change the value only and not the sign.

Levene, Rothen, and Marker[64] reported comprehensive data on the rotary dispersion of a series of configurationally related fatty acids of the general type  $H—\underset{R}{\overset{CH_3}{C}}—(CH_2)_n \cdot COOH$, where n varied from 0 to 1 and R from $C_2H_5—$ to $C_{11}H_{21}—$. All of these acids contain an asymmetric carbon

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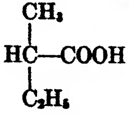
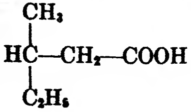
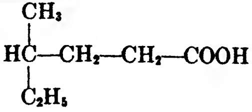
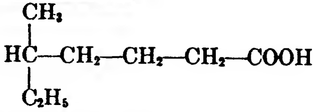
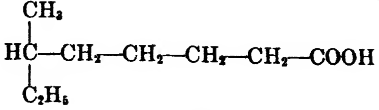
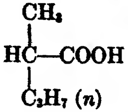
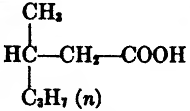
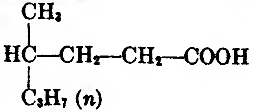
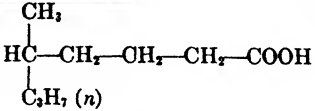
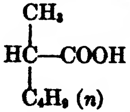
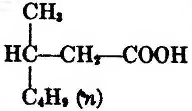
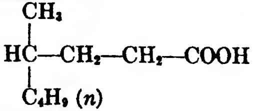
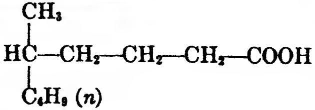
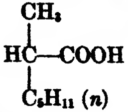
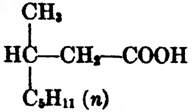
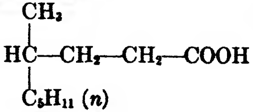
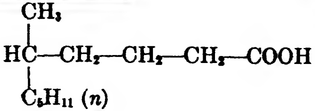
[64] P. A. Levene, A. Rothen, and R. E. Marker, *J. Chem. Phys.*, 1, 662–676 (1933).

TABLE 9

MAXIMUM MOLECULAR ROTATIONS, $[M]_D^{25}$, OF CONFIGURATIONALLY RELATED ALIPHATIC ACIDS CONTAINING A METHYL GROUP ON THE ASYMMETRIC CARBON ATOM

1	2	3	4	5
 $\overset{CH_3}{\underset{C_2H_5}{HC}}—COOH$ −18.0	 $\overset{CH_3}{\underset{C_2H_5}{HC}}—CH_2—COOH$ −10.4	 $\overset{CH_3}{\underset{C_2H_5}{HC}}—CH_2—CH_2—COOH$ −13.6	 $\overset{CH_3}{\underset{C_2H_5}{HC}}—CH_2—CH_2—CH_2—COOH$ −11.1	 $\overset{CH_3}{\underset{C_2H_5}{HC}}—CH_2—CH_2—CH_2—CH_2—COOH$ −12.2
 $\overset{CH_3}{\underset{C_3H_7\,(n)}{HC}}—COOH$ *levo*	 $\overset{CH_3}{\underset{C_3H_7\,(n)}{HC}}—CH_2—COOH$ +3.6	 $\overset{CH_3}{\underset{C_3H_7\,(n)}{HC}}—CH_2—CH_2—COOH$ −6.9	 $\overset{CH_3}{\underset{C_3H_7\,(n)}{HC}}—CH_2—CH_2—CH_2—COOH$ −3.7	
 $\overset{CH_3}{\underset{C_4H_9\,(n)}{HC}}—COOH$ *levo*	 $\overset{CH_3}{\underset{C_4H_9\,(n)}{HC}}—CH_2—COOH$ +6.1	 $\overset{CH_3}{\underset{C_4H_9\,(n)}{HC}}—CH_2—CH_2—COOH$ −4.1	 $\overset{CH_3}{\underset{C_4H_9\,(n)}{HC}}—CH_2—CH_2—CH_2—COOH$ −1.7	
 $\overset{CH_3}{\underset{C_5H_{11}\,(n)}{HC}}—COOH$ *levo*	 $\overset{CH_3}{\underset{C_5H_{11}\,(n)}{HC}}—CH_2—COOH$ +8.1	 $\overset{CH_3}{\underset{C_5H_{11}\,(n)}{HC}}—CH_2—CH_2—COOH$ −1.9	 $\overset{CH_3}{\underset{C_5H_{11}\,(n)}{HC}}—CH_2—CH_2—CH_2—COOH$ −0.6	

atom and are, therefore, optically active. Data pertaining to the molecular rotation of these acids are given in Table 10. These authors determined the rotatory dispersions for a number of acids of Table 10 over a wide range of wave lengths of light extending into the far ultraviolet.

TABLE 10

MAXIMUM MOLECULAR ROTATIONS, $[M]^{25}_{5892.6}$, OF CONFIGURATIONALLY RELATED ALIPHATIC ACIDS WITHOUT SOLVENT

α-Methylbutyric acid	−18.0	γ-Methylcaproic acid	−13.6
Ethyl ester	−22.9		
α-Methylvaleric acid	−21.4	γ-Methylheptylic acid	− 6.9
Ethyl ester	−27.5		
α-Methylcaproic acid	−24.3	γ-Methylcaprylic acid	− 4.1
α-Methylnonylic acid	−27.3	γ-Methylnonylic acid	− 1.9
α-Methyldodecylic acid	−27.5	δ-Methylheptylic acid	−11.1
β-Methylvaleric acid	−10.4	δ-Methylcaprylic acid	− 3.7
Ethyl ester	−11.5		
β-Methylcaproic acid	+ 3.6	δ-Methylnonylic acid	− 1.7
Ethyl ester	+ 0.69		
β-Methylheptylic acid	+ 6.1	δ-Methyldecylic acid	− 0.6
β-Methylcaprylic acid	+ 8.1	ε-Methylcaprylic acid	−12.2
Ethyl ester	+ 4.1		

A number of optically active derivatives of the *n*-aliphatic acids have been prepared in which the activity is derived from the introduced radical. Optically active amyl, bornyl, and methyl esters and the brucine and cinchonine salts of the *n*-aliphatic acids have been prepared and their molecular rotations determined.[65–67]

Natural Acids.—A number of optically active fatty acids have been isolated from natural sources. The principal members of this class of acids are listed in Table 11 together with the values for their specific rotations.

Hydroxy Acids.—When a hydrogen of the methylene chain of a fatty acid is substituted by another atom or radical there is produced in the molecule an asymmetric carbon atom and a plane of asymmetry. For example, if a hydroxyl group replaces a hydrogen atom in oleic acid, the resulting acid is optically active. For this reason, ricinoleic, or 12-hydroxyoleic acid, is optically active whereas oleic acid is not. Its rotation has been reported[68] to vary from $[\alpha]_D = 6.25$ to 7.5. On conversion to its *trans*-isomeride by treatment with oxides of nitrogen its rotation remains the same, both in magnitude and sign, since ricinoleic and ricinelaidic acids

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[65] T. P. Hilditch, *J. Chem. Soc.*, **95**, 1570–1577 (1909). See also H. Christopher and T. P. Hilditch, *J. Chem. Soc.*, **101**, 192–202, 202–207 (1912).

[66] J. Minguin and E. G. de Bollemont, *Compt. rend.*, **134**, 608–610 (1902).

[67] P. A. Guye and L. Chavanne, *Compt. rend.*, **119**, 906–909 (1894); **120**, 452–454 (1895).

[68] P. Walden, *Ber.*, **27**, 3471–3478 (1894).

TABLE 11

SPECIFIC OPTICAL ROTATIONS OF NATURAL FATTY ACIDS

Systematic name	Common name	Empirical formula	Rotation	
			$[\alpha]_D$	T, °C.
12-Hydroxy-$\Delta^{9,10}$-octadecenoic	Ricinoleic	$C_{18}H_{34}O_3$	+ 6.4	22
13-$\Delta^{2,3}$-Cyclopentenyl-*n*-tridecanoic	Chaulmoogric	$C_{18}H_{32}O_2$	+ 60.3	25
11-$\Delta^{2,3}$-Cyclopentenyl-*n*-undecanoic	Hydnocarpic	$C_{16}H_{28}O_2$	+ 69.3	25
9-$\Delta^{2,3}$-Cyclopentenyl-*n*-nonanoic[a]	Alepric	$C_{14}H_{24}O_2$	+ 77.1	25
7-$\Delta^{2,3}$-Cyclopentenyl-*n*-heptanoic[a]	Aleprylic	$C_{12}H_{20}O_2$	+ 90.8	25
5-$\Delta^{2,3}$-Cyclopentenyl-*n*-pentanoic[a]	Aleprestic	$C_{10}H_{16}O_2$	+100.5	25
1-$\Delta^{2,3}$-Cyclopentenyl-*n*-methanoic	Aleprolic	$C_6H_8O_2$	+120.5	25
13-$\Delta^{2,3}$-Cyclopentenyl-$\Delta^{6,7}$-tridecenoic	Gorlic	$C_{18}H_{30}O_2$	+ 60.7	25
*iso*Nonadecanoic	Tuberculostearic	$C_{19}H_{38}O_2$	inactive	...
*iso*Heneicosanoic	Phytomonic	$C_{20}H_{40}O_2$	inactive	...
*iso*Tetracosanoic	...	$C_{24}H_{48}O_2$	+ 5.17	23
*iso*Pentacosanoic	...	$C_{25}H_{50}O_2$	+ 15.60	23
*iso*Hexacosanoic	Phthioic	$C_{26}H_{52}O_2$	+ 12.78	23
*iso*Heptacosanoic	...	$C_{27}H_{54}O_2$	+ 17.11	23
Dihydroxyoctadecanoic	Dihydroxystearic	$C_{18}H_{36}O_4$	− 0.15	50
Mixture of hydroxy acids[b]	Phrenosinic	...	+ 3.33	...
Mixture of hydroxy acids	Leprosinic	...	+ 4	...

[a] Structure assigned by analogy with that of known homologs.
[b] Mixture of α-hydroxydocosanoic, -tetracosanoic, and -hexacosanoic acids.

are geometrical and not optical isomers. The esters of ricinoleic acid are also optically active. Their activities, $[\alpha]_D^{15}$, have been reported[69] to be as follows: methyl ricinoleate 5.20, ethyl ricinoleate 4.48, *n*-propyl ricinoleate 4.35, isobutyl ricinoleate 4.22.

A number of saturated hydroxy aliphatic acids are known to occur naturally, but few of them have been isolated in a pure state. King[70] isolated dihydroxystearic acid, m.p. 141°C., from the sludge deposited on settling commercial ricinoleic acid. Polarization of this acid in warm alcohol solution gave a specific rotation of $[\alpha]_D^{50}$ $-0.15°$, but the author concluded that the observed rotation of 0.7′ was probably within the limits of experimental error.

Chibnall, Piper, and Williams[71] found that phrenosinic acid obtained from the cerebroside, phrenosin, consisted of a mixture of α-hydroxy-*n*-hexacosanoic (15%) and α-hydroxy-*n*-tetracosanoic acids (85%). The purest product obtained melted at 102.3–102.6°C. and had an optical rotation in pyridine of $[\alpha]_D^{22}$ $+3.33°$. For purposes of identification with the

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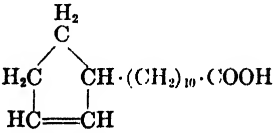
[69] A. Haller, *Compt. rend.*, **144**, 462–466 (1907).
[70] G. King, *J. Chem. Soc.*, **1942**, 387–391.
[71] A. C. Chibnall, S. H. Piper, and E. F. Williams, *Biochem. J.*, **30**, 100–114 (1936).

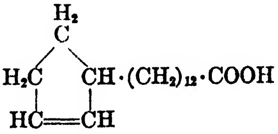
natural acids the α-hydroxy acids of the series C_{13} to C_{18} were prepared, but since they represented racemates they were optically inactive. The results of Chibnall *et al.* were subsequently confirmed by Crowfoot.[72]

An inseparable mixture of optically active hydroxy acids was isolated from the lipids of the leprosy bacillus by Anderson and co-workers[73] and assigned the name leprosinic acid.

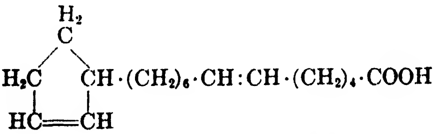
Chaulmoogra Acids.—The most extensive homologous series of naturally occurring optically active acids are those of the group of chaulmoogra acids. Seven acids of this series are known, all consisting of an aliphatic acid having an ω-substituted cyclopentenyl ring. They owe their optical activity to the presence of one or more asymmetric carbon atoms. The structural formulas for the three best known cyclopentenyl substituted acids are given below. The specific rotations and other properties of the acids



Hydnocarpic acid, $C_{16}H_{28}O_2$



Chaulmoogric acid, $C_{18}H_{32}O_2$



Gorlic acid, $C_{18}H_{30}O_2$

TABLE 12

CONSTANTS OF OPTICALLY ACTIVE FATTY ACIDS FOUND IN CHAULMOOGRA OILS[a]

Acid	Molecular weight	M.p., °C.	Specific rotation, $[\alpha]^{25}_{D}$	Iodine value
Chaulmoogric	280.2	68.5	60.3	90.5
Hydnocarpic	252.2	60.5	69.3	100.7
Alepric	224.2	48.0	77.1	113.4
Aleprylic	196.2	32.0	90.8	129.7
Aleprestic	168.1	..	100.5[b]	151.2
Homolog not found	140.1	..	110.5[b]	181.5
Aleprolic	112.1	..	120.5[b]	226.7
Gorlic	278.2	6.0	60.7	182.5

[a] H. I. Cole and H. T. Cardoso, *J. Am. Chem. Soc.*, **61**, 2349–2351, 2351–2353, 3442–3445 (1939).

[b] Calculated.

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[72] D. M. Crowfoot, *J. Chem. Soc.*, **1936**, 716–718.

[73] R. J. Anderson, J. A. Crowder, M. S. Newman, and F. H. Stodola, *J. Biol. Chem.*, **113**, 637–647 (1936).

TABLE 13

CONSTANTS OF ETHYL ESTERS OF OPTICALLY ACTIVE ACIDS FOUND IN CHAULMOOGRA OILS[a]

Compound	Molecular weight	B.p., °C. (10 mm.)	Specific rotation, $[\alpha]^{25}_{D}$	Iodine value	Refractive index, n^{25}_{D}	Specific gravity, 25°/25°
Ethyl chaulmoograte	308.3	222	55.4	82.5	1.4592	0.901
Ethyl hydnocarpate	280.2	200	61.9	90.5	1.4578	0.907
Ethyl aleprate	252.2	174	66.5	100.7	1.4562	0.915
Ethyl aleprylate	224.2	148	79.1	113.4	1.4550	0.925
Ethyl aleprestate	196.2	122[b]	86.5[b]	129.7	1.4538[b]	...
Homolog not found	168.1	96[b]	94.1[b]	151.2	1.4526[b]	...
Ethyl aleprolate	140.1	70[b]	101.8[b]	181.5	1.4514[b]	...
Ethyl gorlate	306.3	232	55.6	167.0	1.4667	0.912

[a] H. I. Cole and H. T. Cardoso, *J. Am. Chem. Soc.*, **61**, 2349–2351, 2351–2353, 3442–3445 (1939).
[b] Calculated.

and ethyl esters of the chaulmoogra series as reported by Cole and Cardoso[74] are given in Tables 12 and 13.

Methylated Acids.—A number of optically active, methylated saturated fatty acids have been isolated from the acetone-soluble fats elaborated by various microorganisms. With the exception of tuberculostearic or 10-methylstearic acid, none of the structures of these acids has been established and in some cases doubt exists concerning the homogeneity o the products. Tuberculostearic acid, $C_{19}H_{38}O_2$ (m.p. 10°C.) and the homologous phytomonic acid, $C_{20}H_{40}O_2$ (m.p. 24°C.) are both presumed to be optically active but possess a rotation too small to be measured.

Phthioic acid, $C_{26}H_{52}O_2$ (m.p. 21–22°C.), and the unnamed homologs corresponding to the formulas $C_{24}H_{48}O_2$ (m.p. 23–24°C.), $C_{25}H_{50}O_2$ (m.p. 17–18°C.), and $C_{27}H_{54}O_2$ (m.p. 20–21°C.) are measurably dextrorotatory.[75]

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[74] H. I. Cole and H. T. Cardoso, *J. Am. Chem. Soc.*, **61**, 2349–2351, 2351–2353, 3442–3445 (1939).

[75] L. G. Ginger and R. J. Anderson, *J. Biol. Chem.*, **156**, 443–451 (1944).

C. PHYSICAL PROPERTIES OF THE FATTY ACIDS

CHAPTER IV

CRYSTAL PROPERTIES

1. Introduction[1]

In Chapter III it was pointed out that many of the chemical, as well as physical, properties of the fatty acids and their derivatives are dependent upon their molecular structure. There are, however, certain properties of fatty acids and their derivatives which are primarily dependent upon their crystal structure, *i. e.*, upon the manner in which the molecules are arranged in the crystal unit or lattice of these substances. The crystal structure and dependent properties of the long chain fatty acids are of considerable theoretical as well as of industrial importance.

Most of our knowledge of the crystal structure of the fatty acids is of recent origin and has been placed on a secure foundation only by the application of x-ray spectroscopy to these and related long chain aliphatic compounds. The present chapter is concerned with a discussion of these structures and the concomitant subjects of crystallography, x-ray diffraction, polymorphism, and change of state, including change from one polymorphic form to another.

2. Crystallography

Only two solid states are recognized from the scientific point of view, namely, crystalline and amorphous, the essential distinction between them being the result of internal order. The order in the crystalline state is reflected in the formation of plane bounding surfaces so oriented that they show some degree of symmetry. In addition to being bounded by plane surfaces, crystals are distinguished from amorphous material by the fact that some of the properties of the solid depend in magnitude upon the direction in which they are measured, *i. e.*, they are *anisotropic*. For example, the refractive index, compressibility, coefficient of thermal expansion, electrical conductivity, and heat conductivity are properties which are direction-dependent in crystals. Amorphous solids are generally re-

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[1] The author wishes to acknowledge the very considerable assistance rendered by Mr. M. E. Jefferson and Mrs. Florence B. Kreeger of the Analytical, Physical Chemical, and Physical Division of the Southern Regional Research Laboratory in the preparation of this chapter, and especially the x-ray diffraction photographs painstakingly prepared from highly purified aliphatic compounds to illustrate the x-ray method for identifying these substances.

garded as liquids of great viscosity and do not possess definite transition points at which they undergo an abrupt change to the liquid state. Pure crystalline solids, on the other hand, have characteristically sharp transitions to the liquid state with the absorption of heat.

Early crystallographers were convinced by the study of the regularity of form and symmetry, the invariance of the angle between typical plane faces, and the phenomenon of cleavage, that crystals were formed by the regular arrangement in space of some fundamental unit. Haüy, in 1784, demonstrated that characteristic forms of calcite, $CaCO_3$, could be obtained by stacking together extremely small cleavage rhombs as the elementary unit. In the century following, mathematicians and crystallographers, among others Seeber,[2] Hessel,[3] Bravais,[4] Fedorov,[5] Barlow,[6] and Schönflies[7] utilizing the laws of symmetry and observations on the external forms of natural crystals, developed a purely geometrical theory of the manner in which space might be divided by parallelohedra to account for the observed forms, and extended it to the representation of these units by points regularly arranged in space, the points now being independent of the "building block" originally chosen. These points are arranged in a regular three-dimensional trellis work which embodies all the symmetry properties of the crystal. This network of points is known as the *space lattice*, a simple example of which is shown in Figure 1.

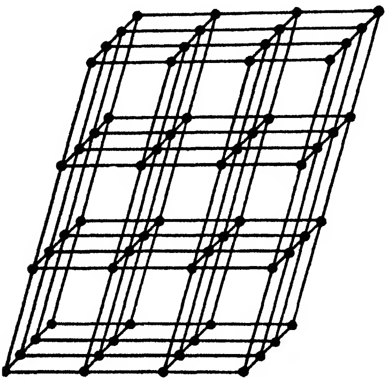

Fig. 1. A space lattice of points.[7a]

These mathematical deductions and conclusions were beautifully verified when Laue's[8] reasoning that, since x-rays were apparently of the same order of magnitude (10^{-8} to 10^{-9} cm.) as atomic dimensions, a crystal might be expected to behave toward this radiation as a three-dimensional

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[2] L. A. S. Seeber, *Ann. Physik,* **76,** 229–248, 349–372 (1824).

[3] J. F. C. Hessel, *Krystallometrie, oder Krystallonomie und Krystallographie auf eigenthümliche weise und mit zugrundelegung neuer allgemeiner lehren der reinen gestaltenkunde, so wie mit vollständiger berücksichtigung der wichtigsten arbeiten und methoden anderer krystallographen. . . Besonders abgedruckt aus Gehler's Phys(ikalisches) Wörterbuche.* Schwickert, Leipzig, 1831.

[4] A. Bravais, *J. école polytech.,* **20,** 101–276 (1851); **19,** 1–128 (1850).

[5] E. S. Fedorov, *St. Petersburg Mineralogischen Gesell.,* **21,** 1–279 (1885); **26,** 433–445 (1890); *Z. Krist.,* **21,** 679–694 (1893); **22,** 70–71 (1894).

[6] W. Barlow, *Sci. Proc. Roy. Dublin Soc.,* **8,** 527–690 (1897).

[7] A. Schönflies, *Krystallsysteme und Krystallstruktur.* Teubner, Leipzig, 1891.

[7a] R. W. G. Wyckoff, *The Structure of Crystals.* 2nd ed., Chemical Catalog Co., New York, 1931, p. 15.

[8] M. Laue, *Sitzber. kais. Akad. Wiss. München,* **1912,** 263–273.

grating, was demonstrated experimentally by Friedrich and Knipping.[9] W. L. Bragg[10] offered a satisfactory interpretation of the observed diffraction pattern which laid the foundation for methods of determining the actual arrangement of atoms in a crystal.

3. X-Ray Diffraction

X-ray diffraction methods, which were first applied to inorganic crystals such as calcite, sodium chloride, etc., and to elemental substances such as metals, sulfur, etc., were later extended to organic compounds including the long chain hydrocarbons, fatty acids, alcohols, esters, glycerides, and ketones. Most of our knowledge of the crystal structure of these substances is due to the work of de Broglie, Friedel, Müller, Malkin, Piper, Shearer, Trillat, and a few others.

Two methods have been generally used, one of which employs a single crystal and the other an oriented layer or film of the substance under examination. The single crystal technique is tedious and extremely difficult but it yields the maximum amount of information concerning the structure of a given crystal. The oriented layer or film method is relatively rapid and is particularly suited for use in determining the identity or the purity of isolated fatty acids, esters, and other aliphatic compounds, and also for determining the relative composition of a mixture of acids, esters, etc. Both methods have been applied to the investigation of the fatty acids and their derived products.

Organic crystals, such as the fatty acids, are molecular in structure rather than atomic as is the case in elemental and inorganic substances. The points on the crystal lattice are occupied by molecules and consequently the unit cells of organic crystals are large. By *unit cell* is meant the smallest element which contains a representation of the lattice, the repetition of which unit builds up the crystal; or it is the smallest parallelopiped which, when repeated, gives the macroscopic crystal.

Although Friedrich[11] examined paraffin wax as early as 1913 by the powder-photograph method, the first attempt to analyze organic compounds was not made until 1921 by W. H. Bragg. The long chain aliphatic compounds were first successfully analyzed by Müller using diffraction photographs obtained with single crystals. By means of this method Müller[12] determined the crystal structure of stearic acid, $C_{18}H_{36}O_2$ and *n*-nonacosane, $C_{29}H_{60}$. These two substances are representative of the crystal structures encountered in long chain aliphatic compounds and they exhibit those

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[9] W. Friedrich, P. Knipping, and M. Laue, *Sitzber. kais. Akad. Wiss. München*, **1912**, 303–322; *Z. Krist.*, **52**, 58–62 (1913); *Le Radium*, **10**, 47–57 (1913).

[10] W. L. Bragg, *Proc. Cambridge Phil. Soc.*, **17**, 43–57 (1912).

[11] W. Friedrich, *Physik. Z.*, **14**, 317–319 (1913).

[12] A. Müller, *Proc. Roy. Soc. London*, **A114**, 542–561 (1927); **A120**, 437–459 (1928); *Trans. Faraday Soc.*, **25**, 347–348 (1929).

TABLE 14

AXIAL DIMENSIONS IN ANGSTROM UNITS AND ANGLES OF INCLINATION OF LONG CHAIN FATTY ACIDS AND RELATED COMPOUNDS[a]

Compound	Formula	a	b	c	β	$a \cdot b$	$\frac{ab}{\sin \beta}$	$\frac{c}{\sin \beta}$	$\frac{a}{\sin \beta}$	ϵ
Lauric acid	$CH_3(CH_2)_{10}COOH$	9.76	4.98	36.9	48° 6′	48.6	36.5	27.6	7.32	0.681
Stearic acid	$CH_3(CH_2)_{16}COOH$	5.55	7.38	48.84	63° 16′	40.94	36.6	43.76	4.95	0.671
Behenolic acid	$CH_3(CH_2)_7C{:}C(CH_2)_{11}COOH$	9.55	4.69	59.10	53° 30′	44.76	36.0	47.51	7.67	0.612
Stearolic acid	$CH_3(CH_2)_7C{:}C(CH_2)_7COOH$	9.55	4.69	49.18	53° 4′	44.76	35.8	39.28	7.63	0.614
Bromostearic acid	$CH_3(CH_2)_{15}CHBrCOOH$	11.04	4.90	52.88	43° 15′	54.13	37.1	36 23	7.56	0.648
Nonacosane	$CH_3(CH_2)_{27}CH_3$	7.45	4.97	77.2	90°	37.0	37.0	77.2	7.45	0.667

[a] S. B. Hendricks, *Chem. Revs.*, 7, 431–477 (1930).

TABLE 15

AXIAL DIMENSIONS IN ANGSTROM UNITS AND ANGLES OF INCLINATION OF LONG CHAIN DICARBOXYLIC ACIDS[a]

Acid	Formula	a	b	c	β	Molecules in elementary cell	$ac \sin \beta$	Distance between end groups
Adipic	$C_6H_{10}O_4$	10.27	5.16	10.02	137° 5′	2	36.18	3.70
Pimelic	$C_7H_{12}O_4$	9.93	4.82	22.12	130° 40′	4	36.26	3.47
Suberic	$C_8H_{14}O_4$	10.12	5.06	12.58	135° 0′	2	36.24	3.73
Azelaic	$C_9H_{16}O_4$	9.72	4.83	27.14	129° 30′	4	36.22	3.47
Sebacic	$C_{10}H_{18}O_4$	10.05	4.96	15.02	133° 50′	2	35.96	3.65
Brassylic	$C_{13}H_{24}O_4$	9.63	4.82	37.95	128° 20′	4	36.41	3.81
Hexadecanedicarboxylic	$C_{18}H_{34}O_4$	9.76	4.92	25.10	131° 10′	2	36.20	3.62
Oxalic	$C_2H_2O_4$	6.46	7.79	6.02	90°	4	. . .	. . .
Succinic	$C_4H_6O_4$	5.07	8.92	5.52	91° 20′	2	. . .	. . .

[a] S. B. Hendricks, *Chem. Revs.*, 7, 431–477 (1930).

characteristics which are common to most compounds of this class, as well as the differences which are attributable to differences in chemical constitution.

As a result of the work of Müller and of others, it is now known that the unit cell of stearic acid is an elongated monoclinic prism containing four molecules. The axial dimensions of the elementary parallelopiped are a = 5.546, b = 7.381, and c = 48.84 Å. The b-axis is perpendicular to the plane ac but the c-axis is inclined so as to produce the angle β between the a- and c-axis of 63° 38′ as shown in Figure 2. The hydrocarbon, n-nonacosane, differs from stearic acid by having its c-axis perpendicular to the plane bc instead of inclined.

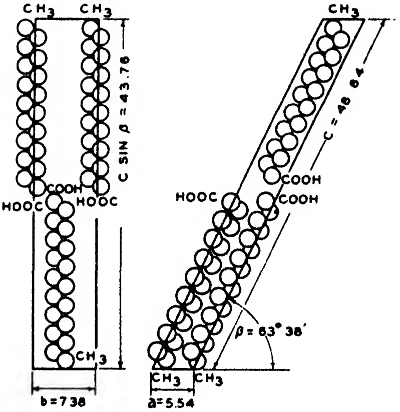

Fig. 2. Diagrammatic representation of the unit cell of a stearic acid crystal.

In Tables 14 and 15 there are recorded data which were collected by Hendricks[13] with reference to the axial dimensions, angle of inclination, etc., for lauric and stearic acids and related compounds. All of the acids in Table 14 are monoclinic prismatic and the unit cell contains four molecules, whereas the hydrocarbon, although it also contains four molecules, is orthorhombic. The dicarboxylic acids listed in Table 15 are also monoclinic. The dicarboxylic acids with an even number of carbon atoms in the chain have but *two molecules in the unit cell,* whereas those with an odd number of carbon atoms in the chain have *four molecules in the unit. cell.*

The chains of these aliphatic molecules are packed regularly with the chain axes parallel in flat sheets or layers of "heads" and "tails" of molecules forming the upper and lower sides or sheets. The direction of easiest cleavage of the crystal is parallel to the sheets or layers. When viewed from above, the upper surface of a sheet or layer of an odd-chain paraffin crystal will consist of a layer of CH_3 groups. The next layer or sheet of molecules will lie below the top layer at a distance equal to the length of the paraffin chain. In the case of stearic acid, the molecules are oriented so that the carboxyl groups are in juxtaposition, consequently a layer or sheet consists of two molecules and the distance between planes, or the thickness of the sheets, is correspondingly increased. Methyl esters behave like stearic acid

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[13] S. B. Hendricks, *Chem. Revs.*, **7**, 431–477 (1930).

in forming oriented double layers, whereas ethyl esters and symmetrical ketones form layers of single molecules.

The distance measured from an x-ray photograph of a compound is the perpendicular distance between planes of identical composition. In the case of the odd-carbon atom paraffins, the distance between planes is equal to the chain length of a single molecule, but in the case of even-carbon atom acids this distance between two like planes of groups corresponds to something less than twice the length of two hydrocarbon chains.[14] In the case of stearic acid, the distance between two like planes of groups is $2l \sin \beta$, where l equals the length of one aliphatic chain and β equals the angle between the c-axis and the plane ac as indicated in Figure 2. As shown in Table 14 the c-axis, or the distance between alternate sheets of *n*-nonacosane, is 77.2 Å. from which it can be calculated that the distance between alternate carbon atoms, *i. e.*, twice the distance between carbon atoms is 2.54 Å. compared with 1.54 Å. for the carbon-carbon distance in the diamond.

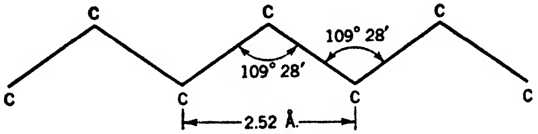

Fig. 3. Diagrammatic representation of the zigzag carbon chain of aliphatic acids.

If it is assumed that the distance between carbon atoms is 1.54 Å., as in the diamond, and that the carbon atoms are arranged in zigzag chains having an angle corresponding to the tetrahedral carbon angle, namely, 109° 28′, then it can be calculated that the distance between alternate carbon atoms should be 2.52 Å. This value agrees with 2.54 Å. obtained by experimental measurement of the c-axis of *n*-nonacosane, and this agreement between calculated and experimental values can be considered as evidence of the zigzag arrangement (Fig. 3) of the carbon atoms in long chain aliphatic compounds.

According to Malkin,[15] this zigzag arrangement of the carbon atoms accounts for the alternation of properties of long chain aliphatic compounds having odd- and even-numbered carbon atoms. In even-numbered carbon chains the end groups are parallel, while in the odd-numbered chains they lie at an angle to each other. This difference in orientation necessitates a difference in the inclination of the chains in the layers which in turn influences the physical properties of the crystals. In the case of the long chain

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[14] S. H. Piper, *J. Soc. Chem. Ind.*, **56**, 61–66T (1937).
[15] T. Malkin, *Nature*, **127**, 126–127 (1931).

aliphatic compounds of an odd or even homologous series, the addition of each pair of CH_2 groups affects the crystal lattice in only one direction, *i. e.*, it increases the cell length or *c*-axis by 4.6 Å. and it is, therefore, possible to identify any member of a homologous series of long chain aliphatic compounds by a single-crystal measurement.

The four molecules composing the unit cell of long chain aliphatic compounds such as *n*-nonacosane and stearic acid are arranged in pairs of superimposed columns, one pair of columns occupying the upper half of the cell and the other pair occupying the lower half of the cell. In Figure 2 (page 85), the second molecule of the lower half of the cell lies in the same plane and directly behind the one in evidence. This arrangement of molecules within the cell, or "packing distance" between adjacent chains is of the order of 3.7 to 4.0 Å., compared to a distance of approximately 1.54 Å. for the distance between carbon atoms in the chain.

It may be stated by way of summary, that x-ray analysis of pure single crystals of fatty acids has provided the following information concerning the crystal structure of these substances.

(1) A single cell consists of four molecules, two of which are in the upper half of the cell and two in the lower half.

(2) The pairs of molecules are oriented with their carboxyl groups in juxtaposition.

(3) The molecules are packed side by side to form sheets which are superimposed in the crystal.

(4) The cross-sectional area of two hydrocarbon chains, *i. e.*, $ab \sin \beta$ is essentially constant and is unaffected by dissimilarity of end groups or atoms.

(5) The long spacings measured by x-ray diffraction are due to the repetition of like planes populated by the chain ends.

(6) The carbon atoms in the long chains possess a zigzag arrangement with a distance of 2.52 Å. between alternate carbon atoms.

(7) The long axes of the carbon chains are inclined or tilted with respect to the parallel sheets.

(8) The inclination or tilting of the carbon chain accounts for the alternation of properties of odd- and even-numbered carbon acids.

(9) Different polymorphic modifications of the same acid contain chains with different angles of inclination or tilt.

The application of x-ray spectroscopy to fatty acids and other long chain aliphatic compounds has not only provided considerable insight into their structures, but it has also provided a means for identifying acids, esters and related compounds and for determining their purity or the composition of homologous mixtures. It has been extensively used for these purposes especially in England by Piper, Malkin, and others, but it has been almost entirely neglected in this country. The most extensive application of x-ray methods to the identification of fatty acids, alcohols, ketones, etc., isolated from natural sources has been due to Chibnall and co-workers.

The foregoing brief discussion is scarcely a satisfactory introduction to x-ray diffraction and crystallography and the interested reader is referred to such standard works as Bragg,[16] Wyckoff,[17] Clark,[18] Davey,[19] Compton and Allison,[20] and Fankuchen[20a] for a comprehensive treatment of the relationships in these fields.

Although the technique of preparing and interpreting x-ray photographs of long chain compounds for analytical purposes has been described by Piper[14,21] and in greater detail by Slagle,[22] a brief recapitulation follows to show the simplicity and utility of this tool for identifying fat products of natural origin.

Figure 4 is a schematic representation of the experimental technique used in photographing the diffraction of a beam of x-rays. A narrow beam of x-rays defined by two slits, *S*, falls on crystal *C* at grazing incidence; the diffracted rays are recorded photographically on the plate at *P*.

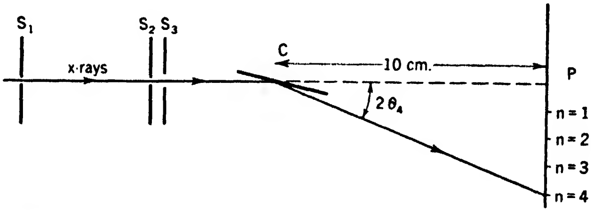

Fig. 4. Schematic representation of x-ray diffraction method.

In the application of x-ray diffraction, advantage is taken of the property of fatty acids, esters, etc., of crystallizing in thin plates. A small amount of fatty acid or ester, enough to produce a layer several tenths of a millimeter thick, is pressed on a thin piece of glass and this mount is placed in the x-ray apparatus at a distance, *CP*, of 5 to 15 cm. The mount is rocked through an angle of 10° to 20°. The exposure which is necessary for satisfactory detail at, say, 10 cm. plate-to-specimen distance, is 30 to 60 minutes. The mount is then rotated 180° and the exposure repeated.

One-half of a typical exposure with calibration lines to permit accurate determination of the plate-to-specimen distance, *CP*, is shown in Figure 5.

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[16] W. H. and W. L. Bragg, ed., *The Crystalline State.* Bell, London, 1933.

[17] R. W. G. Wyckoff, *The Structure of Crystals.* 2nd ed., Chemical Catalog Co., New York, 1931. Supplement for 1930–34 to the 2nd ed. Reinhold, New York, 1935.

[18] G. L. Clark, *Applied X-rays.* 3rd ed., McGraw-Hill, New York, 1940.

[19] W. P. Davey, *A Study of Crystal Structure and Its Applications.* McGraw-Hill, New York, 1934.

[20] A. H. Compton and S. K. Allison, *X-rays in Theory and Experiment.* 2nd ed., Van Nostrand, New York, 1935.

[20a] I. Fankuchen, in *Physical Methods of Organic Chemistry,* Vol. I. A. Weissberger, ed., Interscience, New York, 1945, Chapter 14.

[21] S. H. Piper, A. C. Chibnall, S. J. Hopkins, A. Pollard, J. A. B. Smith, and E. F. Williams, *Biochem. J.*, 25, 2072–2094 (1931).

[22] F. B. Slagle and E. Ott, *J. Am. Chem. Soc.*, 55, 4396–4418 (1933).

A thin slip of mica ($d = 20.4$ Å.) produces the lines indicated by the arrows. The approximately equally spaced lines correspond to successive orders of reflection for which $n = 1,2,3$, etc. (see Fig. 4) in the Bragg equation, $n\lambda = 2d \sin \theta$, where λ is the wave length of the radiation used, θ, the angle of incidence and d, the planar spacing giving rise to the reflection. For large spacings the first order of reflection will be close to the central image necessitating a narrow, well-defined x-ray beam, and an efficient stop; otherwise the direct radiation will fog a considerable area of the plate.

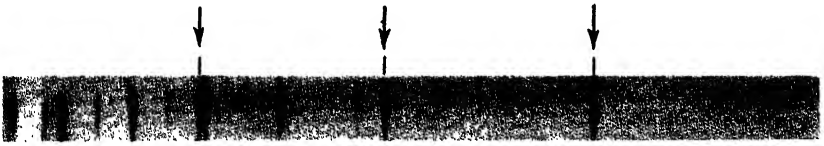

Fig. 5. Typical diffraction pattern from "pressed" layer of long chain hydrocarbon.

The information which such photographs yield is discussed in greater detail in the succeeding pages but it may be profitably summarized here. Figure 6 is a reproduction of the diffraction patterns obtained for the series of fatty acids from C_{16} to C_{21} and for the C_{23} acid, using Cu K_α radiation with a nickel filter (0.0007 in. thick), and a plate distance of 5 cm. The difference in separation of reflections clearly illustrates the "magnification" obtained. For example, the difference in the lengths of the chain in palmitic and stearic acids is 4.6×10^{-8} cm. The alternation of intensity in the first 8 or 9 orders, *i. e.*, n odd (1,3,5, etc.) strong, and n even (2,4,6, etc.)

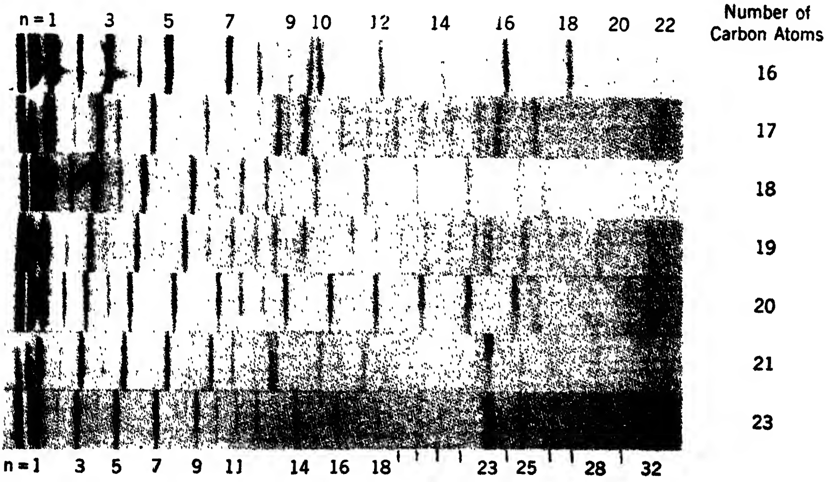

Fig. 6. Effect of chain length on diffraction pattern of *n*-aliphatic acids.

weak, indicates that these acids form layers of double (carboxyl to carboxyl) chain length. This alternation is more marked in odd-numbered than in even-numbered carbon chains.

Figure 7 shows the diffraction pattern obtained from the C_{22} acid and corresponding alcohol and the methyl and ethyl esters. The single chain layer structure of the ethyl ester is indicated by the disappearance of the odd–even order intensity alternation and an increase in the separation of lines.

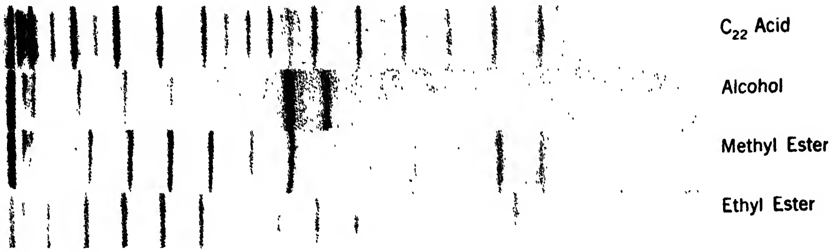

Fig. 7. X-ray patterns of C_{22} acid ana corresponding derivatives.

The presence of side chain substituents, *e. g.*, oxygen, hydroxyl, alkyl, etc., produces another intensity variation. Saville and Shearer[23] showed that in ketones, if the oxygen atom is attached at 1/*m*th of the chain length, the *m*th, 2*m*th, 3*m*th, etc., orders of reflection will tend to disappear. In double molecules the odd–even alternation complicates this effect, but the intensity distribution may still be calculated. An interesting example of this application is found in the work of Velick[24] on the structure of tuberculostearic or 10-methylstearic acid.

Fig. 8. Effect of side chain on diffraction pattern.

A further example of the effect of a side chain substituent on the intensity variation and also of the application of the x-ray method to establishing the identity of natural compounds is illustrated in Figure 8. The upper portion of this figure is a photograph of the diffraction pattern produced by *n*-nonacosane, $C_{29}H_{60}$, and the lower portion that obtained with 10-

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[23] W. B. Saville and G. Shearer, *J. Chem. Soc.*, **127,** 591–598 (1925).
[24] S. F. Velick, *J. Biol. Chem.*, **154,** 497–502 (1944).

nonacosanol, $C_{29}H_{59}OH$, both of which were isolated from the cuticle wax of apples.[25]

The photographs were made with Cu K_α radiation at a 10 cm. crystal-to-plate distance. The crystals were sufficiently well formed to allow pressing against a copper strip as a mount. The presence of twelve orders of reflection from the (0001) plane were clearly visible on the original plate from which the value of d_{hkl} for the plane of greatest spacing was calculated to be 38.0 ± 0.3 Å., (0001) of Al_2O_3, $d = 22.48$ Å., being used for reference. This value corresponds to that found by Piper and co-workers[21] for an aliphatic chain of twenty-nine carbon atoms. The diffraction patterns for the hydrocarbon and secondary alcohol are similar, except that in the case of the long spacing of the alcohol the third, sixth, and ninth orders of reflection are missing, which indicates that the hydroxyl group is attached to the carbon atom one-third the distance from the end of the chain, *i. e.*, either on the ninth or tenth carbon atom. In order to establish which of the two possible positional isomers corresponded to the natural product, both of these alcohols were prepared and other distinguishing properties compared. This comparison, which was made by Piper *et al.*,[21,26] indicated the natural substance to be 10-nonacosanol.

In addition to providing a measure of the chain length, x-ray diffraction patterns are useful in establishing the purity of compounds. The first effect of impurity in quantity is to alter the value of the spacing and to broaden the lines; also it will tend to reduce the number of high orders in a diffraction photograph. Preparations of high purity will give sharp, well-defined and high orders of reflection, and in general, reflections will be registered over the entire angle of rock. Further discussion of the x-ray criteria of purity will be found in the papers of Piper *et al.*[14,26] and Pollard *et al.*[27] Imperfect crystallization cannot necessarily be attributed to impurities; solvent and crystallization procedures should be carefully checked and standard solvents and methods which have been found to produce uniform results should be used whenever practical.

The common occurrence of polymorphic modifications in aliphatic compounds adds a degree of complication to the interpretation of the diffraction patterns. Temperature is usually the predominant factor in the formation of a given polymorphic form. The nature of the solvent and the presence of certain impurities also influence the modification which predominates and these factors must be investigated for any given case. Once the modifications are known and the proper conditions established, it is possible to construct a graph of the spacing of any homologous series as a function of the chain length (see Fig. 9, page 95). For a discussion of

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[25] K. S. Markley, S. B. Hendricks, and C. E. Sando, *J. Biol. Chem.*, **98**, 103–107 (1932).

[26] S. H. Piper, A. C. Chibnall, and E. F. Williams, *Biochem. J.*, **28**, 2175–2188 (1934).

[27] A. Pollard, A. C. Chibnall and S. H. Piper *Biochem. J.* **27** 1889–1893 (1933)

the significance and interpretation of x-ray diffraction patterns of this type with respect to long chain structure the reader is referred to the early papers of Müller[28–30] and Shearer.[31]

4. Polymorphism

In the introduction to this chapter it was pointed out that a number of the properties of fatty acids and related compounds depend on their crystalline structure. It must now be pointed out that these substances can crystallize in more than one solid or polymorphic form and therefore exhibit variations in these properties.

Polymorphic forms are solid phases of the same chemical composition, differing among themselves in crystalline form, free energy, and other physical and chemical properties, but yielding identical liquid or gaseous phases upon fusion or evaporation. This definition differentiates polymorphism from isomerism in which different solid phases or modifications have the same composition but maintain these differences in the liquid or gaseous state. In terms of the phase rule, every polymorphic form exists as a separate phase, and the number of solid phases for a single component is therefore the number of existent polymorphic forms; whereas any system of isomers is a two-component or multicomponent system, since the phases cannot have their composition expressed by less than two terms.

It should, however, be mentioned that these definitions apply to equilibrium conditions and do not exclude the possibility of a metastable crystalline form of a compound melting to form a metastable liquid phase. This phenomenon is well known in organic compounds which melt (metastably) and resolidify as their temperature is raised to that corresponding to a more stable or higher melting form. Also it should be noted that in some cases inversion may be difficult to accomplish experimentally.

Two types of polymorphism are recognized, namely, *enantiotropic* and *monotropic*. In the case of *enantiotropism* the different forms possess vapor pressure curves which approach each other with change in temperature and intersect at a point called the *transition point*, at which point the vapor pressures of the two forms are identical. At such a transition temperature and only there, are both solid phases stable, and at this point an equilibrium exists between them such that the addition of heat will effect a transformation into the form stable at higher temperatures, without, however, raising the temperature (isothermal transition) until the other form has disappeared, since the change occurs at an invariant or *triple point*. Abstrac-

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[28] A. Müller, *J. Chem. Soc.*, **123**, 2043–2047 (1923).
[29] A. Müller and G. Shearer, *J. Chem. Soc.*, **123**, 3156–3164 (1923).
[30] A. Müller and W. B. Saville, *J. Chem. Soc.*, **127**, 599–603 (1927).
[31] G. Shearer, *J. Chem. Soc.*, **123**, 3152–3156 (1923).

tion of heat brings about the reverse change, also at constant temperature. This form of polymorphism is completely reversible in the solid state.

In the second type of polymorphism, namely, *monotropism,* the vapor pressure curves of the two forms do not meet and such forms lack a transition point. Under conditions where both forms can exist, the one form is always stable, and the other metastable. The metastable form always has the higher vapor pressure, and will, therefore, change into the stable form by some process such as distillation. This form of polymorphism is not reversible in the solid state.

The occurrence of polymorphism is commonly observed in long chain aliphatic compounds, and is generally the rule rather than the exception among the long chain fatty acids, esters, glycerides, alcohols, hydrocarbons, etc. Polymorphism is particularly important in the fat and oil industry because the consistency of many products such as lard, butter, shortening, oleomargarine, etc., is dependent on the particular polymorphic modifications which are induced in these products during processing and use. The particular polymorphic form which is assumed when long chain aliphatic compounds crystallize depends on a variety of factors, particularly the purity of the compound, the solvent from which it crystallizes, the presence or absence of particular crystalline nuclei, temperature, rate of cooling, and degree of supercooling. Each polymorphic form is characterized by various properties, such as melting point, resolidification point, heat of crystallization, specific volume, x-ray spacing, etc., which distinguish it from any other form of the same compound. Certain forms are readily distinguishable by microscopic examination or even by visual inspection. Pure long chain hydrocarbons are often observed as dense, opaque crystals, or again as transparent crystals resembling clear ice, corresponding to each of two different polymorphic modifications.

Both enantiotropism (reversible polymorphism) and monotropism (irreversible polymorphism) are exhibited by the monoesters of the fatty acids, whereas the acids themselves exhibit only monotropism.

(*a*) *Polymorphism in n-Aliphatic Acid Series*

In 1939, Francis and Piper[32] published a résumé covering the results of ten years of investigation on the crystal properties of the higher normal aliphatic acids. In the course of these investigations they prepared and examined all of the even numbered fatty acids and their methyl and ethyl esters from C_{14} to C_{38} as well as the odd-numbered fatty acids from C_{17} to C_{29}.

The even-numbered acids were obtained in two polymorphic forms which were differentiated on the basis of their long spacing values and designated

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[32] F. Francis and S. H. Piper, *J. Am. Chem. Soc.*, **61**, 577–581 (1939).

as *B*- and *C*-forms, the *B*-form having the longer spacing. It was established that the aliphatic acids with an even number of carbon atoms generally crystallize from solvents in the unstable modification characterized by *B*-spacings and are irreversibly converted at temperatures about 5°C. below their melting points into the stable modification characterized by *C*-spacings. Slow crystallization of the even-numbered carbon acids from hot glacial acetic acid generally yields the polymorphic form possessing a *C*-spacing, whereas crystallization from benzene generally yields the form possessing the longer *B*-spacing. The marked differences between the x-ray spacings of the *B*- and *C*-forms of stearic acid are illustrated in Figure 8a.

Fig. 8a. X-ray pattern of the *B* (upper) and *C* (lower) forms of stearic acid.

Pure *n*-eicosanoic acid appears to be an exception to this general statement since it was found to yield a mixture of the *B*- and *C*-forms when crystallized from acetic acid. When crystallization of pure even-numbered carbon acids occurs from a melted specimen, the *C*-form is generally produced. Acids having an odd number of carbon atoms give the modification corresponding to the *B*-form, irrespective of the solvent used in crystallization.

TABLE 16

LONG SPACING VALUES OF THE EVEN-NUMBERED NORMAL ALIPHATIC ACIDS[a]

Number of carbon atoms	Crystal spacings, Å.			
	Acids		Methyl esters	Ethyl esters
	B-form	*C*-form		*B*-form
14	. . .	31 60	. . .	. . .
16	39.1	35.60	43.45	. . .
18	43.75	39.75	47.95	25.80
20	48.45	44.15	52.30	. . .
22	52 95	48.3	57.02	29.90
24	57.75	52 6	61.70	32.15
26	62.2	56.25	66 15	34.45
28	67.15	61.05	70.80	36.65
30	71.4	65.2	75.25	38.75
32	76.3	69.25	79.95	41.1
34	80.5	73.3	84.15	43.45
36	85.25	78.1	89.30	46.3
38	90.0	82.1	93.00	48.05
46	108.2	99.05	121.7(?)	57.45

[a] F. Francis and S. H. Piper, *J. Am. Chem. Soc.*, **61**, 577–581 (1939).

Table 17

LONG SPACING VALUES OF THE ODD-NUMBERED NORMAL ALIPHATIC ACIDS[a]

Number of carbon atoms	Crystal spacings, Å.		
	Acid (*B*-form)	Methyl ester	Ethyl ester
17	40.45	46.3	24.75
19	44.50	50.8	26.95
21	49.25	55.25	29.35
23	53.40	60.0	31.50
25	57.65	64.55	33.60
29	66.35	73.75	38.1

[a] F. Francis and S. H. Piper, *J. Am. Chem. Soc.*, **61**, 577–581 (1939).

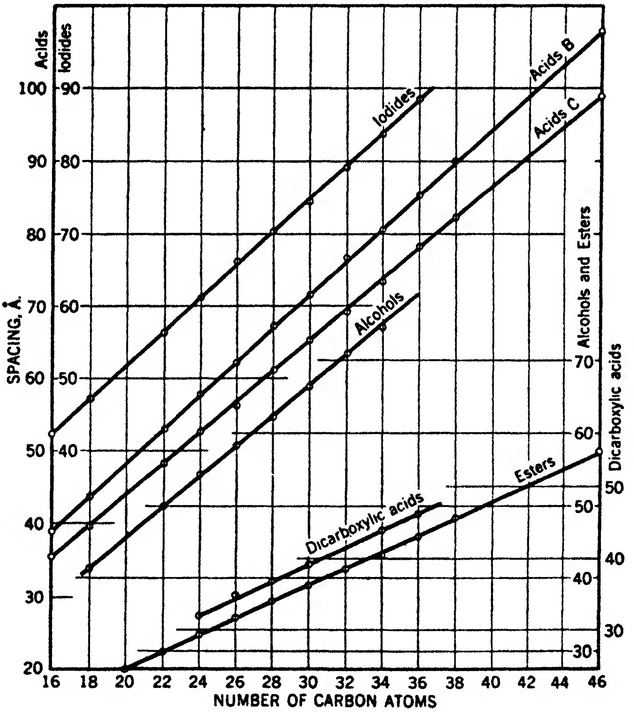

Fig. 9. Variation in spacing values as a function of the number of carbon atoms in long chain aliphatic compounds.[33]

The long spacing values for the fatty acids and the corresponding methyl and ethyl esters as determined by Francis and Piper[32] are given in Tables 16 and 17. If the values of the x-ray spacing for the same polymorphic

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[33] F. Francis, F. J. E. Collins, and S. H. Piper, *Proc. Roy. Soc. London*, **A158**, 691–718 (1937).

modifications of the various homologous series of long chain aliphatic compounds are plotted against the number of carbon atoms in the chain, a series of straight lines are obtained as shown in Figures 9 and 10 which are reproduced from the work of Francis, Collins, and Piper[33] and of Piper.[14] This linearity in the relationship between the number of carbon atoms and spacing values contrasts with the curvilinear relationship or alternation exhibited by other properties of these compounds.

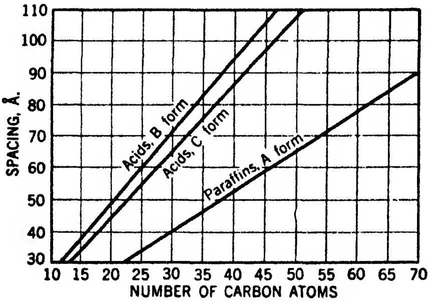

Fig. 10. Variation in spacing values as a function of the number of carbon atoms in the normal paraffins and the two forms of fatty acids.[14]

(b) *Polymorphism in the Methyl and Ethyl Esters*

The polymorphism exhibited by the long chain normal aliphatic acids is relatively uncomplicated compared to that obtaining in the corresponding methyl and ethyl esters. The pure acids exhibit only monotropy and the two forms are readily distinguishable on x-ray examination. Owing to the fact that the acids are irreversibly converted below their melting points to the stable form only one melting point is observed for each acid.

The methyl, and especially the ethyl esters, possess multiple melting points and exhibit both monotropic and enantiotropic polymorphism depending on their chain length and whether they contain an odd or an even number of carbon atoms in the chain. Melting points, rather than x-ray diffraction, have been relied upon to distinguish the polymorphic forms of the esters, and a different system of designating the various modifications has been used. In the case of the acids the two monotropic forms were designated by Piper as *B* and *C* in correspondence with the values of the long spacings, the *B*-form corresponding to the one with the higher value. The various modifications of the esters are designated α, β, γ, etc., in correspondence with the observed melting and transition points. In some cases the modifications distinguished by different melting points have been correlated with differences in x-ray spacings.

The complex nature of the polymorphic behavior of the esters of the long chain aliphatic acids has attracted many investigators whose combined efforts have resulted in considerable clarification, but no complete solution of the problem. Indeed, it is unlikely that such a solution will be forthcoming until quantitative specific heat determinations are made throughout the range of temperatures at which the various polymorphic forms can exist. The technique and applicability, as well as utility, of this type of investigation are now well established,[34-37] and have been applied by Garner *et al.*[38-44] to the determination of the heats of crystallization and specific heats of the fatty acids and the methyl and ethyl esters. However, owing to the limited range, generally 20° to 70°C., over which the specific heat measurements were made, this work is in need of repetition and extension to much lower temperatures.

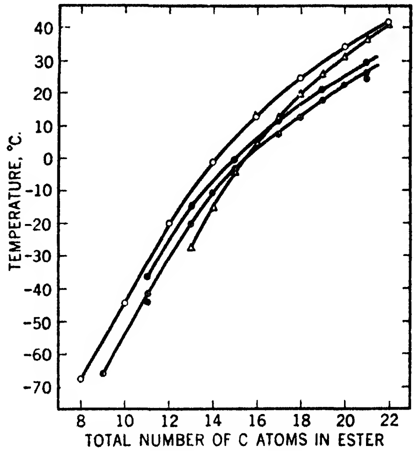

Fig. 11. Freezing and melting point curves of the ethyl esters of the saturated fatty acids:[46] ○, m. p. curve of the β-form of even esters; ●, m. p. curve of the β-form of odd esters; △, f. p. curve of the α-form of the odd and even esters; ⊗, f. p. curve of the γ-form of the odd and even esters.

Francis, Piper, and Malkin[45] observed an unexpected increase in the long spacings of certain equimolecular mixtures of ethyl esters which subsequently led them, as well as others, to investigate the cause of this phenomenon, and thereby to the discovery that ethyl esters exist in two crystalline modifications, one of which is stable over a limited range of temperatures near the melting point. The large spacings were found to be given by the form normally stable only at high temperatures. In the case of mixtures such as were examined by Francis, Piper, and Malkin, the change from the metastable form into the normal stable modification is greatly retarded, consequently the fused mixture solidifies (crystallizes) in the metastable form which is maintained over a considerable period. Since Francis *et al.* prepared their mixed esters by fusion, the binary mixtures were obtained

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[34] A. E. Bailey, S. S. Todd, W. S. Singleton, and G. D. Oliver, *Oil & Soap*, **21**, 293–297 (1944).

[35] G. D. Oliver, W. S. Singleton, S. S. Todd, and A. E. Bailey, *Oil & Soap*, **21**, 297–300 (1944).

[36] A. E. Bailey and G. D. Oliver, *Oil & Soap*, **21**, 300–302 (1944).

[37] A. E. Bailey, M. E. Jefferson, F. B. Kreeger, and S. T. Bauer, *Oil & Soap*, **22**, 10–13 (1945).

[38] W. E. Garner and F. C. Randall, *J. Chem. Soc.*, **125**, 881–896 (1924).

[39] W. E. Garner, F. C. Madden, and J. E. Rushbrooke, *J. Chem. Soc.*, **1926**, 2491–2502.

[40] W. E. Garner and J. E. Rushbrooke, *J. Chem. Soc.*, **1927**, 1351–1358.

[41] W. E. Garner and A. M. King, *J. Chem. Soc.*, **1929**, 1849–1861

[42] A. M. King and W. E. Garner, *J. Chem. Soc.*, **1931**, 578–580.

[43] A. M. King and W. E. Garner, *J. Chem. Soc.*, **1934**, 1449–1456.

[44] A. M. King and W. E. Garner, *J. Chem. Soc.*, **1936**, 1368–1372, 1372–1376.

[45] F. Francis, S. H. Piper, and T. Malkin, *Proc. Roy. Soc. London*, **A128**, 214–252 (1930).

[46] S. A. Mumford and J. W. C. Phillips, *Rec. trav. chim.*, **52**, 176–180, 181–194 (1933).

in the metastable modification which exhibited the enhanced spacing values rather than the expected normal value.

Mumford and Phillips[46] investigated the polymorphic behavior of a large number of pure ethyl esters and their binary mixtures. The thermal data assembled by these authors for the pure esters are reproduced in Table 18 and graphically in Figure 11. Inspection of the curves in Figure 11 indicates that throughout the homologous series, the α-freezing points lie on a smooth curve but the β-melting points alternate, the β-melting point curve of the even esters being higher than and distinct from that of the odd. On examination of the α-freezing point and β-melting point curves it is seen that just as the α-melting point curve intersects the β-melting point curve of the odd esters at, or about the C_{17} member of the series, so in the other direction it will intersect the β-melting point curve of the even esters above C_{22}, *i. e.*, the higher even members, like the odd, will exhibit enantiotropy.

Malkin[47] found that although the α to β transformation of the odd esters

TABLE 18

FREEZING AND MELTING POINTS OF POLYMORPHIC FORMS OF ETHYL ESTERS OF THE SATURATED ACIDS[a]

Total number of carbon atoms	Ester	Freezing point of α-form	Melting point of β-form: Even esters	Melting point of β-form: Odd esters	Freezing point of γ (C_1)-form
8	Hexoate	. . .	(f. p.) −67.5	. . .	. . .
9	Heptoate	. . .	. . .	. . .	−66.1
10	Octoate	. . .	(f. p.) −44.75	. . .	. . .
	. . .	. . .	(f. p.) −43.1	. . .	. . .
11	Nonoate	. . .	. . .	*ca.* −35	*ca.* −42
	. . .	. . .	. . .	(f. p.) −36.7	. . .
	. . .	. . .	. . .	. . .	−44.45
12	Decoate	. . .	−20.3	. . .	. . .
		. . .	(f. p.) −19.9	. . .	. . .
13	Undecoate	−27.8[b]	. . .	−15.0	−20.5
14	Laurate	−15.5[b]	− 1.8	. . .	*ca.* −11[b]
		. . .	. . .	. . .	? −10.65
15	Tridecoate	− 4.8[b]	. . .	− 0.8	*ca.* −3.5
16	Myristate	4.45[b]	12.3	. . .	. . .
17	Pentadecoate	11.95	. . .	*ca.* 11.5[b]	*ca.* 7[b]
18	Palmitate	19.3	24.1	. . .	*ca.* 12[b]
		19.4	24.18	. . .	. . .
19	Margarate	25.25	. . .	20.6	17.2
20	Stearate	30.8	33.5	. . .	*ca.* 22[b]
		30.9	33.4	. . .	. . .
21	Nonadecoate	35.7	. . .	28.9	25.6
		35.5	. . .	. . .	24.5
22	Eicosoate	40.5	41.0	. . .	. . .

[a] S. A. Mumford and J. W. C. Phillips, *Rec. trav. chim.*, **52**, 181–194 (1933).
[b] Indicates extrapolated values.

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[47] T. Malkin, *J. Chem. Soc.*, **1931**, 2796–2805.

was definitely enantiotropic, reversibility did not occur in the case of the even esters, but as pointed out by Mumford and Phillips,[46] the β-melting points would lie very close to the α-freezing points and reversibility might therefore be difficult to detect. The freezing points of the γ(C_1)-modifications of the esters appear to fall on a curve which is approximately parallel to, but lower than, the β-melting point curve of the odd esters, and intersecting the α-freezing point curve at or near the C_{15} member of the series.

In most cases the particular polymorphic form which is obtained with pure esters can be recognized and identified, and the α- to β-, or β- to α-transitions can be readily determined. However, it has been observed that, when ethyl undecanoate cools, it forms large, hard, semitransparent crystals having a freezing point of −20.5°C. and a melting point of −19.5°, but, on rubbing, these crystals change exothermally into a softer, more granular and opaque form melting at −15°C. Neither of these forms is the transparent α-modification. Ethyl pelargonate, the next lower odd ester, also exhibits two high melting crystalline forms, the large hard variety, freezing point about −42°C. changing very readily into the softer modification, freezing point about −35.5°C. Mumford and Phillips[46] concluded that of these two forms the higher melting, stable form is the β-modification and the lower melting, unstable form is a third or γ-modification.

Further evidence of the existence of this third modification was obtained by Mumford and Phillips during an examination of the cooling curves of the α-forms of ethyl margarate and mixtures with its homologs. These curves exhibited two arrests which were designated, respectively, C_1 and C_2. The second of these arrests apparently corresponded to the transition to the β-modification, whereas, the first arrest corresponded to the transition from the α-form to an unknown form. It was concluded by these authors that the α- to β-transition of ethyl margarate is complex and occurs through an intermediate C_1-modification. The latter modification persists throughout a series of solid solutions in many of the mixtures in which ethyl margarate is a component. For example, mixtures of ethyl palmitate and ethyl margarate exhibit this C_1-form throughout the series of binary mixtures containing up to 70 mole per cent of ethyl margarate. In the case of ethyl margarate and ethyl nonadecanoate, it persists throughout the whole range of compositions. In the case of binary mixtures containing ethyl margarate as one component, it is possible by extrapolation to determine the freezing point of the C_1-modification of the other member of the binary mixture. These extrapolated values are indicated in Table 18 by superscript *b*. This C_1-modification which appears in the case of binary mixtures containing ethyl margarate would seem to correspond to the unstable γ-form which is observed in the case of pure ethyl undecanoate and ethyl pelargonate. Its persistence, at least in metastable form, results from the addition of the second component to produce the binary mixture.

TABLE 19

MELTING POINTS OF ACIDS OF EVEN CARBON CONTENT AND THEIR ESTERS[a]

Carbon content of acid	Acids			Methyl esters				Ethyl esters				
				β			γ	α			β	γ
	S. p.	R. p.	M. p.	S. p.	R. p.	M. p.	M. p.	S. p.	R. p.	M. p.	S. p.	M. p.
12	43.75	...	....	...	..	...	...	−15.5	...	...	−1.7	...
14	53.65	53.9	54.4	18.37	..	18.8	...	4.45	...	...	11.0	...
16	62.60	62.4	62.9	29.20	..	...	30.55	19.4	...	...	23.20	24.4
18	69.39	69.2	69.6	37.85	37.7	38.7	39.1	31.05	30.95	31.4	...	33.9
20	....	74.9	75.35	45.41	45.2	45.8	46.6	40.36	40.15	40.54	...	41.65
22	79.70	79.6	79.95	51.84	51.7	52.7	53.3	47.80	47.7	48.25	...	48.7
24	83.90	83.8	84.15	57.42	57.5	57.8	58.4	54.20	54.2	54.35	...	54.8
26	87.41	87.2	87.7	62.50	62.5	62.9	63.45	59.60	59.5	59.95	...	60.2
28	....	90.4	90.9	...	66.4	66.7	67.5	64.22	64.3	64.6	...	...
30	....	93.2	93.6	70.3	70.4	70.8	71.7	68.30	68.35	68.45	...	...
32	....	95.5	96.0	...	73.6	74.1	74.9	(72.0)	72.0	72.5	...	...
34	98.00	97.8	98.2	77.0	76.9	77.2	77.9	75.30	75.2	75.4	...	...
36	(99.7)	99.4	99.9	...	79.9	80.3	80.9	78.31	78.3	78.6	...	...
38	(101.5)	...	101.6	...	82.3	82.7	83.1	(80.8)	80.3	80.55	...	...
46	....	106.5	106.85	...	91.0	91.4	91.7	90.22	90.3	90.5	...	...

[a] F. Francis and S. H. Piper, *J. Am. Chem. Soc.*, **61**, 577–581 (1939).

Mumford and Phillips concluded from their investigations that ethyl esters of the fatty acid series from C_{12} upwards exhibit three distinct kinds of alternation of polymorphic type as follows:

(*1*) Alternating *monotropy*, with esters up to C_{16}; the α-forms of both odd and even numbers being metastable and unobtainable except in mixtures.

(*2*) Alternating *monotropy* and *enantiotropy* with esters from C_{16} to C_{22}; the α-forms of the odd members being stable near the melting point, and those of the even members metastable but unobtainable.

(*3*) Alternating *enantiotropy* with esters above C_{22}; the α-forms of both odd and even members being stable in the vicinity of the melting point.

Evidence based on the observations relative to the existence of a $\gamma(C_1)$-modification of the ethyl esters of the odd-numbered acids from C_9 to C_{21} indicates that these esters may be trimorphic.

Smith[48] has summarized the available information up to 1939 relative to the polymorphism of the ethyl esters as follows: At least three kinds of polymorphism are observed. For the esters up to ethyl myristate, the opaque β-forms of both even and odd members are stable and the transparent α-forms are metastable (*monotropic polymorphism*); from ethyl myristate to ethyl eicosanoate, α-forms of the odd members are stable near the melting point and change enantiotropically to the β-forms on cooling; α-forms of the even members are metastable (except in mixtures) and change monotropically to the β-forms; above ethyl eicosanoate, the α-forms of both odd and even members are stable near the melting point (*monotropic polymorphism*).

The x-ray spacings of the methyl esters of the fatty acids from C_{16} to C_{46} are given in Tables 16 and 17. The corresponding melting points as reported by Francis and Piper[32] are reproduced in Tables 19 and 20. Inspection of the data in Table 19 indicates that the melting points of the γ-modifications of the methyl esters of the C_{16} to C_{36} series of acids are approximately 1.0 to 1.5°C. above their resolidification points. If the melting point is determined for that modification (β-form) which separates on crystallization from the melt and before the temperature has fallen more than 1°C., it is found that in most cases a lower melting point is obtained which is about 0.5°C. above the resolidification point. The two forms of methyl esters can, therefore, be distinguished by determining the melting point, solidification point, and remelting point. The lower of the two values corresponds to the β-form and the higher to the γ-form. The methyl esters of the odd-numbered acids are classified in a similar manner.

The resolidification of the liquid methyl esters is very slow and in the lower members of the series it cannot be observed in a capillary tube with

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[48] J. C. Smith, *Ann. Repts. Progress Chem.*, **35,** 257 (1939).

TABLE 20

MELTING POINTS OF ACIDS WITH ODD CARBON CONTENT AND THEIR ESTERS[a]

Carbon content of acid	Acids			Methyl esters				Ethyl esters		
				β			γ	S. p. from graph esters even acids	R. p.	M. p.
	S. p.	R. p.	M. p.	S. p.	R. p.	M. p.	M. p.			
17	60.81	60.85	61.3	...	28.1	28.6	29.7	25.4 (25.15)	25.4	25.7
19	68.8	68.2	68.65	38.64	38.4	38.9	39.3	35.95 (36.05)	35.8	36.1
21	73.5	73.7	74.3	...	46.6	47.2	47.6	44.18	43.95	44.5
23	78.69	78.4	79.1	...	53.5	54.0	54.4	51.05	51.1	51.4
25	82.91	82.7	83.5	...	59.2	59.5	60.0	56.9	56.85	57.15
29	...	89.7	90.3	...	68.3	68.8	..	66.35	66.3	66.6

[a] F. Francis and S. H. Piper, *J. Am. Chem. Soc.*, 61, 577–581 (1939).

any degree of certainty. The velocity of the change, however, increases as the series is ascended, but it never appears to be as great as that of the corresponding ethyl esters.

In addition to the two melting points corresponding to the β- and γ-modifications that can be observed in the methyl esters, there is another phenomenon which can be observed if the molten ester is allowed to cool a few degrees below its resolidification point and the temperature then raised slowly. If, under these conditions, the solid esters are illuminated by transmitted light they appear to be translucent, and certain of the methyl esters are seen to become opaque about 0.4° to 0.7°C. below the melting point of the γ-modification. It has been assumed that this transformation may be due to the formation of liquid crystals.[32,49]

Malkin[49] determined the long spacings of the α- and β-forms of the methyl, ethyl, propyl, butyl, and amyl esters of palmitic, margaric, and stearic acids which are given in Table 21. According to Malkin the spac-

TABLE 21

LONG SPACINGS OF α- AND β-FORMS OF VARIOUS ESTERS OF PALMITIC, MARGARIC, AND STEARIC ACIDS

Ester	Palmitate		Margarate		Stearate	
	α	β	α	β	α	β
Methyl	...	21.6		23.3		23.9
		diff. = 1.4		diff. = 1.3		diff. = 1.6
Ethyl	...	23.0	27.1	24.6	28.6	25.5
		diff. = 0.8		diff. = 0.9		diff. = 0.7
Propyl	27.6	23.8	28.6	25.5	30.1	26.2
						diff. = 1.5
Butyl	28.8	...	30.1	...	31.4	27.7
						diff. = 1.1
Amyl	...	...	31.45	...		28.8

[49] T. Malkin, *Trans. Faraday Soc.*, 29, 977–982 (1933).

ings of the α-forms correspond to planes separated by vertical zigzag chains, whereas those of the shorter β-forms correspond to tilted chains. The α-forms were found to give only one side spacing of 4.2 Å., while the β-forms give the two side spacings usually associated with long chain compounds, namely, 3.7 and 4.2 Å. The esters therefore appear to behave in a manner similar to paraffins[60] and the alcohols,[61] where the absence of the shorter side spacing in the α-form is attributed to rotation of the molecule about the chain axis.

5. Thermal Properties and Crystal State

As previously mentioned, each crystalline phase or polymorphic modification of the fatty acids and esters is characterized by a number of specific thermal properties. Any change in the physical state of these substances must necessarily be accompanied by a corresponding change in those properties, and it is evident, therefore, that their quantitative determinations should provide additional information concerning the existence of specific phases and the transitions from one phase to another. The thermal properties of the fatty acids and esters which are readily amenable to quantitative measurement are specific heat and heat of transition from one phase to another, including transition from one polymorphic form to another in the solid state, and the transition from solid to liquid or liquid to solid. The heat of transition from solid to liquid is more generally referred to as the heat of fusion and that from liquid to solid as the heat of crystallization.

The heat of crystallization or fusion and the heat of transition from one crystalline form to another are latent heats and occur at constant temperatures. They are entirely analogous to the latent heat of vaporization. The latent heat of any transformation is the amount of heat absorbed or evolved per unit of quantity of product transformed in the direction indicated, or in other words, it may be positive or negative. By specific heat is meant the quantity of heat necessary to raise the temperature of one gram of a substance through one degree centigrade at any temperature.

(a) *Specific Heat and Heat of Transition*

Our present knowledge of the specific heats, heats of crystallization, and heats of transition of the long chain fatty acids, esters, and related compounds is due primarily to the work of Garner and co-workers extending over a period of nearly twenty years. During this period these workers made many quantitative measurements of the thermal properties of these compounds and applied the results to the elucidation of their crystal struc-

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[60] A. Müller, *Proc. Roy. Soc. London*, **A127**, 417–430 (1930); **A138**, 514–530 (1932)
[61] J. D. Bernal, *Z. Krist.*, **83**, 153–155 (1932).

TABLE 22

HEATS OF CRYSTALLIZATION AND TRANSITION AND SPECIFIC HEATS OF EVEN-NUMBERED CARBON ACIDS FROM ACETIC TO CEROTIC

Acid	Setting point, ° K.	Q, heat of crystn., kg.-cal./mole	ΔQ per 2 CH$_2$, kg.-cal.	Specific heat of solid, $\sigma_s(t_1^0 - t_2^0)$, cal./g.	Specific heat of liquid, $\sigma_l(t_1^0 - t_2^0)$, cal./g.	Mean specific heat of liquid (m.p. to 30° above), cal./g.
Acetic	289.5	2.77	....	....	....	..
Butyric	270	2.64	−0.13	....	....	..
Caproic	271.5	3.60	0.96	0.4495 (−10 to −33)	0.5105 (23–0)	0.51
Caprylic	289.5	5.11	1.51	0.4650 (12–0)	0.5050 (46–18)	0.51
Capric	304.5	6.69	1.58	0.5009 (24–0)	0.4989 (65–35)	0.50
Lauric	316.8	8.75	2.06	0.5116 (39–19)	0.5146 (78–48)	0.51
Myristic	326.7	10.74	1.99	0.5209 (43–24)	0.5157 (84–23)	0.52
Palmitic	335.8	12.98	2.24	0.4920 (53–22)	0.5416 (68–22)	0.54
Stearic	343.7	...	1.98	.... 0.4597 (56–20)	....	..
Arachidic	349.5	16.95	1.98	0.4772 (66–20)	0.5663 (100–22)	0.57
Behenic	353.2	18.75	....	0.4854 (71–18)	0.5556 (109–80)	0.56
Lignoceric	356.1	21.10	....	0.4656 (78–18)	0.5855 (109–87)	0.59
Cerotic	360.4	...	....	0.4789 (70–17)	0.5712 (109–79)	0.57

TABLE 23

HEATS OF CRYSTALLIZATION AND TRANSITION AND SPECIFIC HEATS OF ODD-NUMBERED CARBON ACIDS FROM FORMIC TO PENTACOSANOIC

Acid	Setting point, ° K.	Q, heat of crystn., kg.-cal./mole	ΔQ per 2 CH$_2$, kg.-cal.	Heat of transition $\alpha \to \beta$, kg.-cal./mole	Specific heat of solid $\sigma(t_1^0 - t_2^0)$, cal./g.	Specific heat of liquid $\sigma(t_1^0 - t_2^0)$, cal./g.	Mean specific heat of liquid (m.p. to 30° above), cal./g.
Formic	281.5	2.52	....	..	....	....	..
Propionic	251	2.26	−0.26	..	....	....	..
Valeric	253	...	....	..	....	....	..
Heptanoic	261.8	3.58	....	..	0.4752 (−15 to −35)	0.4928 (30–0)	0.49
Pelargonic	285.5	4.85	1.27	1.37	0.4220 (24–0)α 0.3653β	0.5044 (44–18)	0.50
Undecanoic	301.5	5.99	1.14	1.84	0.5323 (+1 to −9)α 0.4069 (15–1)β	0.5190 (67–36)	0.52
Tridecanoic	314.7	8.02	2.03	0.94	0.4307α 0.4322β	0.5456	0.55
Pentadecanoic	325.5	10.30	2.28	1.20	0.4668α 0.4603β	0.5316	0.53
Margaric	334.5	12.22	....	1.55	0.4236–0.5063 (53–18)β	0.5604 (99–64)	..
Tricosanoic	350.4	17.60	....	1.62	0.4166–0.5603 (71–18)β	0.5762 (108–87)	..
Pentacosanoic	353.6	20.00	....	1.47	0.4146–0.5351 (72–20)β	0.5769 (110–88)	..

tures. In 1926 Garner, Madden, and Rushbrooke[39] summarized their work and that of others on the thermal properties of the normal aliphatic acids.

These data included all the even acids from acetic to arachidic and the odd acids from formic to pentadecanoic. In 1929 Garner and King[41] extended the series of even acids to *n*-hexacosanoic and of the odd acids to *n*-pentacosanoic.

These data, which include the setting point, heat of crystallization, heat of transition from α- to β-form in the solid state, and the specific heats of the solid and liquid forms of the normal fatty acids, are reproduced in Tables 22 and 23. Corresponding thermal data for the methyl and ethyl esters of the series lauric to triacontanoic acid were summarized by King and Garner[43,44] in 1934 and 1936 and extended by Francis, King, and Willis[52] in 1937 to include ethyl tetratriacontanoate. These data are reproduced in Table 24.

According to Garner and co-workers, the data in Table 22 for the even acids higher than C_{10} can be expressed in two equations as follows:

$$Q = 1.03\,n - 3.61 \tag{1}$$

$$Q/T = 0.002652\,n - 0.0043 \tag{2}$$

which can be combined to give the following expression for the setting point:

$$T = (1.03\,n - 3.61)/(0.002652\,n - 0.0043) \tag{3}$$

Similarly, the data in Table 23 for the odd acids in the α-form from C_{11} to C_{25} can be expressed as in the form:

$$Q = 0.9651\,n - 4.49 \tag{4}$$

$$Q/T = 0.002505\,n - 0.0071 \tag{5}$$

which, when combined, give the following expression for the setting point:

$$T = (0.9651\,n - 4.49)/(0.002505\,n - 0.0071) \tag{6}$$

Graphical treatment of the data in Table 24 gave the expression:

$$T = (1.083\,n - 4.15)/(0.002839\,n - 0.00185) \tag{7}$$

for the melting points of the even methyl esters, and the expression:

$$T = (0.8389\,n - 5.58)/(0.00224\,n - 0.00904) \tag{8}$$

for the melting points of the odd ethyl esters.

When the data for the melting points of the ethyl esters of the even-numbered carbon acids are plotted against the number of carbon atoms in the acid chain (Fig. 12), two curves are obtained which intersect in the

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[52] F. Francis, A. M. King, and J. A. V. Willis, *J. Chem. Soc.*, **1937**, 999–1004.

TABLE 24

HEATS OF CRYSTALLIZATION AND TRANSITION AND SPECIFIC HEATS OF ETHYL AND METHYL ESTERS OF NORMAL ALIPHATIC ACIDS

Corresponding acid	Setting point			Heat of crystn., Q, kg.-cal./mole		Heat of transition, α–β at s.p., cal./mole	Specific heats, cal./g.		
	Calc. °K.	Obs.					Solid		Liquid
		°K.	°C.	α-form	β-form		α-form	β-form	
Ethyl Esters of Even-Numbered Carbon Acids									
Lauric	270.1β	271.3β	−1.70β	....	9.745	....	..	0.34	0.48
Myristic	284.1β	284.0β	11.0β	....	11.17	....	..	0.50	0.50
Palmitic	295.9β	296.2β	23.2β	....	12.68	....	..	0.39	..
	292.3α	292.3α	.....	....	....	....	..	..	0.50
Stearic	305.9β	306.4β	.....	....	14.31	....	..	0.45	..
	304.2α	304.1α	31.05α	9.436	....	4.874	0.92	..	0.50
Arachidic	313.4α	313.4α	40.36α	10.93	16.39	5.46	0.72	0.44	0.53
Behenic	321.0α	320.8α	47.8α	12.42	18.63	6.21	0.65	0.44	0.55
n-Tetracosanoic	327.1α	327.2α	54.2α	13.82	20.57	6.75	0.72	0.42	0.53
n-Hexacosanoic	332.4α	332.6α	59.6α	15.22	22.66	7.44	0.73	0.43	0.53
n-Triacontanoic	341.0α	341.3α	68.3α	17.93	25.98	8.05	0.79	0.45	0.55
n-Tetratriacontanoic	....	348.2α	75.19α	19.75	30.48	10.73	1.24	0.43–0.58	0.55
Ethyl Esters of Odd-Numbered Carbon Acids[a]									
				V-form	T-form	V to T	V-form	T-form	
n-Pentadecanoic	285.1	285	.....	....	....	....	..	..	..
Margaric	299.0	292.2	25.15	8.66	12.62	3.96	0.76	0.44	0.50
n-Nonadecanoic	309.1	309.1	36.05	10.32	14.74	4.42	0.64	0.46	0.50

TABLE 24 (*Continued*)

Methyl Esters of Even-Numbered Carbon Acids									
Myristic	290.5	291.4	18.35	....	10.63	....	..	0.48	0.53
Palmitic	302.5	302.1	29.05	....	13.23	....	..	0.44	0.52
Stearic	311.4	310.8	37.78	....	15.40	....	..	0.43	0.51
n-Eicosanoic	318.7	318.4	45.41	....	17.62	....	..	0.42	0.52
Behenic	324.5	324.8	51.84	....	19.68	....	..	0.42	0.54
Methyl Esters of Odd-Numbered Carbon Acids									
n-Nonadecanoic	....	311.6	38.64	10.24	14.87	4.63	0.62	0.45	0.51

[a] T = tilted chain in unit cell; V = vertical chain in unit cell.

TABLE 25

AVERAGE THERMAL VALUES FOR INDIVIDUAL MEMBERS OF SEVERAL HOMOLOGOUS SERIES OF ALIPHATIC COMPOUNDS[a]

	Series[b]	Heat of crystn. per CH_2, kg.-cal.	Entropy per CH_2 group, $\times 10^6$	Av. sp. heat of solid forms, cal./g.	Av. sp. heat of liquid for range 30° above m.p. cal./g.	Area of hydrocarbon chain, $Å^2$	Convergence temp. (calc.) °K.	Heat of crystn. of terminal groups, kg.-cal.
Tilted forms	Even acids	1.03	2652	0.48	0.53	18.3	388.5	−1.55
	Odd acids	0.97	2505	0.44	0.54	...	385.2	−2.56
	Even methyl esters	1.08	2839	0.43	0.52	...	381.5	−1.98
	(T) Hydrocarbons	1.0	...	0.44	0.57	18.3	...	....
	(T) Ethyl esters	1.04	...	0.43	0.52	18.5	...	....
Vertical forms	(V) Odd ethyl esters	0.84	2240	0.63	0.50	...	...	−3.90
	(V) Even ethyl esters	0.71	1796	0.71	0.52	19.6	394.2	−1.86
	(V) Even hydrocarbons	0.61	1491	1.05	0.57	19.9	408.0	−0.53

[a] A. M. King and W. E. Garner, *J. Chem. Soc.*, 1936, 1368–1372, 1372–1376.
[b] T and V have the same significance as in Table 24.

vicinity of $n = 20$. The two curves (A, Fig. 12) represent the melting points of two different crystalline forms (α and β) of the esters. The β-forms are stable at the melting point for members below $n = 20$ while the α-forms are stable above this value. The equations for these curves are (up to $n = 20$):

$$(9) \qquad T_m = (0.7630\,n + 0.63)/(0.00179\,n + 0.01475)$$

and (above $n = 20$):

$$(10) \qquad T_m = (0.7081\,n - 3.28)/(0.001796\,n - 0.0012).$$

The equations for T make it possible to predict a maximum or convergence temperature for the melting points of each homologous series. In the case of the even-numbered fatty acids this convergence temperature is 115.5°C. or 388.5°K. (see Table 25, column 7). As a matter of fact, in all of the homologous series of long chain aliphatic compounds there is a convergence temperature at about 120°C. owing to the fact that the methylene chain ultimately becomes the dominant factor in determining the melting point.

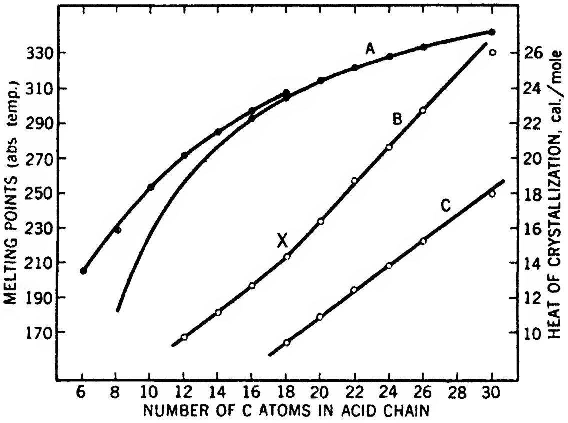

Fig. 12. Melting points and heats of crystallization as a function of the length of the hydrocarbon chain of ethyl esters of the n-fatty acids according to King and Garner[43] (A) melting point curves of α- (●) and β- (⊗) forms of ethyl esters; (B) heats of crystallization of the β- or tilted forms; (C) heats of crystallization at the setting point of the α- or vertical forms; (X) point of inflection in slope of heat of crystallization of β-forms.

In contrast to the convergence of melting points of the odd- and even-numbered carbon acids with increase in chain length, the curves for the heats of crystallization diverge up to the tenth member and from there on are parallel. The heats of crystallization are linear above decanoic acid as indicated by equations (*1*) and (*4*).

The mean specific heats of the acids in the liquid state over a temperature range of approximately 30°C. above the melting point show no evidence of alternation but increase slightly as the series is ascended. The average mean specific heat of the stable form of the solid acids at the melting point is 0.46 cal. per g. which is somewhat lower than the mean specific heat for the same acids in the liquid state.

The data given in Tables 22, 23, and 24, as well as other data of Garner and co-workers which are not reproduced here, were expressed by King and Garner[44] as a series of constants or average values for the individual members of several homologous series of aliphatic compounds as indicated in Table 25. The lower members of the homologous series show anomalies in the melting points, heats of crystallization, and related properties, but in the case of carbon chains of ten or more atoms these anomalies disappear. For example, considering the odd and even homologous series above C_{10}, it is observed that the molar heat of crystallization increases linearly with the number of methylene groups in the hydrocarbon chain and that the increment in the heat of crystallization (Table 25, column 2), due to the introduction of a methylene group into the chain, becomes constant for the higher members of any one series; also, that the increment in the entropy of crystallization (Table 25, column 3) per methylene group is constant for any one homologous series.

An examination of the increments per methylene group for different series shows that the long chain compounds may be divided into two distinct classes. In one group are those compounds for which the increments in the heats of crystallization and the entropies of crystallization are the same within the limits of experimental error. This group possesses specific heats for the solid in equilibrium with the melt which are normal in the sense that the values are lower than those for the liquid states (Table 25, column 4 and 5). X-ray analyses of the solids in this group have shown that the axes of the hydrocarbon chains are tilted with respect to the planes containing the terminal groups.

In the second group are found the hydrocarbons and ethyl esters whose increments in the heats and entropies of crystallization are lower, and whose specific heats, cross-sectional areas, and coefficients of expansion are higher than those of the first group. Also, the values vary from one series to another. X-ray analysis shows that in this group the chains are vertical with respect to the planes containing the terminal groups.

Garner and co-workers[43,44] have applied their thermal data to the explanation of the baffling subject of alternation in the melting points between the even and odd members of the various homologous series of long chain aliphatic compounds. Their thermal data, as well as that of other workers with respect to other physical properties of these compounds, indicate that alternation is due essentially to differences in crystalline structure. For a more detailed discussion of the theory of melting of the fatty acids and esters the reader should consult the above-mentioned publications of Garner *et al.* and the review of the subject by J. C. Smith.[48]

(*b*) *Melting and Freezing Points*

The foregoing discussion of polymorphism in relation to the thermal properties of fatty acids and esters has included many references to melting and resolidification phenomena, primarily as characterizing criteria of the crystal states of these compounds. Aside from their significance in relation to polymorphism, melting and freezing points are useful in establishing the identity and relative purity of naturally occurring acids and their derivatives.

The melting point and freezing point are defined as the temperature at which solid crystals of a substance are in equilibrium with the liquid phase under its own vapor. If this equilibrium condition is approached by cooling the liquid, the temperature is referred to as the freezing point, and if approached by heating the solid, it is referred to as the melting point.

Most crystalline compounds, if chemically and physically homogeneous and thermochemically stable up to a temperature at which they will exist as a liquid, possess a sharp and invariant melting point. Whether this melting point is observed or not in the case of any particular compound, such as a fatty acid or ester, depends on many factors, among which are its purity, thermochemical stability, and the method of determining the melting point.

Chemical homogeneity alone does not necessarily insure that the compound will possess an invariant melting point since the melting point can be affected by the presence of another polymorphic form of the same molecular species. For example, the presence of a second polymorphic form, usually metastable above its inversion temperature, may result in the observation of a melting range anywhere between the melting point of the lower form and that of the higher melting form.

In the case of a chemically and physically homogeneous compound, the principal factor affecting the observed value of the melting point is the method and apparatus used in its determination. The melting point observed by the usual capillary-tube method is generally higher, sometimes by one to two degrees, than that observed with large samples by the heating-curve method. The various factors, as well as the thermodynamic considerations and phase rule applications involved in determining melting and freezing points, are discussed by Skau and Wakeham.[53] The types of apparatus and their effects on the melting point have been discussed by

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[53] E. L. Skau and H. Wakeham, in *Physical Methods of Organic Chemistry*. Vol. I. A. Weissberger, ed., Interscience, New York, 1945, Chapter 1.

Tseng,[54] Francis and Collins,[55] Markley,[56] Hershberg,[57] and others.

Francis and Collins[55] conducted a painstaking investigation into the factors involved in the capillary-tube method of determining the melting, setting, and resolidification points of the fatty acids and esters. The factors investigated included the type of apparatus, the size of the capillary tube, amount of material used, effect of traces of impurities, etc. They concluded from this work that the *setting point* is the only thermal characteristic of the transition between solid and liquid states that can be reproducibly and reasonably accurately determined experimentally by means of the capillary-tube method; also, that the melting point obtained by the capillary-tube method is invariably higher than the setting or true melting point, as determined by another apparatus described by Francis and Collins in the same paper.

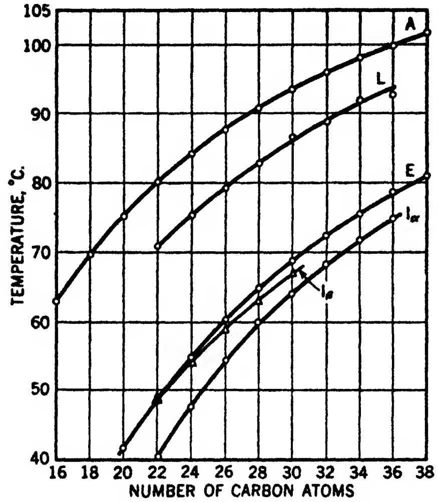

Fig. 13. Melting point as a function of the number of carbon atoms in (A) acids, (L) alcohols, (E) ethyl esters, and (I_α) and (I_β) iodides.[33]

When the apparatus and technique of Francis and Collins is employed for determining the melting point by the capillary-tube method, the difference between the setting and melting points is much smaller compared to other similar methods. The particular type of apparatus employed by them renders it possible to keep the substance under close observation at temperatures very near the melting point and, hence, it is possible to detect the existence of metastable forms fusing within one degree of each other.

Francis and co-workers[32,33] employed the apparatus and technique described by Francis and Collins for the determination of the melting, setting, and resolidification points of the fatty acids and their derivatives of the series C_{12} to C_{38}. From the graphical reproduction of these data[33] in Figure 13, it is evident that the melting points of the homologous series of even-numbered fatty acids, alcohols, ethyl esters, and alkyl iodides, each lie on a smooth curve which tends to become parallel to the *x*-axis as the chain length increases. As previously mentioned, the ultimate convergence

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[54] Chao-Lun Tseng, *J. Chinese Chem. Soc.*, 1, 143–182 (1933).
[55] F. Francis and F. J. E. Collins, *J. Chem. Soc.*, 1936, 137–142.
[56] K. S. Markley, *Ind. Eng. Chem., Anal. Ed.*, 6, 475 (1934).
[57] E. B. Hershberg, *Ind. Eng. Chem., Anal. Ed.*, 8, 312–313 (1936).

temperature was calculated by King and Garner[44] to be about 120°C. for all long chain aliphatic compounds.

The fact that the melting points of the even-numbered acids lie on the same curve is evidence that at the melting point each member of the homologous series was in the same polymorphic form, namely, the high-melting *C*-form, into which the *B*-form passes irreversibly about 5°C. below the melting point. If, however, the comparison had included the alternate odd-numbered acids obtained by crystallization from solvent, alternation in the melting points of the odd- and even-numbered acids would have been observed, since the odd-numbered acids crystallize in the *B*-form irrespective of the solvent used in crystallization. With the exception of eicosanoic (arachidic) acid which gives a mixture of *B*- and *C*-forms, only the *C*-form is obtained on crystallization of the even acids from glacial acetic acid.

The melting point relationships of the methyl and ethyl esters are considerably more complicated than those of the fatty acids owing to the greater complexity of their polymorphic behavior which has already been discussed. The complexity of the melting point phenomena exhibited by the ethyl esters is illustrated by the melting and freezing point data which were presented in Table 18 (page 98) and Figure 11 (page 97) and discussed in connection with the dimorphic behavior of these substances. This discussion is recapitulated in part in the following pages.

It has been mentioned that if the melting points of the ethyl esters of the even- and odd-numbered acids are separately plotted against the number of carbon atoms, each series falls on a smooth curve (Fig. 11), but if they are plotted on the same curve alternation is observed. The alternation, however, results from the comparison of the melting points of different polymorphic forms in the two series, namely, the opaque β-forms of the esters of the even acids and the transparent α-forms of the esters of the odd acids. When, however, the comparison is made with the strictly comparable α-forms the alternation disappears and the entire series of ethyl esters of even- and odd-numbered acids lie on the same curve.[46,48,58]

Phillips and Mumford[58] have pointed out that the esters of the even-numbered acids exhibit monotropic dimorphism, and that the different stabilities of the transparent α-forms are due to the fact that the α-forms of the odd esters *are the stable form,* but those of the even esters *are the metastable form* in the vicinity of the melting point. The β-forms of the even esters are stable up to their melting points, whereas the β-forms of the odd esters undergo transition into the corresponding α-forms below their melting points. However, this simple alternation does not hold throughout the whole series but only for esters above C_{16}. Below this, both even and odd members exist in monotropic modifications, the melting points of the

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[58] J. W. C. Phillips and S. A. Mumford, *J. Chem. Soc.*, **1932**, 898–906.

stable β-forms alternating, but the freezing points of the metastable α-forms falling on a smooth curve.[46,58]

In addition to the α- and β-forms of the ethyl esters, a third modification designated as the $\gamma(C_1)$-form has been observed on cooling the melted ester. In the case of ethyl margarate, for example, the $\gamma(C_1)$-modification crystallizes without supercooling and changes spontaneously into the higher melting β-form, but except when stabilized by the presence of homologs, its existence is masked by the enantiomorphic α to $\gamma(C_1)$ and the monotropic $\gamma(C_1)$ to β transitions which take place simultaneously in the solid phase.

The melting and setting point data (Tables 19 and 20) for the fatty acids and their methyl and ethyl esters which were obtained by Francis and Piper[32] have already been discussed in connection with the polymorphism exhibited by these substances. Unfortunately, Francis and Piper designated the various melting and setting points which they observed by the Greek letters α, β, and γ, which leads to some confusion owing to the fact that Malkin, Mumford, Smith, and others have used the same symbols to refer to polymorphic crystalline states which are not necessarily the same as those existing at the melting or resolidification points referred to by Francis and Piper.

The observed melting point of the methyl esters of the even series, crystallized from either benzene or glacial acetic acid, are designated by Francis and Piper as γ-melting points (Table 19, page 100, column 8). As previously mentioned, these values lie between 1.0 and 1.5°C. above their respective resolidification points (Table 19, column 6). The melting point made on the form which crystallizes from the melt and before the temperature has fallen more than about 1°C., is designated as the β-melting point and is found to be about 0.5°C. above the resolidification point. In the case of the even esters, a liquid crystalline state appears to occur on cooling the melted ester a few degrees below the resolidification point and then raising the temperature to within 0.4° to 0.7°C. of the γ-melting point, or in some cases at 1°C. below the β-melting point.

The melting points of the ethyl esters crystallized from solvent are, as in the case of the methyl esters, designated as γ-melting points and the melting points made after resolidification and cooling about 1°C. are termed α-melting points (Table 19, column 11).

For purposes of ready reference and comparison, there have been assembled in Table 26 the melting and freezing point data for most of the fatty acids, and methyl and ethyl esters of the normal aliphatic series from C_1 to C_{38}. An effort has been made to select the best value for the form which is most likely to be observed with a pure compound by the capillary melting point method. However, in many cases there is no supplemental information available relative to the specific crystalline modification which existed at the observed melting point, consequently some of the recorded melting points may correspond to metastable forms.

TABLE 26

MELTING POINTS OF NORMAL SATURATED ALIPHATIC ACIDS AND THEIR METHYL AND ETHYL ESTERS

Acids and esters	Number of carbon atoms	Acid		Methyl ester		Ethyl ester[a]	
		M.p., °C.	F.p., °C.	M.p., °C.	F.p., °C.	M.p., °C.	F.p., °C.
Formic	1	8.4	...	−99.8	...	−80.5	...
Acetic	2	16.6	...	−98.1	...	−83.6	...
Propionic	3	−22	...	−87.5	...	−72.6	...
Butyric	4	− 7.9 (− 4.7)	−19	−95	...	−93.3	...
Valeric	5	−59 (−34.5)	...	...	...	...	...
Caproic	6	− 3.4	− 3.2	...	...	...	−67.5
Heptanoic	7	−10.5	− 6.3	...	...	...	−66.1
Caprylic	8	16.7	16.3	−41	...	...	−44.8
Pelargonic	9	12.5	12.2	...	...	−44.4	−36.7
Capric	10	31.6	31.2	−18	...	−20.3	−19.9
Undecanoic	11	29.3	28.1	...	...	−15.0	−20.5 (−27.8)
Lauric	12	44.2	43.9	5(?)	...	− 1.8	−11 (−15.5)
Tridecanoic	13	41.5	41.8	...	...	− 0.8	− 3.5 (− 4.8)
Myristic	14	53.9	54.1	18.8	18.4	12.3	4.45 (11.0)
Pentadecanoic	15	52.3	52.5	...	...	11.5	11.9 (7.0)
Palmitic	16	63.1	62.8	30.6	29.2	24.4γ	19.4 (23.2)
Margaric	17	61.3	60.9	29.7	28.1	25.7γ	25.4
Stearic	18	69.6	69.3	39.1	37.8	33.9γ	31.0
Nonadecanoic	19	68.6	68.8	39.3	38.6	36.1γ	35.9
Arachidic	20	75.3	74.9	46.6	45.4	41.6γ	40.4
Heneicosanoic	21	74.3	73.7	47.6	46.6	44.5	44.1
Behenic	22	79.9	79.7	53.3	51.8	48.7γ	47.8
Tricosanoic	23	79.1	78.7	54.4	53.5	51.4γ	51.1
Lignoceric	24	84.2	83.9	58.4	57.5	54.8γ	54.2
Pentacosanoic	25	83.5	82.9	60.0	59.2	57.2γ	56.8
Cerotic	26	87.7	87.4	63.5	62.5	60.2γ	59.6
Heptacosanoic	27	...	...	...	...	...	...
Montanic	28	90.0	90.4	67.5	66.4	64.6α	64.3
Nonacosanoic	29	90.3	89.7	68.8	68.3	66.6γ	66.3
Melissic	30	93.6	93.2	71.7	70.4	68.4α	68.3
Hentriacontanoic	31	...	...	...	...	...	...
Dotriacontanoic	32	96.0	95.5	74.9	73.6	72.5α	72.0
Tritriacontanoic	33	...	...	...	...	...	...
Tetratriacontanoic	34	98.2	98.0	77.9	77.0	75.4α	75.3
Pentatriacontanoic	35	...	...	...	...	...	...
Hexatriacontanoic	36	99.9	99.7	80.9	79.9	78.6α	78.3
Heptatriacontanoic	37	...	...	...	...	...	...
Octatriacontanoic	38	101.6	101.5	83.1	82.3	80.6α	80.3

α and γ refer to melting point designations as used by Mumford and Phillips.[46]

(c) *Phase Diagrams*

In the absence of more precise methods (x-ray diffraction, specific heat curve, etc.) of identification, the determination of the degree of purity or the composition of a mixture of fatty acids, may be made by the assistance of phase diagrams of binary systems of these substances. Many such diagrams, or the data from which they may be constructed, have been published. Phase diagrams have also been constructed for various binary and ternary systems of fatty acid esters, amides, anilides, alcohols, etc. Not all of the data which have been published for these systems are of equal reliability, since the compounds used in some investigations have not been of the highest purity, and the techniques employed have not always been the most precise.

The earliest work on the temperature–composition relationships of the fatty acids was done prior to the development of precision equipment for making temperature measurements and before rigid criteria of purity had been established for the fatty acids and their derivatives. In some cases reinvestigation has established the relative accuracy and reliability of existing temperature–composition data while in others no replicated data are available. Both melting point–composition and freezing point–composition data have been used in the construction of temperature–composition diagrams. Freezing point data are preferable for construction of temperature–composition curves because the freezing point is more reproducible than the melting point and less likely to be influenced by the appearance of metastable polymorphic forms. Oddly enough, few of these systems have been critically examined from the standpoint of classical phase rule criteria, hence the exact nature of some of the observed inflections and *liquidus–solidus* phases are not entirely understood.

Temperature–composition curves have been constructed for a number of binary systems of even-numbered fatty acids, which may be classified on a basis of their components as consisting of: (*1*) two saturated acids, (*2*) one saturated and one unsaturated acid, (*3*) two unsaturated acids of geometrically similar form, and (*4*) two unsaturated acids of geometrically different form.

The possible ternary systems are more numerous because of the greater possible number and variation of combinations which may occur by the introduction of a third component into each of the above-mentioned four systems. However, relatively few of these systems have been investigated.

Binary systems of mixtures of even- and odd-numbered adjacent acids have also been investigated but these have been principally confined to the saturated fatty acid series.

Binary Systems of Saturated Acids.—All of the binary systems of adjacent pairs of even-numbered saturated fatty acids from caproic, C_5H_{11}-

COOH, to tetratriacontanoic, $C_{33}H_{67}COOH$, have been investigated. Because of its historical significance, frequency of its investigation, and because it exhibits the characteristics typical of all the binary systems of saturated acids, that comprised of palmitic and stearic acids will be discussed first and the other systems will be related to it.

Of the various binary systems of aliphatic acids, palmitic–stearic has been most frequently investigated, followed by the palmitic–margaric and stearic–margaric systems. The impetus for the investigation of these three systems arose primarily from the repeated and conflicting reports of the occurrence of margaric acid in natural fats and oils. The existence of margaric acid in natural products is now no longer considered even a remote probability and the phase diagrams for these systems have, therefore, lost much of their original interest and utility. The binary and ternary systems of the higher acids of the series are at the present time of much more utility, because such mixtures of naturally occurring acids are difficult to resolve.

Probably the earliest examination of the palmitic–stearic acid system was made by Heintz[59] in 1854. The sample of stearic acid used melted at 69.2°C. and the palmitic acid at 62.0°C. indicating that they were relatively pure products especially for that time. Melting and solidification points were determined over the entire composition range. De Visser[60] reported a similar investigation of the palmitic–stearic acid system but determined only the freezing points. Palmitic and stearic acids for this investigation were obtained from vegetable butters containing but one or the other of these two acids, in addition to little else except oleic acid. They were rigorously purified and apparently represented extremely pure products; the palmitic acid solidified at 62.618°C. and the stearic acid at 69.320°C. Fifty-gram samples were used for each freezing point determination and thirty-four determinations were made throughout the composition range. The purity of the acids used and the precision of the measurements are probably as great as any prior or subsequent investigation of this system. Shriner, Fulton, and Burks[61] investigated the ternary system consisting of palmitic–margaric–stearic acids and each of the three binary systems of these acids. The acids used by these investigators melted 1° to 2°C. below the generally accepted values indicating the presence of impurities, which is also reflected in lack of sharpness of the intersections in their freezing point–composition curves.

Smith[62] investigated the binary systems of palmitic–margaric and stearic–margaric acids (Fig. 14) and recalculated the data of de Visser for

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[59] W. Heintz, *Ber. Akad. Wiss. Berlin*, **1854**, 207–213; *Chem.-pharm. Centr.*, **25**, 585–589 (1854); *J. prakt. Chem.*, **63**, 168–169 (1854).

[60] L. E. O. de Visser, *Rec. trav. chim.*, **17**, 182–189 (1898).

[61] R. L. Shriner, J. M. Fulton, and D. Burks, Jr., *J. Am. Chem. Soc.*, **55**, 1494–1499 (1933).

[62] J. C. Smith, *J. Chem. Soc.*, **1936**, 625–627.

the palmitic–stearic acid system to a mole percentage basis in order to express the latter's results on a comparable basis with his own. The melting and freezing point data indicate that the acids prepared by Smith were probably the purest ever used in investigating the above-mentioned binary systems. Francis, Collins, and Piper[33] examined the system of palmitic–stearic acids and constructed a complete phase diagram (Fig. 15) for both the melting point–composition and the setting point–composition relationships. The same system was examined by Schuette and Vogel[63] together with a number of other binary systems (Figs. 17 and 18) which will be discussed later; also by Ravich and Vol'nova,[63a] Carlinfanti and Levi-Malvano,[63b] and others.

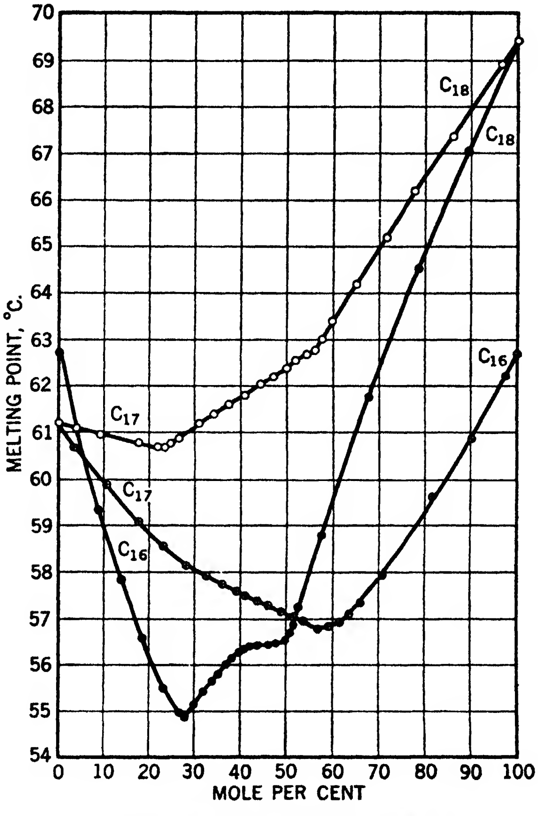

Fig. 14. Melting point–composition diagram for the binary systems of palmitic–stearic, palmitic–margaric, and stearic–margaric acids according to J. C. Smith.[62]

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[63] H. A. Schuette and H. A. Vogel, *Oil & Soap*, **17**, 155–157 (1940).

[63a] G. B. Ravich and V. A. Vol'nova, *Compt. rend. acad. sci. U.R.S.S.*, **37**, 59–62 (1942).

[63b] E. Carlinfanti and M. Levi-Malvano, *Gazz. chim. ital.*, **39**, II, 353–375 (1909).

The melting and freezing points for palmitic, stearic, and margaric acids obtained by various investigators, referred to above, together with those obtained by Francis and Piper,[32] are given in Table 27. The variation in the observed melting and freezing points reflects both the differences in purity of the acids and differences in the techniques employed in making the determinations.

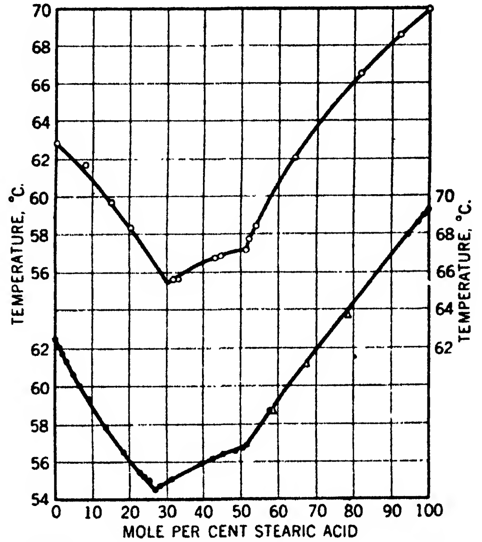

Fig. 15. Melting and setting point–composition curves for palmitic-stearic acid system according to Francis, Collins, and Piper:[33] ○, m. p.; ●, setting points; Δ, de Visser's data.

Table 27

MELTING AND FREEZING POINTS OF PALMITIC, STEARIC, AND MARGARIC ACIDS USED BY VARIOUS INVESTIGATORS IN CONSTRUCTING TEMPERATURE–COMPOSITION CURVES

Palmitic acid		Stearic acid		Margaric acid		Investigator
M.p., °C.	F.p., °C.	M.p., °C.	F.p., °C.	M.p., °C.	F.p., °C.	
62.0[a]	.....	69.2	.....	....	...	von Heintz (1854)
....	62.618[b]	...	69.320[b]	....	...	de Visser (1898)
62.3[a]	60.70	69.7[a]	68.40	60.0[a]	59.35	Shriner *et al.* (1933)
63.5[a]	62.67	70.5[a]	69.42	61.5[a]	61.17	Smith (1936)
62.85[a]	62.53	69.9[a]	69.32	....	...	Francis, Collins, and Piper (1937)
62.9[a]	62.4	69.2[a]	69.6	60.85[a]	61.3	Francis and Piper (1939)
....	62.22	...	68.85	....	...	Schuette and Vogel (1940)

[a] Capillary-tube method.

[b] Fifty-gram sample.

As previously mentioned, the temperature–composition curve of the system, palmitic–stearic acid, is typical of all the adjacent even-numbered pairs of the fatty acid series. The phase diagram of this system (Fig. 15) consists of segments of three smooth curves, which in some portions are nearly linear, intersecting at a minimum or eutectic melting point and at an incongruent melting point corresponding to 27.5:72.5 mole per cent and 50:50 mole per cent, respectively, of stearic and palmitic acids.

The minimum melting point represents a eutectic point, or the invariant temperature at which the phase reaction of the system, upon removal of heat without change in temperature, results in the disappearance of the liquid phase. The other transition corresponds to dimolecular compound formation and incongruent melting, or to a meritectic point.[64]

Oddly enough, both the dimolecular compound and the eutectic of palmitic and stearic acids are often obtained by crystallization of a mixture of these two acids from organic solvents. Since the melting point of any mixture of palmitic acid containing from about 5% to about 65% of stearic acid lies below the melting point (61.3°C.) of pure margaric acid, it is understandable why such mixtures, when obtained from natural sources, could have been mistaken for margaric acid.

The phase diagrams of the odd and even binary mixtures of palmitic–margaric and stearic–margaric acids exhibit similar but less sharp intersections. The lack of sharpness may be due to the effect of different polymorphic forms occurring in the solid state when even- and odd-numbered acids are mixed, or to a lack of purity in one or both of the acids in the mixture, or to both of these conditions. Shriner *et al.*[61] concluded that compound formation did not occur in the even–odd systems. However, it is probable that the presence of small amounts of impurities in their acids tended to obliterate or obscure intersections in the temperature–composition curve. The slightly lower freezing points and the lack of sharp intersections in the binary mixtures investigated by Schuette and Vogel[63] are likewise indicative of the lack of extreme purity in their original acids. Francis, Collins, and Piper[38] stated that the setting points of palmitic and stearic acids recorded by previous investigators of these binary systems indicate that their preparations contained small quantities of impurities and the characteristics of the phase diagrams appear to confirm this statement.

The temperature–composition curves (see Fig. 14, page 117) of Smith[62] are characterized by relatively linear segments and sharp intersections as well as by the occurrence of an inflection at a composition corresponding to 40:60 mole per cent of stearic–palmitic acid. This latter inflection, which has also been observed by other workers, somewhat resembles a congruent melting point.

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[64] S. T. Bowden, *The Phase Rule and Phase Reactions.* Macmillan, London, 1938.

The temperature–composition curves for the series of binary pairs of adjacent even-numbered acids from caproic to tetratriacontanoic are reproduced in Figures 16 to 19.

The curves for the systems composed of caproic–caprylic, caprylic–capric, and capric–lauric acids (Fig. 16) are from the publication of Grondal and Rogers.[65] The acids used by these investigators possessed sharp melting points and correspond to those given in Table 26. Each of the melting phase diagrams consists of three segments of smooth curves intersecting at a sharp minimum or eutectic point and at an incongruent melting or meritectic point, similar in all respects to the palmitic–stearic acid system. Minimum melting points occur at about 27.5 mole per cent and incongruent melting points at about 40 to 47 mole per cent of the higher acid.

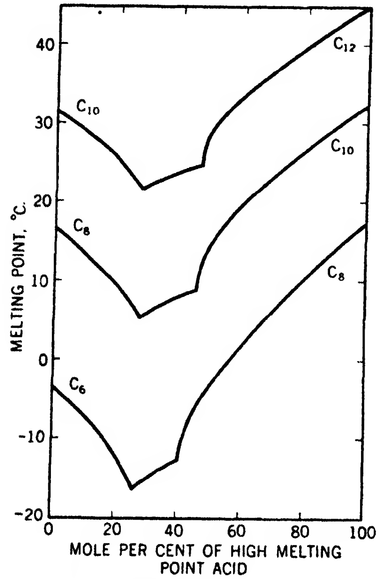

Fig. 16. Melting point–composition curves for the binary systems caproic–caprylic, caprylic–capric, and capric–lauric acids according to Grondal and Rogers.[65]

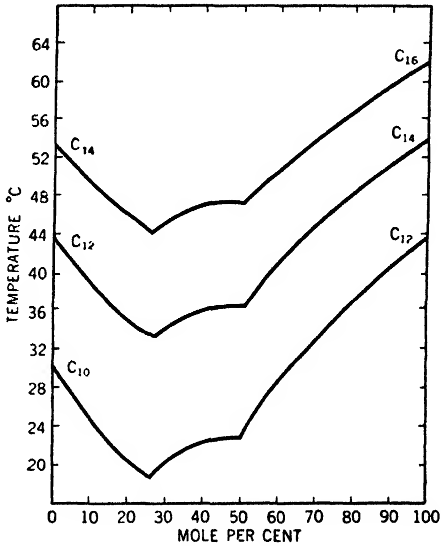

Fig. 17. Melting point–composition curves for the binary systems capric–lauric, lauric–myristic, and myristic–palmitic acids according to Schuette and Vogel.[66]

Kulka and Sandin[67] investigated the adjacent even-numbered binary systems consisting of capric–lauric and myristic–lauric acids, and the odd–

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[65] B. J. Grondal and D. A. Rogers, *Oil & Soap*, **21**, 303–305 (1944); see also H. A. Schuette and H. A. Vogel, *Oil & Soap*, **22**, 238–240 (1945).

[66] H. A. Schuette and H. A. Vogel, *Oil & Soap*, **16**, 209–212 (1939).

[67] M. Kulka and R. B. Sandin, *J. Am. Chem. Soc.*, **59**, 1347–1349 (1937).

even system undecanoic–lauric. The phase diagrams of the first two systems show sharp intersections at 27.5 mole per cent of the higher acid. The odd–even system did not exhibit sharp intersections but rather a definite change in slope near the middle of the system indicative of compound formation.

The capric–lauric and lauric–myristic acid systems were also investigated by Schuette and Vogel.[66] The diagrams for these systems and that of myristic–palmitic acid by the same workers are reproduced in Figure 17.

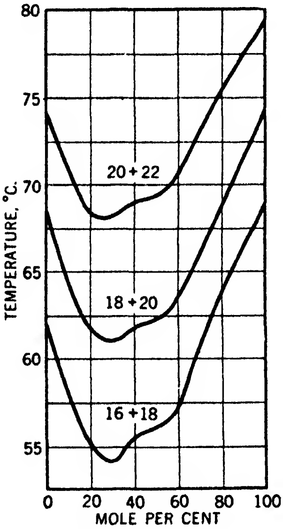

Fig. 18. Freezing point–composition curves for the binary systems palmitic–stearic acids, stearic–arachidic acids, and arachidic–behenic acids as replotted from the data of Schuette and Vogel.[63]

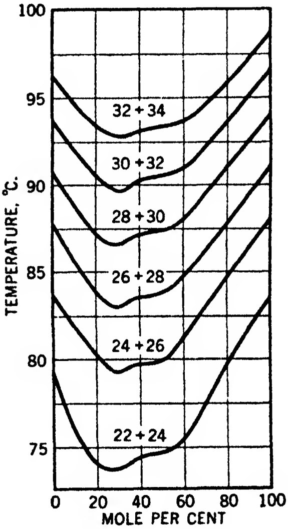

Fig. 19. Freezing point–composition curves of the system behenic–lignoceric acids from data of Schuette and Vogel[63] and melting point–composition curves for the binary systems, C_{24} to C_{34}, from data of Piper *et al.*[68]

The curves, which have been redrawn for purposes of comparison, exhibit the same structure as the lower molecular weight series except for the somewhat greater departure from linearity in the middle segment. Minimum melting points occur at about 26 mole per cent of the higher acid and incongruent melting occurs very near the 50:50 mole per cent composition.

Figure 18 represents the freezing point–composition curves obtained by plotting the data of Schuette and Vogel[63] for the binary systems palmitic–

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[68] S. H. Piper, A. C. Chibnall, and E. F. Williams, *Biochem. J.*, 28, 2175–2188 (1934).

stearic, stearic–arachidic, and arachidic–behenic acids. Figure 19 consists of the curve obtained from similar data of Schuette and Vogel[63] for behenic–lignoceric acids and the melting point–composition curves from the data of Piper, Chibnall, and Williams[68] for the remaining binary acid systems from C_{24} to C_{34}. The curves in Figures 18 and 19 are plotted on the same scale. In all of these curves sharp minima and incongruent melting points are absent and they exhibit only a continuous change in slope in the general vicinity where intersections should occur.

The lack of sharp intersections in the systems composed of the higher fatty acids has been explained by their lower tendency toward strong association and compound formation and greater tendency toward formation of solid solutions. However, this cannot be the case in the palmitic–stearic acid system which has been shown by various workers to give sharp intersections (Figs. 14 and 15) and it would not be expected that they would disappear abruptly with the next higher binary acid (stearic–arachidic) system. Whatever may be the explanation for the lack of sharp intersections in the highest molecular weight systems, their absence in the palmitic–stearic and the stearic–arachidic acid systems (Fig. 18) would appear to be due either to lack of purity of the original acids or to some inadequacy in technique. A similar difference in the apparent purity of the original materials is evident by comparing the curves of Schuette and co-workers[69] for the binary pairs composed of tetracosanoic–hexacosanoic, hexacosanoic–octacosanoic, octacosanoic–triacontanoic acids, with similar curves obtained by Piper *et al.*[68] While the curves of both authors show a tendency toward more rounded intersections, those of the former authors have almost disappeared and indeed do so in the two highest molecular weight systems.[70]

Various binary systems of adjacent pairs of odd- and even-numbered acids have been investigated. In addition to the undecanoic–lauric, palmitic–margaric, and margaric–stearic acid systems which have already been discussed, those comprised of docosanoic–tricosanoic and tricosanoic–tetracosanoic acids have been investigated by Chibnall, Piper, and Williams.[71] These authors also constructed melting point–composition curves for the odd-numbered binary acid systems consisting of tricosanoic–pentacosanoic and pentacosanoic–heptacosanoic acids.

All of the melting point–composition diagrams of binary mixtures composed of even-numbered aliphatic acids which have been examined to date are similar in character and consist of a series of solid solutions, a eutectic mixture with a minimum melting point, and 1:1 compound formation indicated by an incongruent melting point. The evidence of bimolecular compound formation is now accepted and appears to have been securely

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[69] H. A. Schuette, R. M. Christenson, and H. A. Vogel, *Oil & Soap*, **20**, 263–265 (1943).
[70] H. A. Schuette, D. A. Roth, and R. M. Christenson, *Oil & Soap*, **22**, 107–109 (1945).
[71] A. C. Chibnall, S. H. Piper, and E. F. Williams, *Biochem. J.*, **30**, 100–114 (1936).

established by the work of Jantzen,[72] who took special precautions to obtain equilibrium in his systems.

It has also been shown by x-ray examination that the unit cell of pure crystalline acids consists of double layers with the carboxyl groups in juxtaposition. Other evidence has demonstrated that in the liquid state these acids are similarly associated in double molecules or compounds.[73] When two substances exist in double molecules, as for example *A–A* and *B–B*, respectively, it may be expected that equimolar mixtures of these compounds should yield some of the compound *A–B* and indeed such is the case. According to Guy and Smith,[74] equimolar compounds are also formed in the binary systems palmitamide–stearamide and palmitanilide–stearanilide. Whether similar mixtures of methyl esters form double molecules is still debatable. It has been inferred from x-ray measurements[47] that methyl palmitate and methyl stearate crystallize in double molecules. Examination of the binary systems of esters has not given definite proof of the existence of double molecules probably owing to their polymorphic behavior and because of the tendency toward stabilization of metastable forms near the middle of the system. The greater stability of the transparent form of the methyl esters seems to indicate a weakness toward formation of double molecules which is in accord with the fact that the molecular weights of methyl esters in solution are normal.

Binary Systems of Saturated and Unsaturated Acids.—The temperature–composition diagrams of a number of binary systems consisting of a saturated and an unsaturated acid have been examined by several investigators. These systems are represented by oleic–palmitic, oleic–stearic, erucic–behenic, and those formed with the corresponding geometrical isomerides, elaidic–palmitic, elaidic–stearic, isoerucic (brassidic)–behenic, and those of the diethenoid acid, linoleic–palmitic and linoleic–stearic.

The systems composed of oleic–palmitic, oleic–stearic, elaidic–palmitic, and elaidic–stearic acids have been investigated by Carlinfanti and Levi-Malvano,[75] Lapworth, Pearson, and Mottram,[76] Koczy and Griengl,[77] Smith,[78] Ravich, Vol'nova, and Kuz'mina,[79] and others. While all of these workers obtained melting point–composition curves for these systems, which are generally similar in character, only those of Smith will be dis-

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[72] E. Jantzen, *Z. angew. Chem.*, **44**, 482–483 (1931).

[73] P. Waentig and G. Pescheck, *Z. physik. Chem.*, **93**, 529–569 (1919).

[74] J. B. Guy and J. C. Smith, *J. Chem. Soc.*, **1939**, 615–618.

[75] E. Carlinfanti and M. Levi-Malvano, *Gazz. chim. ital.*, **39 II**, 353–375, 375–385 (1909).

[76] A. Lapworth, L. K. Pearson, and E. N. Mottram, *Biochem. J.*, **19**, 7–18 (1925).

[77] W. Koczy and F. Griengl, *Monatsh.*, **57**, 253–290 (1931).

[78] J. C. Smith, *J. Chem. Soc.*, **1939**, 974–980.

[79] G. B. Ravich, V. A. Vol'nova, and T. N. Kuz'mina, *Compt. rend. acad. sci. U.R.S.S.*, **29**, 88–90 (1940).

cussed. The phase diagrams in Figure 20, reproduced from the publication of Smith, are typical of the saturated–monounsaturated acid systems.

The acids employed by Smith were extremely pure judged by their melting and freezing points and the nature of the melting point–composition curves. All of the systems were found to be of the eutectic type and in the oleic–stearic system the eutectic occurs at about 2.5 mole per cent of stearic acid. None of the systems gives in the *liquidus* curve any indication of compound formation such as is found in binary mixtures of long chain saturated acids. According to Smith, it was not expected that oleic acid would readily yield compounds, but elaidic acid, because of its higher melting point and because of the structure of the *trans*-chain, might be expected to combine readily with palmitic or stearic acid. The behavior of oleic acid in solution indicates that it is less completely associated than stearic acid, but x-ray measurements of elaidic acid crystals definitely show that the unit cells contain double molecules (long spacing 48.95 Å. as in the case of palmitic acid and stearic acid (long spacing 46.2 Å., metastable form).

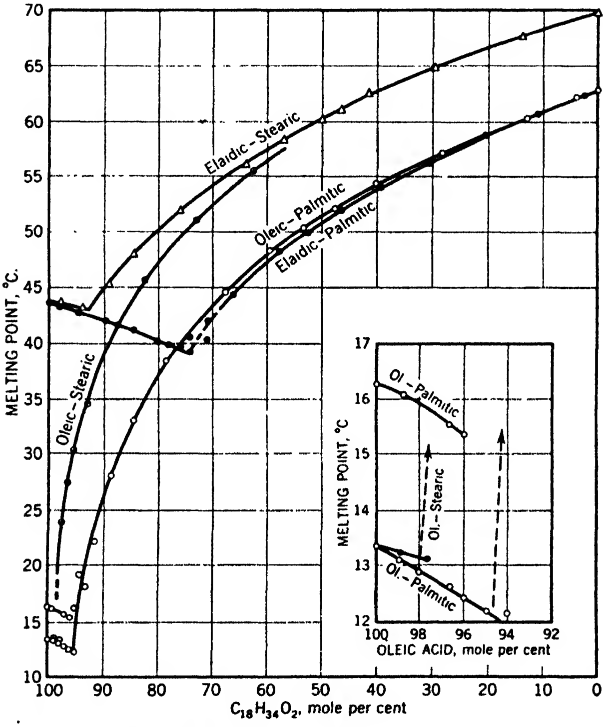

Fig. 20. Melting point–composition curves for the binary systems oleic–palmitic, oleic–stearic, elaidic–palmitic, and elaidic–stearic acids according to Smith.[78]

Lutton[79a] reported x-ray diffraction data for the two polymorphic forms of oleic acid, melting respectively at approximately 13° and 16°C. According to Lutton, the very striking differences observed in the patterns of the two forms point to profound differences in crystalline structure. The lower melting form, with its main short spacing of 4.19 Å., its long spacing of 40.5 Å., and its relatively strong intensity for the odd orders of long spacing, suggests similarities in structure to the *B*- and *C*-forms of stearic acid. On the other hand, the higher melting form is probably unique in crystal structure among the forms of long chain monocarboxylic acids for which diffraction data have thus far been reported. This form has main short spacings of 4.65 and 3.67 Å., a long spacing of 84.4 Å. (possibly 42.2 Å.), and a very irregular and unusual distribution of intensity among the various orders of long spacing.

It should be noted that in the eutectic region, two melting points are obtained for the binary mixture oleic–palmitic acid corresponding to the α- and β-forms of the unsaturated acid.[78,80] With lower concentrations of oleic acid only the α-form appears to be stable. The formation of a eutectic at about 2.5 mole per cent of palmitic or stearic acid with oleic acid is particularly important in the preparation of the pure unsaturated acid by low temperature crystallization. The failure of this method to yield pure oleic acid results from the fact that the eutectic separates when mixed fatty acids containing these components are submitted to low temperature fractionation. It is necessary, therefore, to separate the solid and liquid acids by distillation either before or after the oleic acid is separated by crystallization.

The binary system comprising the C_{20} acids, namely, erucic–behenic and brassidic(isoerucic)–behenic acids, were investigated by Mascarelli and Sanna.[81] The melting point–composition curves are entirely analogous to the oleic–palmitic and elaidic–palmitic systems exhibiting eutectic formation in the region of 2 to 8 mole per cent of the saturated acid.

The binary systems linoleic–palmitic and linoleic–stearic acids were investigated by Koczy and Griengl[77] who found no evidence of eutectic or compound formation, but merely a continuous series of solid solutions. However, their temperature–composition curves begin at a concentration of 5% saturated acid and any eutectic formed below this composition would not have been observed. Also the purity of their unsaturated acid (m.p. −15°C.) is questionable.

Binary Systems of Geometrically Similar Unsaturated Acids.—Only a few binary systems composed of unsaturated acids of the same isomeric

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[79a] E. S. Lutton, *Oil & Soap*, **23**, 265–266 (1946).

[80] G. B. Ravich, V. A. Vol'nova, and T. N. Kuz'mina, *Acta Physicochim. U.R.S.S.*, **14**, 403–413 (1941).

[81] L. Mascarelli and G. Sanna, *Atti accad. Lincei*, **24**, II, 91–97 (1915).

form and different degrees of unsaturation have been investigated. These include principally oleic–linoleic, oleic–linolenic, and linoleic–linolenic acids. The first mentioned system was examined by Koczy and Griengl[77] and by Stewart and Wheeler.[82] The two latter systems were also investigated by Stewart and Wheeler and the phase diagrams obtained by them are reproduced in Figures 21 to 23.

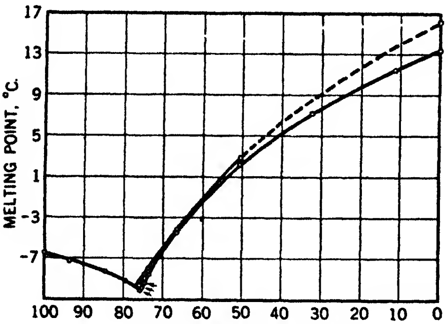

Fig. 21. Melting point diagram of oleic–linoleic acid system. The upper curve is the β-form of oleic acid.[82]

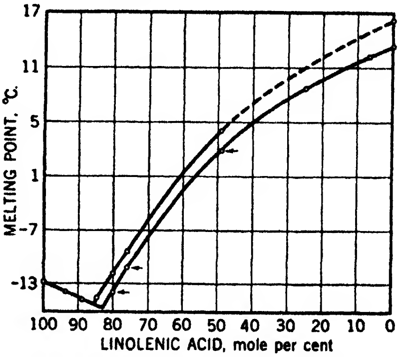

Fig. 22. Melting point diagram of oleic–linolenic acid system. The upper curve is the β-form of oleic acid.[82]

The oleic acid used in their investigations melted at 13.4°C. (α-form) and 16.2°C. (β-form), and contained about 0.3% of saturated acids. Linoleic acid was prepared by debromination of tetrabromostearic acid and may have contained one or more isomers of linoleic acid. It melted at −6.5°C. and solidified at −7.2°C. The linolenic acid was prepared by debromination of hexabromostearic acid and may have contained isomeric linolenic acids. It melted at −12.8°C. and solidified at −13.4°C.

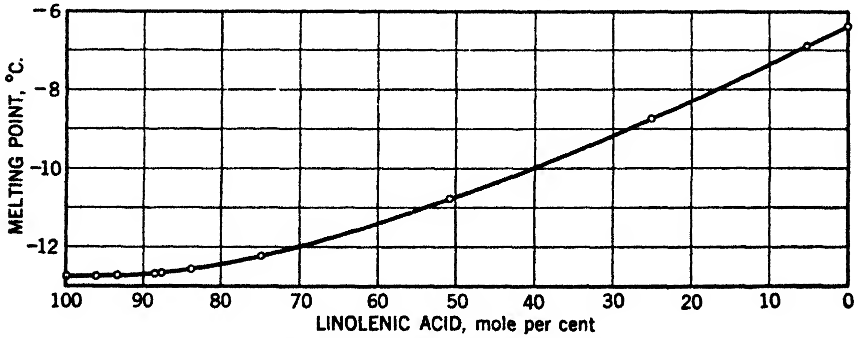

Fig. 23. Melting point diagram of linolenic–linoleic acid system.[82]

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[82] H. W. Stewart and D. H. Wheeler, *Oil & Soap*, 18, 69–71 (1941).

Oleic acid forms with linoleic and linolenic acids similar series of binary mixtures (Figs. 21 and 22). Over certain portions of the melting point–composition curves, two melting points were noted corresponding to the two forms of oleic acid. Eutectic formation was observed between linoleic acid and the two forms of oleic acid, one at −10°C. corresponding to a composition of 75.2:24.8 mole per cent linoleic and α-oleic acids, the other at −9.8°C. corresponding to a composition of 76.3:23.7 mole per cent of linoleic and β-oleic acids. Similar eutectics were observed at 82.7 and 85.5 mole per cent of linolenic acid at −15.7°C. and −15.1°C. for the α- and β-forms, respectively. No evidence of compound formation was observed in either of these two binary systems. In contrast to this behavior, the linoleic–linolenic acid system gave only a continuous series of solid solutions (Fig. 23).

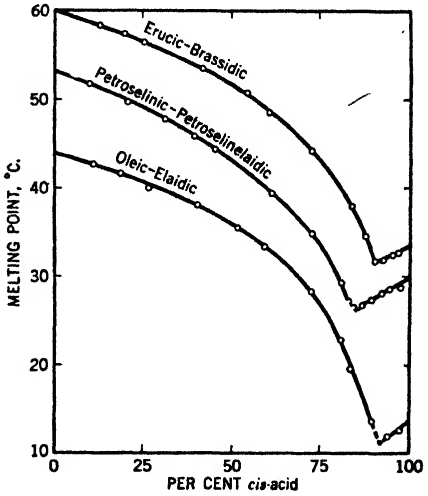

Fig. 24. Melting point diagrams of the binary systems of oleic–elaidic, petroselinic–petroselaidic, and erucic–brassidic acids according to Griffiths and Hilditch.[83]

Binary Systems of Geometrically Different Unsaturated Acids.—Several binary systems consisting of geometrical isomers of unsaturated acids have been examined by means of phase diagrams. These include principally oleic–elaidic, petroselinic–petroselaidic, and erucic–brassidic (isoerucic) acids. The related system of elaidic–linoleic acid has also been investigated.

Phase diagrams for the first three mentioned systems have been examined by Griffiths and Hilditch[83] and are reproduced in Figure 24. The oleic–elaidic acid system was also investigated by Koczy and Griengl[77] and the erucic–brassidic acid system by Mascarelli and Sanna.[81] With the exception of the curves obtained by Koczy and Griengl, all of the phase diagrams are qualitatively similar. Each system exhibits eutectic formation in the region of 85 mole per cent of the *cis*-form of the acid with no evidence of compound formation. The system of elaidic–linoleic acid examined by Koczy and Griengl consisted only of a series of solid solutions. The failure of most of Koczy and Griengl's phase diagrams to exhibit minimum melting points is apparently due to the lack of purity in their original acids. This is especially evident when their binary phase diagrams are compared with similar curves for the several ternary systems which they investigated.

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[83] H. N. Griffiths and T. P. Hilditch, *J. Chem. Soc.*, **1932**, 2315–2324.

6. Application of Crystal Property Data for the Identification of Natural Acids

The data relative to the crystal properties of the long chain aliphatic acids which have been brought together in the preceding pages, are fairly complete, and in the main relatively accurate, although they will probably require some revision when purer compounds and more refined techniques become available. They are, however, sufficiently accurate to permit their application in determining (*1*) the identity of a given pure acid, (*2*) the degree of purity of a given acid, (*3*) the composition of a binary mixture of acids, (*4*) the presence of branching in the hydrocarbon chain, and (*5*) the presence and location of polar substituents in the hydrocarbon chain.

In order to identify and characterize a saturated fatty acid, it is required that the long spacing of the x-ray diffraction photograph be correct to at least 0.2% and that the reflections should give sharp lines and a large number of orders. With the use of proper solvents, well-defined crystals of the correct polymorphic form should be obtained and the $(n + 1)$th or $(n + 2)$th orders of reflection of the diffraction photograph should show strong and sharp reinforcements.

Lack of purity is indicated by small and poorly developed crystals, alteration in the spacing value, few orders of reflection, and oftentimes in a broadening of the lines. Since imperfect crystallization may result from the use of improper solvents, as well as from the presence of impurities, and because the particular polymorphic form assumed may be influenced by temperature, it is necessary to exercise care in the selection of the solvent and maintenance of the proper temperature conditions during the preparation and examination of long chain fatty acids.

The melting and setting points should be accurate to 0.05°C. and should differ less than 0.1°C. unless there is a transition near the melting point. Since 1.0% of palmitic acid will lower the melting point of stearic acid by no more than 0.24°C., and 20 mole per cent of tetracosanoic acid added to tricosanoic acid will lower the melting point of the latter acid by only 0.45°C., the necessity for extreme accuracy in determining melting and setting points is obvious.

In this connection it should be mentioned again that melting points determined by the usual capillary-tube method are generally 0.5° to 2°C. higher than the true melting point. For accurate determination of the melting point, from 1 to 3 g. of material should be used and the temperature should be determined with a standardized thermometer immersed in the bath liquid or preferably with a standardized thermocouple immersed in the sample. Where only small amounts of material are available the procedures of Piper *et al.*[21] or of Francis and Collins[55] are recommended.

According to Francis and Piper,[32] a determination of the acid alone, or of one of its esters, can be misleading, but identity can be established with certainty from the melting point and resolidification point of the acid, and a measurement of the crystal spacings of a specimen obtained by crystallization from *benzene* and of another specimen crystallized from *acetic acid.* As previously mentioned, each of these solvents produces a different polymorphic form of the naturally occurring acids, but the same forms in the case of the odd-numbered synthetic acids.

If the acid is not a pure substance, but is a binary mixture of saturated acids, the composition of the mixture may be determined by comparison of the spacing value and the melting and setting points of mixtures of known composition, *i.e.*, by location of the melting point on the phase diagram. These criteria may not in themselves be sufficient to identify the mixture and comparison may also have to be made with the corresponding methyl or ethyl ester.

CHAPTER V

SPECTRAL PROPERTIES

1. Introduction

It was mentioned in the previous chapter that x-ray spectroscopy depended on the fact that the crystal lattice, or the arrangement of atoms or molecules within a crystal, was of such nature and dimensions that it could act as a three-dimensional grating for the diffraction of light in the region of 10 to 150 Å. It was seen that this form of spectroscopy could be applied to measuring the distances between carbon atoms in long chain compounds such as the higher fatty acids and also to the determination of the number and arrangement of the molecules in a unit cell or crystal.

When a molecule is exposed successively to more or less monochromatic radiation of various frequencies, it may possess the ability to absorb the radiant energy corresponding to certain of these frequencies. This absorbed energy will increase the internal energy (electronic, vibrational, or rotational) of the molecule. For a given molecule, the particular type of energy increase will depend upon the amount of energy in the incident light. Thus, ultraviolet radiation may increase the electronic energy of the molecule, whereas infrared radiation will usually possess only energy enough to enhance the vibrational or rotational states. Absorption at a given frequency will depend upon the molecular structure of the compound, *i. e.*, on a particular grouping which can have an electronic, vibrational, or rotational change of state by exactly the energy associated with the given frequency.

A study of the particular components of various molecular structures which absorb at certain frequencies, or a study of the particular frequencies absorbed by molecules of unknown structures is known as absorption spectroscopy. It might be expected that the application of this form of spectroscopy to the examination of fats and oils and their derivatives would yield considerable information concerning the chemical structures of these substances. Actually, the investigation of the behavior of all the available types of radiation with respect to fats and fat products has made possible a considerable expansion in our knowledge of the nature and conjugation of their *chromophoric* groups, the nature of substituent groups, and the configuration of the groups within the molecule.

Another application of absorption spectroscopy depends on the fact that a considerable body of spectroscopic data for well-defined substances already exists in the literature and it is, therefore, possible by analogy with these known spectra to classify those of fats and oils and their derivatives, even though their structures may not be known. In fact, this method can be applied along with available chemical data in ascertaining the approximate structure of many of these substances of unknown structure. Once the spectrum of a fatty compound is known, spectroscopy has further utility as an analytical method for the quantitative determination of this compound in mixtures. In all these applications absorption spectroscopy, including visual, infrared, and ultraviolet, has made rapid progress in recent years with respect to the chemistry of fats, oils, and associated lipids.

The following discussion is intended to indicate the value of absorption spectroscopy as a tool for investigating fatty acids and fatty acid derivatives, and the general types of information which may be derived from the application of spectrophotometry to these substances. Lack of space precludes detailed descriptions of the apparatus and methods of measuring the frequency or intensity of the various types of spectra which are discussed here, but a number of excellent monographs and articles are available which treat in detail of the theory of spectroscopy, laboratory equipment, and methods of obtaining and measuring various types of spectra and the reader should consult them for information on these subjects.[1-5]

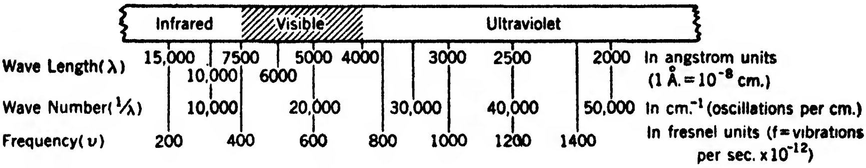

Fig. 25. Relative spectral regions and units used in delimiting them.[5]

Since this chapter is concerned with absorption spectra ranging from the far ultraviolet on the one hand, to the far infrared on the other, it is in order to define the limits of the wave lengths of light included in each region and the terms used to describe them. The various spectral regions are shown

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[1] W. R. Brode, *Chemical Spectroscopy.* 2nd ed., Wiley, New York, 1943.

[2] J. H. Hibben, *The Raman Effect and Its Chemical Applications.* Reinhold, New York, 1939.

[3] E. S. Miller, *Quantitative Biological Spectroscopy.* Burgess, Minneapolis, 1939.

[4] R. B. Barnes, R. C. Gore, U. Liddel, and V. Z. Williams, *Infrared Spectroscopy.* Reinhold, New York, 1944.

[4a] R. E. Burk and O. Grummitt, *Major Instruments of Science and Their Applications to Chemistry.* Interscience, New York, 1945.

[5] J. P. Kass, "Ultraviolet Absorption Studies of Drying Oils," in *Protective and Decorative Coatings,* Vol. IV. J. J. Mattiello, ed., Wiley, New York, 1944, pp. 362–405.

diagrammatically in Figure 25. It is evident, from this figure, that various units are used to designate the regions of the spectrum or the character of a given type of radiation. These units are wave length, wave number, and frequency and are designated by the symbols λ, $1/\lambda$ or ν, and ν, respectively. They are introconvertible and bear the following relation to one another:

$$\frac{1}{\text{wave length}} = \text{wave number} = \frac{\text{frequency}}{\text{speed of light}}$$

or:

$$\frac{\text{speed of light}}{\text{wave length}} = \text{frequency} = \text{speed of light} \times \text{wave number}$$

It follows that:

$$\frac{1}{\text{wave length (in Å.)}} \times 10^8 = \frac{1}{\text{wave length (in m}\mu)} \times 10^7 = \text{wave number (in cm.}^{-1}$$

and:

$$\frac{10^8}{\text{wave number (in cm.}^{-1})} = \text{wave length (in Å.)}$$

and:

$$\text{wave number (in cm.}^{-1}) \times 3 \times 10^{-2} = \frac{3 \times 10^6}{\text{wave length (in Å.)}} = \frac{3 \times 10^5}{\text{wave length (in m}\mu)} = \text{frequency (in } f)$$

and:

$$\frac{3 \times 10^6}{\text{frequency (in } f)} = \text{wave length (in Å.)}$$

All of these units, as well as others, are currently in use either by arbitrary choice or as a matter of necessity. For many purposes it is immaterial which units are used, but in some instances involving theoretical considerations and relationships between absorption spectra and the presence of chromophoric groups in the molecule, it is essential that the frequency scale be employed. For example, if the absorption in the ultraviolet is compared with fundamental bands in the infrared, as was done by Mowry, Brode, and Brown[6] in the case of isomerized arachidonic acid, it is essential that the absorption maxima be expressed in terms of frequencies, *e. g.*, in fresnels or vibrations per second $\times\ 10^{-12}$.

Generally, preference will be given in this chapter to use of wave lengths, λ in angstroms, and frequencies, f in fresnels or vibrations per second $\times\ 10^{-12}$. Some of the graphical data reproduced from other sources express

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[6] D. T. Mowry, W. R. Brode, and J. B. Brown, *J. Biol. Chem.*, **142,** 671-678 (1942).

wave lengths in mμ when referring to the ultraviolet, and μ when referring to the infrared regions. The relations of these units to angstroms are as follows: 1 μ = 1000 mμ = 10,000 Å., or 1 Å. = one ten-millionth of one millimeter, 1 mμ = one millionth of one millimeter, 1 μ = one thousandth of one millimeter.

In addition to absorption spectroscopy which has just been discussed, another branch of spectroscopy, namely, the Raman effect, is useful in investigating the characteristics of fat molecules. Owing to the difference in the magnitude of the frequencies and frequency shifts involved in the Raman effect as compared to the radiation involved in absorption spectroscopy, and because of the theoretical relation of the Raman effect to the internal structure of the molecule, wave numbers, $1/\lambda$ or $\bar{\nu}$, *i. e.*, number of waves per centimeter, rather than wave lengths, are used to designate the radiation involved.

2. Raman Spectra

It is no doubt true, as stated by Hibben,[7] that few physical discoveries have resulted in greater stimulation to investigations in a particular field than has the discovery of the Raman effect by Sir C. V. Raman in 1928. The application of Raman spectra to the investigation of organic compounds has yielded much valuable information concerning the internal characteristics of the molecule. By means of Raman spectra, it has been possible to determine the strength of bonds between atoms in their normal state and to calculate the frequency and amplitude of atomic vibrations. In some cases it has been possible to determine the spatial configuration and the anisotropy of the molecule. From this information the specific heats, relative heats of dissociation, and the heats of fusion of pure organic compounds may be estimated.

Despite the wide utility of the Raman effect in the field of organic chemistry, it has found only limited application in the field of fats and oils. The Raman spectra of only a few of the normal, straight chain fatty acids have been examined. They include the members of the homologous series from formic, HCOOH, to capric acid, $CH_3(CH_2)_8COOH$. The corresponding methyl and ethyl esters, methyl ketones, acid anhydrides, and acid chlorides have also been investigated. These investigations, which are due principally to Kohlrausch and co-workers,[8,9] were primarily concerned with the characteristic frequency shifts resulting from the presence of carbonyl groups in these compounds. The data with reference to the lower

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[7] J. H. Hibben, *Chem. Revs.*, **13**, 345–478 (1933).

[8] K. W. F. Kohlrausch and A. Pongratz, *Ber.*, **B66**, 1355–1369 (1933).

[9] K. W. F. Kohlrausch, F. Köppl, and A. Pongratz, *Z. physik. Chem.*, **B21**, 242–255; **B22**, 359–372 (1933).

frequency shifts of the aliphatic acids have been compiled by Hibben[10] whose publication should be consulted.

Raman Spectra of Unsaturated Fatty Acids

Many investigations have been made with respect to effect of ethylenic bonds on the Raman spectra of organic compounds, and especially the relation of the frequency shifts to *cis-trans*-isomerism. McCutcheon, Crawford, and Welsh[11] appear to be the first to apply Raman spectra to an investigation of the *cis-* and *trans*-isomers of the C_{18} unsaturated acids. The characteristic Raman shifts of the ethyl esters of the C_{18} unsaturated acids, observed by McCutcheon *et al.*, are given in Table 28.

TABLE 28

RAMAN LINES CHARACTERISTIC OF UNSATURATED ETHYL ESTERS[a]

Oleate	Elaidate	Linoleate	β-Linoleate	Linolelaidate	Linolenate
		953 1	952 1		954 0
	962 1				
974 3 *d*		972 5 *d*	973 4 *d*	977 1	971 2
					1250 1
1267 7 *d*	1269 1	1264 7 *d*	1264 7 *d*	1261 2 *d*	1265 6 *d*
		1643 6 *d*	1643 5 *d*		
1655 8 *p*		1658 10 *p*	1657 10 *p*	1656 10 *p*	1656 9 *p*
	1669 8 *p*			1668 5 *d*	
3009 6 *p*	3008 3 *p*	3012 5 *p*	3012 5 *p*	3009 2 *p*	3013 8 *p*

[a] J. W. McCutcheon, M. F. Crawford, and H. L. Welsh, *Oil & Soap*, **18**, 9–11 (1941). Frequency shifts, $\Delta\bar{\nu}$; relative intensities (scale 0–10) and polarizations are listed separately; *p* = polarized, *d* = depolarized.

Previous work has established the fact that the ethylenic bond in all compounds of the type RCH═CHR′ gives rise to a frequency in the neighborhood of $\Delta\bar{\nu}$ 1650 and that for *cis*-compounds, this frequency is $\Delta\bar{\nu}$ 10 to 20 less than for the *trans*-compound. It is also characteristic of ethylenic compounds that a Raman line occurs at approximately $\Delta\bar{\nu}$ 3010 and that this line has about twice the intensity in *cis*-compounds as in the corresponding *trans*-compounds. The characteristic ethylenic frequency in ethyl oleate was found by McCutcheon *et al.* to be 14 units lower than in ethyl elaidate and the intensity of the line at $\Delta\bar{\nu}$ 3009 to be approximately twice as strong for ethyl oleate as for ethyl elaidate, which observations are additional confirmation of the *cis-* and *trans*-configurations, respectively, for oleic and elaidic acids.

McCutcheon and co-workers[11] concluded from the examination of the Raman data obtained with α- and β-linoleates, that these two substances

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[10] J. H. Hibben, *Chem. Revs.*, **18**, 1–232 (1936).

[11] J. W. McCutcheon, M. F. Crawford, and H. L. Welsh, *Oil & Soap*, **18**, 9–11 (1941).

were identical, thus substantiating the authors' conclusions[12] as well as those of Riemenschneider, Wheeler, and Sando[13] and of Kass and Burr[14] in this respect. However, these conclusions are at variance with those of Frankel and Brown[15] and others, as has been previously mentioned in connection with the geometrical isomerism of these compounds. It is significant that the Raman data led McCutcheon to conclude that the elaidinization reaction of linoleic acid produces a reversal of not one, but of both double bonds from the *cis-* to the *trans*-configuration, *i. e.*, linolelaidic acid is the *trans-trans*-form of this acid and ordinary linoleic acid, the *cis-cis*-form. On the basis of the Raman and infrared spectra of ethyl linolenate, McCutcheon concluded that the linolenate possessed a *cis-cis-cis*-arrangement of the double bonds.

Although on the whole, these conclusions are correct and correspond with the generally accepted chemical evidence, some peculiarities of the Raman spectra which he obtained should be pointed out. It is well established, as stated by McCutcheon, that the *trans*-forms of compounds of the type RCH═CHR′ exhibit a greater frequency shift than the corresponding *cis*-forms. However, the relative weakness of the carbonyl shift as compared with the ethylenic one shown in the Raman diagram contained in the original publications of McCutcheon is somewhat anomalous, and the significance of the hydrogen frequency near $\Delta\bar{\nu}$ 3012 seems to be overemphasized. Frequencies do occur in this region for the simpler ethylene compounds, but there is apparently no frequency in this region in compounds containing more than six carbon atoms in the chain. However, it is in this region that a harmonic of the deformation vibration would appear, but it should not be polarized. As has been pointed out by Hibben,[2] the difference between the carbon-hydrogen symmetrical vibration and the *cis*- and *trans*-forms of dichloroethylene is very small.

3. Visible Absorption

The fatty acids are colorless substances and hence do not exhibit absorption in the visual range, *i. e.*, with wave lengths of light from about 4000 to 7000 Å. This is true also of pure glycerides, but it is not true of the natural fats and oils since they contain varying amounts of pigments which are capable of absorption in the visible region of the spectrum. For example, the presence of gossypol, which has a characteristic absorption band at 3660 Å., carotene with a band at 4500 Å., or chlorophyll with a band at 6600 Å., can be readily ascertained by visual absorption measurements.

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[12] J. W. McCutcheon, *Can. J. Research*, **B16**, 158–175 (1938).

[13] R. W. Riemenschneider, D. H. Wheeler, and C. E. Sando, *J. Biol. Chem.*, **127**, 391–402 (1939).

[14] J. P. Kass and G. O. Burr, *J. Am. Chem. Soc.*, **61**, 1062–1066 (1939).

[15] J. S. Frankel and J. B. Brown, *J. Am. Chem. Soc.*, **65**, 415–418 (1943).

4. Infrared Absorption

Infrared radiation or infrared light is similar in character and general properties to ordinary visible light and is a result of wave emission at the velocity of light from a body oscillating with a definite frequency. Infrared radiation suffers absorption and reflection exactly as does visible light. Because the infrared region begins at the point where the visible region ends, and because the human eye varies with respect to the limiting sensitivity at both ends of the visible spectrum, it is not possible to define exactly the infrared region.

The visible spectrum is usually assumed to extend from 4000 to 7500 Å., and the infrared spectrum may be considered as the region above 7500 Å. The latter is generally divided into the short or near infrared from 7500 Å. (0.75 μ) to 10,000 Å. (1 μ), a middle region extending from 10,000 to 60,000 Å. (6 μ), and a lower or far infrared above 60,000 Å. The upper limit of the far infrared region is generally undefined, but it may be considered as overlapping the lower Hertzian region of radio frequencies.

Many organic compounds which exhibit no marked absorption in the visible region may possess characteristic absorption in the infrared. In practice, a substance whose infrared absorption spectrum it is desired to determine, is irradiated with infrared light from a standard source and the percentage of transmission determined over a series of wave lengths. The percentage of light transmitted for each wave length is plotted against the wave length and a curve is drawn through all the points to give a spectral transmittancy curve. It has been found that specific absorption maxima which are observed in various organic compounds can be attributed to the presence of particular atomic groups in the molecule and are generally unaffected by spatial configuration. For example, the *d*- and *l*-forms of pinene have identical spectra. Certain atomic groupings, as, for example, the amino, methyl, and hydroxyl groups give rise to specific absorption bands.

Barnes, Liddel, and Williams[16] investigated the infrared absorption spectra of 363 synthetic and natural organic compounds and prepared a library of representative absorption curves for comparison with others which may be obtained with unknown compounds. These curves which were taken in the region of 5 to 13 μ of the infrared spectrum have been published in a serially numbered collection. Among these spectrographs are several fatty acids, glyceride oils, and related substances. These substances, together with the catalog number of the corresponding graph, are listed in Table 29.

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[16] R. B. Barnes, U. Liddel, and V. Z. Williams, *Ind. Eng. Chem., Anal. Ed.*, **15**, 659–709 (1943).

TABLE 29

INFRARED ABSORPTION SPECTRA CURVES CATALOGUED BY BARNES, LIDDEL, AND WILLIAMS[a]

Substance	Graph No.
Acetic acid, allyl ester	167
Acetic acid, methyl ester	161
Acetic acid, polyvinyl ester	165
Acetic acid, vinyl ester	166
Acrylic acid, *n*-butyl ester	171
Acrylic acid, ethyl ester	169
Acrylic acid, ethyl ester, polymer	170
Acrylic acid, methyl ester	168
Adipic acid, diallyl ester	188
Caproic anhydride	158
Ethylene glycol	91
Lauric acid, methyl ester	175
Linseed oil	199
Linseed oil, ethyl esters	206
Linseed oil, methyl esters	205
Neat's-foot oil	200
Neofat, methyl ester	207
Octadecadienoic acid, methyl ester	194
Oleic acid, methyl ester	176
Propionic acid, ethyl-β-ethoxy ester	164
Sebacic acid, diallyl ester	189
Soybean oil	201
Tripalmitin	203
Tristearin	202
Triundecylenin	197
Tung oil	198
Tung oil, methyl esters	204
Undecylenic acid	228

[a] *Ind. Eng. Chem., Anal. Ed.*, **15**, 659–709 (1943).

Infrared Spectra of Unsaturated Fatty Acids

McCutcheon *et al.*[11] determined the infrared absorption spectra of the ethyl ester of oleic, elaidic, linoleic, linolelaidic, and linolenic acids. In the spectral transmission curves which are reproduced in Figure 26, the ratio of the transmission of the unsaturated ester to that of ethyl stearate is plotted against the wave length of the transmitted radiation. Strong absorption is observed in the region of 6.0 μ (60,000 Å.) in the case of the esters of oleic, linoleic, and linolenic acids, while elaidic and linolelaidic acids exhibit relatively weaker and wider absorption bands in this region. In the case of ethyl linolenate a secondary absorption occurs in the region of 5.25 μ (52,500 Å.). On a basis of theoretical considerations, *cis*-acids should exhibit a strong absorption characteristic of the double bond in the region of 6.0 μ (60,000 Å.). McCutcheon failed to observe a strong absorption with ethyl elaidate and linolelaidate in this region. He interpreted the difference in absorption characteristics of ethyl linoleate and ethyl linolelaidate in the region of 6.0 μ (60,000 Å.) as proof of the *cis-cis-* and *trans-trans-*configurations, respectively, of these two esters.

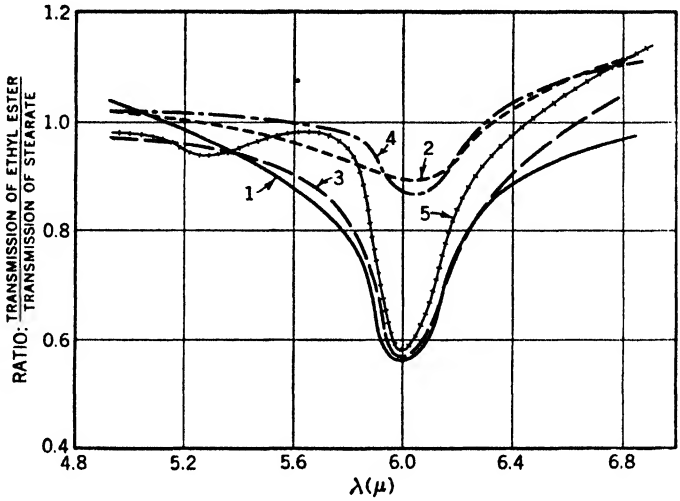

Fig. 26. Infrared spectral transmission curves of the ethyl esters of oleic (1), elaidic (2), linoleic (3), linolelaidic (4), and linolenic (5) acids according to McCutcheon *et al.*[11]

As previously mentioned, McCutcheon concluded on the basis of the Raman and infrared spectra that the linolenate possessed a *cis-cis-cis-*configuration. However, the dissimilarity between the absorption curve of the linolenate as compared to the curves for the oleate and linoleate is in need of clarification.

Gamble and Barnett[17] examined the infrared absorption of the methyl, glycol, and glyceryl esters of oleic, linoleic, linolenic, and elaeostearic acids. The absorption spectra curves of the glyceryl esters are reproduced in Figures 27 and 28. All of the glyceryl esters show an absorption in the region of 6 μ (60,000 Å.), characteristic of the double bond. The elaeostearate exhibits an additional strong absorption at 10.0 μ (100,000 Å.) which is ascribed by the authors to the presence of conjugation. However, a feeble absorption in the same region is evident in the other esters and may indicate traces of conjugated acids in the products examined. The absorption at 8.4 μ (84,000 Å.) is attributed to the presence of an oxygen linkage.

Gamble and Barnett also determined the infrared absorption spectra of methyl oleate and methyl elaeostearate (Fig. 29) before and after exposure to ultraviolet light. After the exposure of methyl elaeostearate to ultra-

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[17] D. L. Gamble and C. E. Barnett, *Ind. Eng. Chem.*, **32**, 375–378 (1940).

violet light, the strong absorption band at 3.4 μ (34,000 Å.) was found to have shifted to 3.1 μ (31,000 Å.). A strong absorption at 2.9 μ (29,000 Å.)

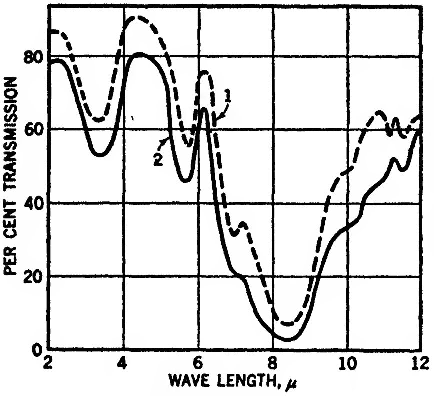


Fig. 27. Infrared absorption spectra of glyceryl trioleate (1) and trilinoleate (2).[17]

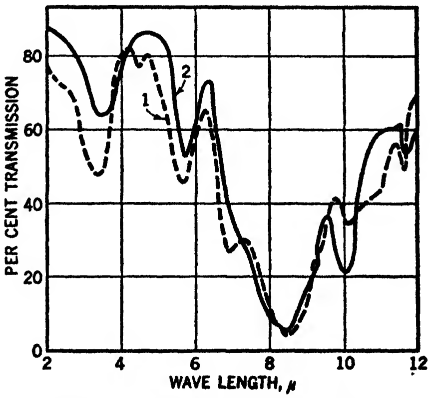


Fig. 28. Infrared absorption spectra of glyceryl trilinolenate (1) and trielaeostearate (2).[17]

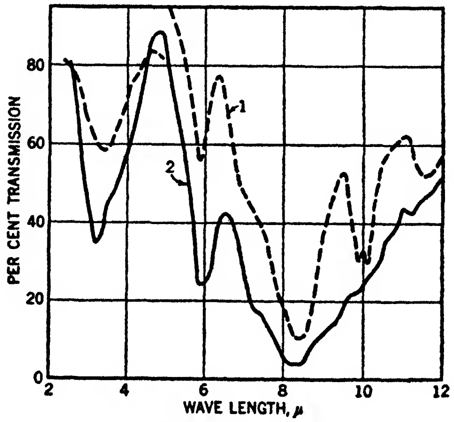
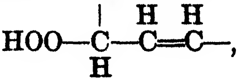


Fig. 29. Effect of ultraviolet radiation on the infrared absorption spectra of methyl elaeostearate[17]: (1) unexposed; (2) after 1500 hours in mercury arc.

is normally attributed to the presence of a hydroxyl group and the shift of the band at 3.4 μ (34,000 Å.) toward 2.9 μ (29,000 Å.) is attributed to the introduction of hydroxyl groups. It is probable, however, that the shift is due to the formation of a hydroperoxido group,



$\mathrm{HOO{-}\overset{|}{\underset{H}{C}}{-}\overset{H}{C}{=}\overset{H}{C}{-}}$, which is readily formed even in oleic acid when irradiated with ultraviolet light in the presence of oxygen.

5. Ultraviolet Absorption

Ultraviolet radiation or light is similar in character and properties to ordinary light but is constituted of shorter wave lengths. The ultraviolet region of the spectrum is assumed to extend from the lower visible region, *i. e.*, 4000 Å. to below 1000 Å. Ordinary spectroscopic equipment is generally adapted to measurements in the region from 3500 to about 2000 Å., but equipment can be built which permits measurements to be made in the far ultraviolet. With specially sensitized photographic plates and an evacuated spectrograph Schumann succeeded in reaching 1200 Å., and by the addition of fluorite optics Lyman made measurements down to 500 Å. Thus, the lower limits of the ultraviolet may be considered as overlapping the region of x-ray spectra which was discussed in the preceding chapter (page 83–92).

As in the case of absorption in the visible region, ultraviolet absorption is associated with a specific type of structure, *i. e.*, with the presence of ultraviolet *chromophores* in the molecule, rather than with the molecule as a whole. This type of absorption differs from infrared absorption by virtue of the fact that the former is associated with a chromophore absorbing electronic energy, whereas the latter is associated only with simple atom groupings involving vibrational or rotational energies. The ultraviolet absorption spectrum may, however, be affected to some extent by the molecular environment or substituents attached to the chromophores, as well as by the nature of the solvent in which the measurements are made.[18,19]

Of the various types of absorption spectroscopy which may be applied to the investigation of fatty substances, ultraviolet absorption appears to possess the greatest theoretical and practical utility. This type of spectroscopy can be applied to the identification of specific compounds, the determination of chemical homogeneity, the detection of the presence of specific linkages or configurations in the molecule, and for the quantitative estimation of specific components in a mixture. As will become evident in the following pages, ultraviolet spectroscopy has been applied with increasing frequency and fertility to a wide range of problems in the field of fats and oils and their associated products.

It was originally thought that unsaturated aliphatic hydrocarbons did not exhibit selective absorption in the ultraviolet region, but it is now known that such compounds absorb strongly in the far ultraviolet and it is in this region that all long chain fatty acids must be examined. The satu-

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[18] H. Booker, L. K. Evans, and A. E. Gilliam, *J. Chem. Soc.*, **1940**, 1453–1463.

[19] M. M. Graff, R. T. O'Connor, and E. L. Skau, *Ind. Eng. Chem., Anal. Ed.*, **16**, 556–557 (1944).

rated hydrocarbons, alcohols, and ethers are so transparent, when pure, that they are excellent solvents for measurements at wave lengths above 2000 Å.[19]

With the introduction of a carboxyl group, or one ethylenic bond in the hydrocarbon chain, specific absorption appears. With two double bonds present in the hydrocarbon chain several arrangements are possible. They may be in isolated positions as in 1,4-pentadiene, $CH_2{=}CHCH_2CH{=}CH_2$; attached to the same carbon atom[19a] as in ethylallene or 1,2-pentadiene, $CH_2{=}C{=}CHCH_2CH_3$; or in a conjugated position as in 1,3-pentadiene, $CH_2{=}CHCH{=}CHCH_3$. The absorption differs for each of the three types of arrangements of the pair of double bonds, the position of the maximum absorption increasing in wave length in the above order.

Mixed fatty acids of glyceride oils exhibit absorption above 2000 Å. owing to the presence of carboxyl and ethylenic groups. The saturated fatty acids show small differences in their absorption bands but the unsaturated acids absorb more strongly owing to the effect of both the ethylenic linkages and the carboxyl group. The presence of a hydroxyl group such as occurs in ricinoleic acid, appears to have little effect on the nature of the ultraviolet absorption in the region above 2000 Å.

(a) *Ultraviolet Spectra of the Fatty Acids*

The ultraviolet absorption spectra characteristic of the various types of pure fatty acids have been assembled by Kass[5] into a composite graph which is reproduced in Figure 30.

Examination of the individual curves of Figure 30 reveals the fact that the absorption above 2000 Å. due to the carboxyl group in the saturated acids is very weak, whereas the introduction of a second ultraviolet chromophoric group in the form of a double bond in oleic acid increases the absorption. The geometric isomer, elaidic acid, exhibits an absorption above 2000 Å. similar to oleic acid but shifted about 50 Å. toward the longer wave lengths. The higher absorption in the longer wave lengths in elaidic acid as compared to oleic acid may be due to the presence of oxygenated or other compounds rather than to a difference in structure. Ricinoleic acid exhibits a similar but greater shift in the same region and all three acids exhibit relatively similar absorptions in the region from 2200 to 2400 Å.

The introduction of a triple bond as in stearolic acid appears to produce a shift of the spectral curve in the region of 2200 to 2600 Å. Whether the entire shift can be attributed to the substitution of the triple bond for a double bond, or whether the shift, especially in the longer wave lengths, is due to partial oxidation or rearrangement during preparation of the acid cannot be stated with certainty at the present time. Increasing the number

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[19a] Cumulative double bonds.

of double bonds as in linoleic and linolenic acids increases the absorption in the region of shorter wave lengths.

As previously mentioned, the presence of conjugated double bonds markedly increases the absorption, especially in the region between 2200 and 2400 Å. Not only is the absorption increased but the specific maxima characteristic of each system of conjugated double bonds (diene, triene, tetraene, etc.) becomes evident. The presence of a diene system of double bonds is characterized by an absorption band at about 2300 Å. as may be observed (Fig. 30) in the curves for $\Delta^{9,10,11,12}$- and $\Delta^{10,11,12,13}$-linoleic acid.

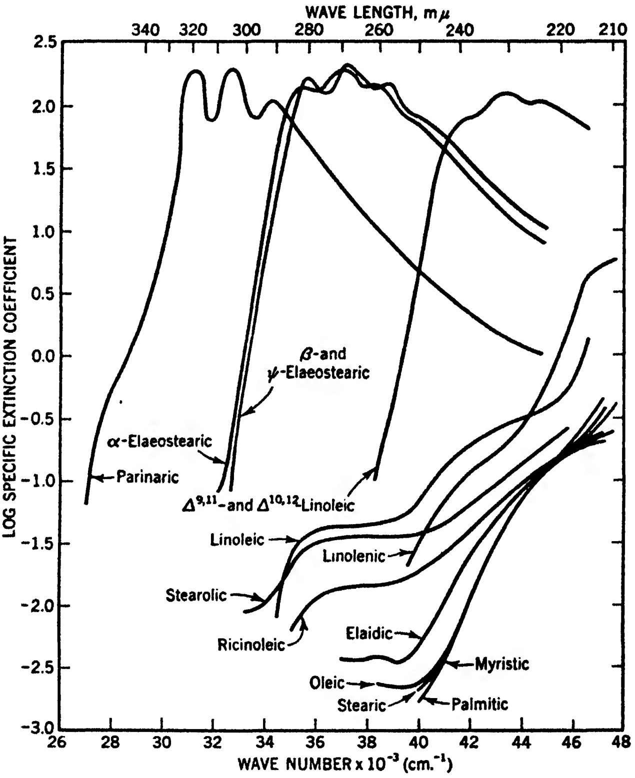

Fig. 30. Characteristic ultraviolet absorption spectra of fatty acids.[5a]

Triene conjugation is characterized by absorption bands at about 2700 Å. and differs slightly for *cis*- and *trans*-forms as may be seen in the curves for α- and β-elaeostearic acids. Tetraene conjugation is characterized by absorption bands at about 3080 and 3200 Å.

The relationship between the ultraviolet spectral curve and unsaturation is even more clearly emphasized by the graph of Barnes, Rusoff, Miller, and Burr,[20] reproduced in Figure 31. The five acids or esters range in increasing number of double bonds from zero in stearic to four in methyl arachidonate. The absorption values are plotted as the logarithm of the molecular extinction coefficients, ϵ, against wave lengths in angstroms and are extended to 2100 Å. at which value the greatest differences in absorption due to the double bond(s) are observable. At 2100 Å. the molecular extinction coefficients were found to be: stearic, 60; oleic, 180; methyl linoleate, 2500; methyl linolenate, 10,000; and methyl arachidonate, 14,500. Arachidonic acid with an iodine number four times that of oleic acid has a spectral absorption at 2100 Å., approximately eighty times as great.

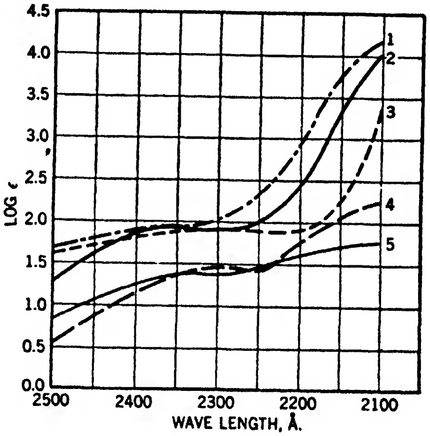

Fig. 31. Effect of unsaturation on the molecular extinction coefficients of fatty acids at various wave lengths[20]: (1) methyl arachidonate; (2) methyl linolenate; (3) methyl linoleate; (4) oleic acid; (5) stearic acid.

Recently, Rusoff, Platt, Klevens, and Burr[20a] extended the investigation of the ultraviolet absorption of the fatty acids into the Schumann region (to 1700 Å.) in which the saturated and nonconjugated unsaturated acids exhibit specific absorption. A wide variety of acids and esters, representing saturated and unsaturated, conjugated and nonconjugated, and *cis*- and *trans*-configurations, were examined. The compounds which were obtained from various sources and by different methods of preparation were not all of the same degree of homogeneity, but absorption spectra measurements on the whole confirmed most of the previous measurements made on these compounds and in addition provided for the first time information

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[20] R. H. Barnes, I. I. Rusoff, E. S. Miller, and G. O. Burr, *Ind. Eng. Chem., Anal. Ed.*, 16, 385–386 (1944).

[20a] I. I. Rusoff, J. R. Platt, H. B. Klevens, and G. O. Burr, *J. Am. Chem. Soc.*, 67, 673–678 (1945).

concerning the nature of the absorption for most of the compounds in regions below 2100 Å.

The saturated acids (acetic, caprylic, and myristic) were shown to have one broad band with a maximum at about 2050 Å., and another region of very intense absorption beginning at 1850 Å. and still rising steeply at 1730 Å., the limit of the measurements.

Oleic and elaidic acids exhibited strong absorption in the region of 2000 to 1700 Å. with a maximum about 1830 Å. The curve for elaidic acid was shifted approximately 40 Å. toward the visible end of the spectrum and the maximum absorption was *increased* about 15%. The authors concluded that the increased absorption at 2350 Å. was probably due to a trace of conjugated acid. On the other hand, the curves for ethyl linolenate and linolenelaidate showed that the absorption of the elaidinized product was shifted 25 Å. toward the visible end of the spectrum and the maximum absorption in the region of 1900 Å. was *decreased* about 11%.

It is notable that myristic acid measured in a polar solvent (ethanol), and oleic acid and the nonconjugated polyunsaturated acids measured in nonpolar solvents, exhibited various amounts of absorption in the region of 2300 Å., whereas myristic acid in a nonpolar solvent exhibited only a steeply rising curve in this region. The authors, like most other workers in this field, attribute the absorption at 2300 Å. in these compounds to the presence of diene conjugation. However, this assumption seems inadequate to explain the difference in absorption in this region of the same sample of myristic acid measured in two different solvents, and the method of preparation renders the presence of diene conjugation in the samples of oleic acid highly improbable. It would appear that some chromophore other than diene is present in these compounds.

(*b*) *Quantitative Expression of Absorption Data*

Before proceeding with a discussion of the literature and applications of ultraviolet absorption, it is necessary to mention the methods which have been used by various authors in expressing their data.

Since the objective of different investigators of ultraviolet absorption phenomena has differed, the mode of presenting the results has varied and intercomparison is sometimes difficult. Some authors have expressed their data in percentages of light absorbed or transmitted, while others have used absorption or extinction coefficients. Furthermore, there has been no uniformity in the units used to express the absorption and extinction coefficients or even the magnitude and position of the absorption. It is common European practice to use absorption coefficients while American practice leans more toward the use of logarithms to the base 10 and the consequent extinction coefficients.

Van der Hulst[21] has published ultraviolet absorption data for a number of unsaturated fatty acids in the form of curves in which extinction coefficients, log E (concentration in gram moles per liter), or log K (concentration in grams per liter) are plotted against the wave length. Kraybill *et al.*[22–24] expressed their results in terms of the specific absorption, *i. e.*, specific $\alpha = (\log_{10} I_0/I)/cl$, where α is the absorption coefficient; I_0, the intensity of radiation transmitted by the solvent; I, the intensity of radiation transmitted by the solution; c, the concentration of solution in g. per 1000 ml.; and l, the length in cm. of solution through which the radiation passes. Beadle and Kraybill[24] have published a table of reference values in terms of absorption coefficients at various wave lengths obtained for alkali-isomerized linoleic, linolenic, and arachidonic acids. These values, which obtain only for the specific conditions of alkali isomerization used by the authors, are given in Table 30.

TABLE 30

REFERENCE VALUES FOR USE IN ULTRAVIOLET SPECTROPHOTOMETRIC ANALYSIS OF FATTY ACIDS[a]

Isomerized fatty acid soap	Relative absorption coefficients[b]			
	2340 Å.	2680 Å.	3010 Å.	3160 Å.
Linoleic	86	..	..	..
Linolenic	60.9	53.2	..	..
Arachidonic	59.3	53.4	25.8	22.6

[a] B. W. Beadle and H. R. Kraybill, *J. Am. Chem. Soc.*, **66**, 1232 (1944).

[b] These values apply only to the conditions of alkali isomerization used by Beadle and Kraybill.

Moore and co-workers,[25–29] Brode *et al.*,[30,31] Burr and co-workers,[32,33] and others have used extinction coefficients, $E^{1\%}_{1\text{ cm.}}$, to express absorption values as a function of wave length in angstroms, although Brode *et al.*[1,30]

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[21] L. J. N. van der Hulst, *Rec. trav. chim.*, **54**, 639–643, 644–650 (1935).

[22] J. H. Mitchell, Jr., H. R. Kraybill, and F. P. Zscheile, *Ind. Eng. Chem., Anal. Ed.*, **15**, 1–3 (1943).

[23] J. H. Mitchell, Jr., and H. R. Kraybill, *Ind. Eng. Chem., Anal. Ed.*, **13**, 765–768 (1941).

[24] B. W. Beadle and H. R. Kraybill, *J. Am. Chem. Soc.*, **66**, 1232 (1944).

[25] W. J. Dann and T. Moore, *Biochem. J.*, **27**, 1166–1169 (1933).

[26] T. Moore, *Biochem. J.*, **31**, 138–154 (1937).

[27] J. Houston, A. G. Cotton, S. K. Kon, and T. Moore, *Biochem. J.*, **33**, 1626–1629 (1939).

[28] E. M. Cruickshank, J. Houston, and T. Moore, *Biochem. J.*, **33**, 1630–1634 (1939).

[29] T. Moore, *Biochem. J.*, **33**, 1635–1638 (1939).

[30] D. T. Mowry, W. R. Brode, and J. B. Brown, *J. Biol. Chem.*, **142**, 671–678 (1942).

[31] W. R. Brode, J. W. Patterson, J. B. Brown, and J. Frankel, *Ind. Eng. Chem., Anal. Ed.*, **16**, 77–80 (1944).

[32] E. S. Miller and G. O. Burr, *Proc. Soc. Exptl. Biol. Med.*, **36**, 726–729 (1937).

[33] F. A. Norris, I. I. Rusoff, E. S. Miller, and G. O. Burr, *J. Biol. Chem.*, **139**, 199–206 (1941). See *Ind. Eng. Chem., Anal. Ed.*, **16**, 385–386 (1944).

TABLE 31[a]

CONVERSION FACTORS[b] FOR ABSORPTION AND EXTINCTION COEFFICIENTS[c]

Coefficients		Absorption coefficients[d] (involving logarithms to base *e*)				Extinction coefficients (involving logarithms to base 10)			
		$\frac{\text{liters}}{\text{moles} \times \text{cm.}}$	$\frac{\text{ml.}}{\text{moles} \times \text{cm.}}$	$\frac{\text{liters}}{\text{g.} \times \text{cm}}$	$\frac{\text{ml.}}{\text{g.} \times \text{cm.}}$	$\frac{\text{liters}}{\text{moles} \times \text{cm.}}$	$\frac{\text{ml.}}{\text{moles} \times \text{cm.}}$	$\frac{\text{liters}}{\text{g.} \times \text{cm.}}$	$\frac{\text{ml.}}{\text{g.} \times \text{cm.}}$
Absorption coefficients	$\frac{\text{liters}}{\text{moles} \times \text{cm.}}$	1	0.001	M[e]	$0.001M$	2.303	2.303×10^{-3}	$2.303M$	$2.303 \times 10^{-3}M$
	$\frac{\text{ml.}}{\text{moles} \times \text{cm.}}$	1000	1	$1000M$	M	2303	2.303	$2303M$	$2.303M$
	$\frac{\text{liters}}{\text{g.} \times \text{cm.}}$	$\frac{1}{M}$	$\frac{0.001}{M}$	1	0.001	$\frac{2.303}{M}$	$\frac{2.303 \times 10^{-3}}{M}$	2.303	2.303×10^{-3}
	$\frac{\text{ml.}}{\text{g.} \times \text{cm.}}$	$\frac{1000}{M}$	$\frac{1}{M}$	1000	1	$\frac{2303}{M}$	$\frac{2.303}{M}$	2303	2.303
Extinction coefficients	$\frac{\text{liters}}{\text{moles} \times \text{cm.}}$	0.434	0.434×10^{-3}	$0.434M$	$0.434 \times 10^{-3}M$	1	0.001	M	$0.001M$
	$\frac{\text{ml.}}{\text{moles} \times \text{cm.}}$	434	0.434	$434M$	$0.434M$	1000	1	$1000M$	M
	$\frac{\text{liters}}{\text{g.} \times \text{cm.}}$	$\frac{0.434}{M}$	$\frac{0.434 \times 10^{-3}}{M}$	0.434	0.434×10^{-3}	$\frac{1}{M}$	$\frac{0.001}{M}$	1	0.001
	$\frac{\text{ml.}}{\text{g.} \times \text{cm.}}$	$\frac{434}{M}$	$\frac{0.434}{M}$	434	0.434	$\frac{1000}{M}$	$\frac{1}{M}$	1000	1

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[a] T. R. Hogness and V. R. Potter, "Spectrometric Studies in Relation to Biology," *Ann. Rev. Biochem.*, **10**, 509–530 (1941).

[b] To convert values of coefficients designated by the units in the top row into values designated by units in the first vertical column, multiply by the factor in the corresponding space.

[c] Coefficients indicated by units.

[d] The terms "absorption" and "extinction" have often been used interchangeably.

[e] M refers to molecular weight of solute.

prefer the use of frequencies expressed in fresnels or vibrations per second × 10^{-12}.

Hogness and Potter[34] have discussed in detail the various methods of expressing absorption data as they relate to Beer's law and have prepared a table of conversion factors for absorption and extinction coefficients (Table 31).

(c) *Applications of Ultraviolet Spectroscopy to the Examination of Fatty Acids*

No attempt will be made to review all of the literature on the ultraviolet absorption of the fatty acids and esters, but a few of the more important applications will be mentioned and the significance of the results pointed out.

Monoethenoid Acids.—Van der Hulst[21] determined the ultraviolet absorption spectra of so-called *chemically pure* and *optically pure* ethyl oleate. Whereas, the *optically pure* preparation showed no absorption maximum in the region of 2400 to 2550 Å., the *chemically pure* product exhibited a series of maxima between 2150 and 3350 Å., which was attributed to the presence of polymerization and oxidation products. Van der Hulst also observed that $\Delta^{2,3}$-oleic acid in which the ethylenic bond is conjugated with the carbonyl double bond in the carboxyl group possessed a strong absorption in the region of 2300 Å. although no distinct maximum was observable.

Polyethenoid Acids.—No specific absorption was observed by van der Hulst[21] with *optically pure* ethyl 9,12-linoleate, but the conjugated $\Delta^{9,10,11,12}$-linoleic acid gave a distinct maximum, attributable to diene conjugation, at 2300 Å. which has also been reported by other workers as occurring at 2300, 2320, and 2350 Å. depending on the nature of the product under investigation.

Ordinary linolenic acid, like linoleic acid, does not exhibit specific absorption maxima, but Dingwall and Thomson,[35] van der Hulst,[21] and others found that the conjugated positional isomer, elaeostearic acid, exhibited strong absorption with three maxima in the region of 2600 to 2800 Å. due to triene conjugation Alpha and β-elaeostearic acids were observed to possess similar absorption curves but the curve of the β-acid was shifted approximately 40 Å. toward the shorter wave lengths.

(*1*) *Alkali Isomerization.*—The detection by Dann and Moore[25] of absorption maxima at 2300 and 2700 Å. in fats which had been subjected to prolonged saponification with alcoholic potash established the fact that isolated double bonds are capable of being shifted to conjugated positions

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[34] T. R. Hogness and V. R. Potter, "Spectrometric Studies in Relation to Biology," *Ann. Rev. Biochem.*, 10, 509–530 (1941).

[35] A. Dingwall and J. C. Thomson, *J. Am. Chem. Soc.*, 56, 899–901 (1934).

by chemical treatment. Moore[26] observed that prolonged saponification of linseed oil with alcoholic potash resulted in a partial conversion of the 9,10,12,13,15,16-linolenic acid to a conjugated acid having strong absorption maxima at 2300 Å. and 2700 Å. Kass and Burr[36] found that a more rapid rearrangement could be brought about by reacting linolenic acid with concentrated solutions of potash in anhydrous butanol or ethylene glycol. They applied this method to the production of pseudo-elaeostearic acid (10,11,12,13,14,15-octadecatrienoic acid, m.p. 79°C.; methyl ester, m.p. 41°C.) from the unsaturated fatty acids of linseed oil.

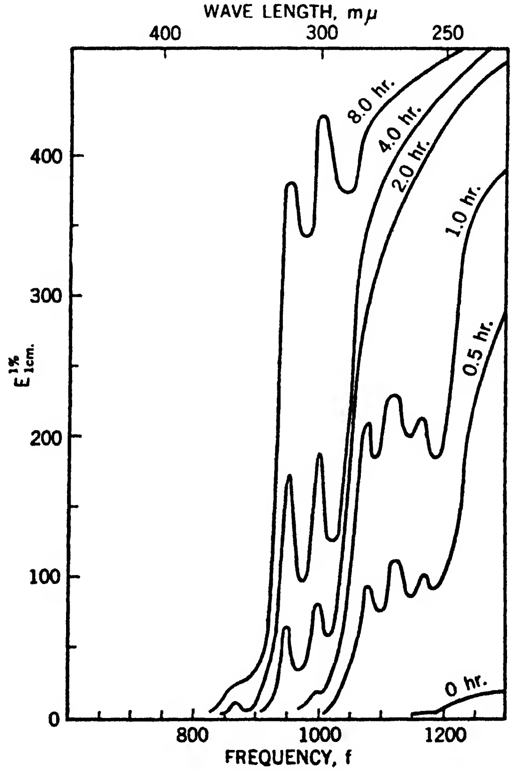

Fig. 32. Spectrophotometric changes during alkali isomerization of arachidonic acid.[30]

Following the catalytic hydrogenation of tung oil, Moore[29] found that the absorption maximum at 2700 Å. was reduced, and that a maximum was produced at 2300 Å., thus substantiating the fact that the absorption at 2700 Å. is due to the presence of three conjugated double bonds and the

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[36] J. P. Kass and G. O. Burr, *J. Am. Chem. Soc.*, **61**, 3292–3294 (1939).

absorption at 2300 Å. to two conjugated double bonds. Moore also observed that the prolonged saponification of a large variety of fats and oils containing linoleic acid resulted in the development of appreciable absorption at 2300 Å., thus proving that this type of saponification results in the formation of varying amounts of conjugated linoleic acid from ordinary linoleic acid. The marine oils, when similarly treated, developed absorption maxima at both 2300 and 2700 Å. indicating the formation of doubly and triply conjugated acids.

Mowry, Brode, and Brown[30] investigated the changes in the absorption which occurred in arachidonic acid during alkali isomerization. Methyl arachidonate was saponified with potassium hydroxide in ethylene glycol solution. Samples were removed at intervals from the saponification mixture and examined with respect to their absorption properties. The curves are shown in Figure 32 in which the change in the absorption, as the isolated double bond system is shifted to a conjugated system, is readily discernible. The extinction values at 2350, 2700, and 3000 Å. indicate the quantities of two, three, and four double bonds which are conjugated. The new acid containing four double bonds in conjugated positions was isolated by crystallization from petroleum ether at −20°C. Judged by its melting point, 95–98°C., the product was not of very high purity.

Mowry, Brode, and Brown,[30] made the theoretically important observation that the three well-defined absorption maxima observed with the isomerized arachidonic acid in absolute ethanol at frequencies of 952, 1000, and 1048 *f* and the inflection at 1100 *f* with respective values of $E^{1\%}_{1\,\text{cm.}}$ of 2200, 2400, 1900, and 700, corresponded to the 20th, 21st, 22nd, and 23rd multiples of a fundamental infrared band at 47.6 *f*. These values check those of Kuhn and Grundmann[37] for the hydrocarbon, $\Delta^{2,3,4,5,6,7,8,9}$-decatetraene which has a similar system of conjugated double bonds.

(*2*) *Effect of Bleaching on the Absorption Spectra of Unsaturated Fatty Acids.*—During the early applications of absorption spectroscopy, it was recommended that optically pure unsaturated acids be prepared by treatment with bleaching earth as a final step in their purification. However, the method cannot be applied to polyethenoid acids and probably not to monoethenoid acids even under the mild conditions recommended by the original proponents.

Mitchell and Kraybill[38] observed that treatment of methyl linoleate and ethyl linolenate with bleaching earth effected a change in the ultraviolet absorption of these esters. The change was found to be especially marked if the esters were first oxidized by blowing with air before treatment with bleaching earth.

Treatment of oxidized linoleic esters with bleaching earth produced an

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[37] R. Kuhn and C. Grundmann, *Ber.*, **71**, 442–447 (1938).

[38] J. H. Mitchell, Jr., and H. R. Kraybill, *J. Am. Chem. Soc.*, **64**, 988–994 (1942).

absorption band at 2680 Å. characteristic of triene conjugation, whereas similar treatment with alkali produced a band at 2320 Å. characteristic of diene conjugation. Similar treatment of oxidized linolenic esters produced bands at 2860, 3000, and 3160 Å. characteristic of tetraene conjugation as

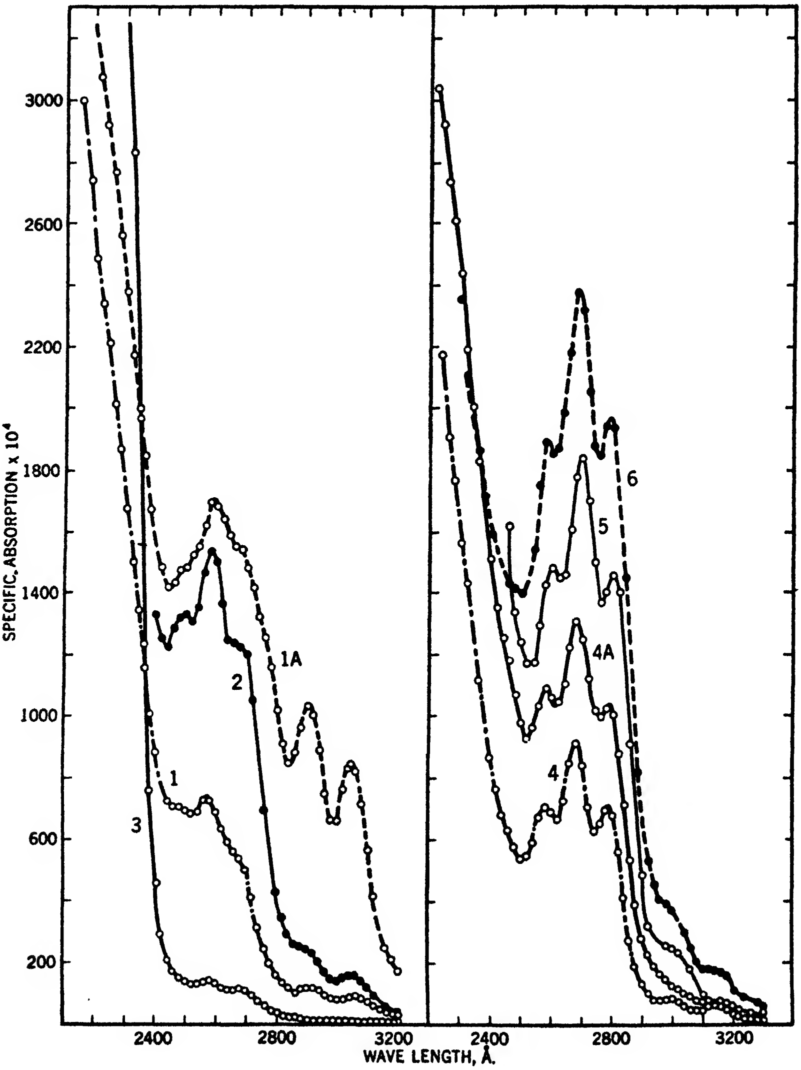

Fig. 33. Comparison of the absorption spectra of bleached and untreated polyethenoid esters and oils[38]: (1) ethyl linolenate; (1A) ethyl linolenate treated with Fuller's earth; (2) mixture of linoleate and linolenate treated with Fuller's earth; (3) methyl oleate; (4) methyl linoleate; (4A) methyl linoleate treated with Fuller's earth; (5) unbleached soybean oil plus tung oil (0.11%); (6) bleached corn oil.

well as a band at 2680 Å. whereas alkali treatment of linolenic esters gave rise to bands at 2680 and 2320 Å. characteristic of triene and diene conjugation, respectively. The characteristic absorption curves for these products are shown in Figure 33.

These results may be interpreted to indicate that treatment with alkali results in a shift of isolated double bonds already present in a polyunsaturated acid to conjugated positions, while treatment with bleaching earth causes the introduction of a new double bond in linoleic and linolenic acids in such a way that they are in conjugated positions. Since this result occurs only when the acid has been oxidized prior to treatment with bleaching earth, it may be concluded that the bleaching earth is acting as a dehydrating agent to remove the elements of water to produce new double bonds in conjugated positions. Several mechanisms by which the oxidation and dehydration might occur were postulated by the authors but proof is lacking as to their validity.

(*3*) *Preparation of Spectroscopically Pure Unsaturated Acids.*—Ultraviolet spectroscopy is particularly useful in determining the purity of polyunsaturated acids as has been demonstrated by Brode *et al.*[31] These authors examined a total of ten specimens of linoleic acid prepared by debromination of α- and β-tetrabromostearic acid. Di-, tri-, and tetraene conjugated acids were found in all samples in proportions varying from 0.46% in the best sample to 6.4% in the worst sample.

Wood and co-workers[39] determined the percentage of di-, tri-, and tetraene conjugation in various preparations of linoleic and linolenic acids and their corresponding chlorides used in the preparation of pure synthetic glycerides of known structure.

The utility of the spectroscopic method as an aid in preparing highly pure polyunsaturated acids is illustrated by the following examples.[40] The ultraviolet absorption spectra of four preparations of linoleic acid shown in Figure 34 were obtained by debromination of tetrabromostearic acid prepared from the same sample of corn oil. However, only by the introduction of one refinement after another in the generally accepted method of preparing linoleic acid was it possible to obtain the highly pure product shown in the last of the four spectral curves.

The preparation illustrated by the first curve of Figure 34 was obtained from tetrabromostearic acid (m.p. 114.2–115.0°C.) prepared according to the method of McCutcheon.[12] The tetrabromides were debrominated in ethyl ether according to the method of Frankel and Brown[15]; the ether was removed by evaporation *in vacuo* at room temperature and the acids fractionally distilled at 0.4 mm. pressure.

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[39] T. R. Wood, F. L. Jackson, A. R. Baldwin, and H. E. Longenecker, *J. Am. Chem. Soc.*, **66**, 287–289 (1944).

[40] R. T. O'Connor, D. C. Heinzelman, M. Caravella, and S. T. Bauer, *Oil & Soap*, **23**, 5–9 (1946).

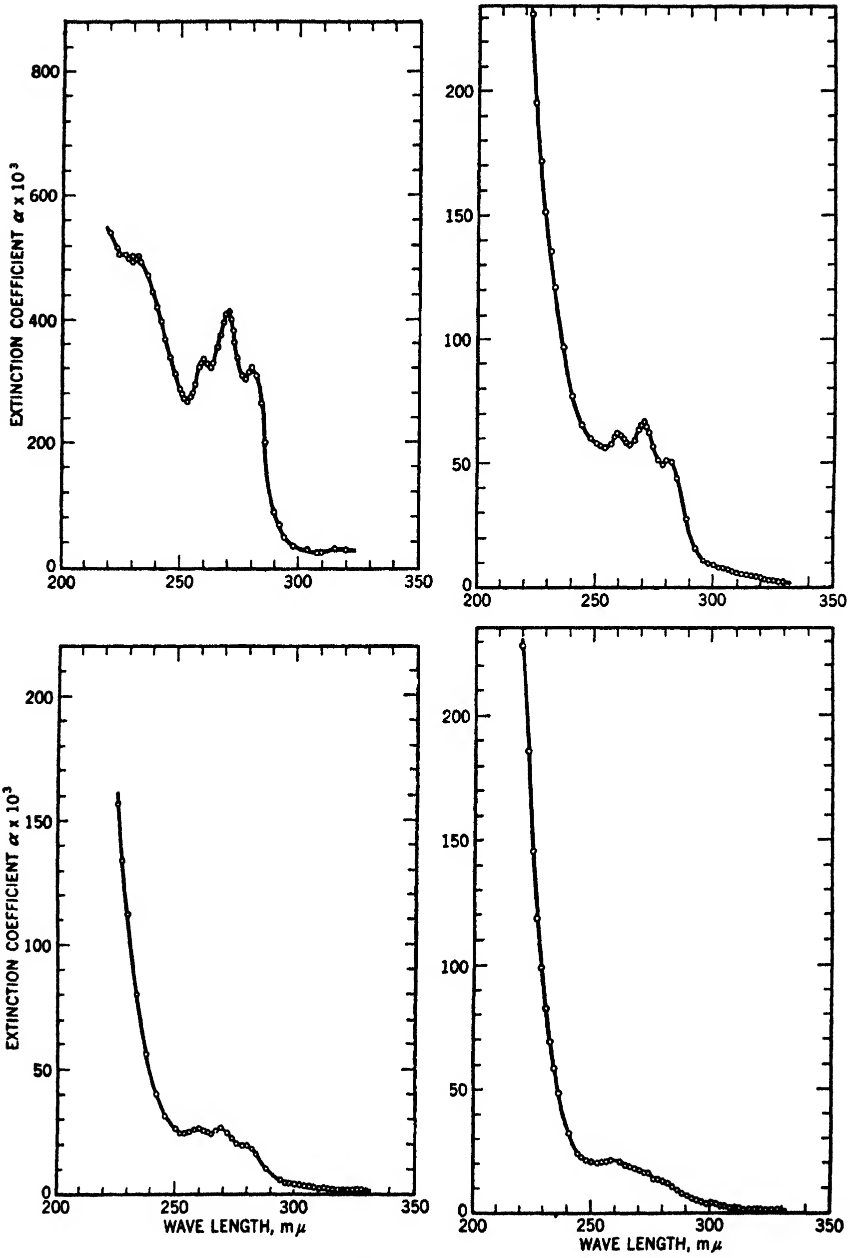

Fig. 34. Ultraviolet absorption spectra of four specimens of linoleic acid of different degrees of purity, measured in optically pure cyclohexane. Note that the first curve is on a scale different from the others because of the greater intensity of absorption of the conjugated impurities in this sample.

The product illustrated by the second curve was prepared from tetrabromostearic acid similar to that used in the first preparation, except that the bromides were dissolved in high boiling petroleum ether (Skellysolve L) and the solution treated with activated carbon. After crystallization of the bromides from petroleum ether, they were dissolved in ethyl ether, reprecipitated by the addition of petroleum ether, and recrystallized from Skellysolve L. The recrystallized tetrabromostearic acid melted at 115.5–115.8° C. Fractional distillation of the regenerated acid was carried out in a molecular still at 113–115°C. at 5 μ pressure to give the final product.

The preparation illustrated by the third curve of Figure 34 was obtained from thrice-crystallized tetrabromostearic acid, once from ethyl ether and twice from Skellysolve L. The tetrabromide (m.p. 115.5–115.8°C.) was debrominated in peroxide-free ether, and the ether solution of free acid filtered under an atmosphere of carbon dioxide, dried over sodium sulfate, and refiltered under the same conditions. The ether was evaporated under reduced pressure and the residual acid fractionally distilled at 113–115°C. at 4 μ pressure to obtain the final product.

The preparation represented by the fourth curve was prepared from the same tetrabromostearic acid but debromination was carried out in an atmosphere of nitrogen freed of oxygen by passage over hot copper. All subsequent steps were conducted as before but always in the presence of oxygen-free nitrogen, followed finally by molecular distillation at 113.0°C. and 1 μ pressure.

The increased purity of each succeeding preparation of linoleic acid is illustrated by the spectral curves and the analytical data in Table 32. The results of these and related investigations emphasize the necessity for the rigid exclusion of oxygen during the preparation of unsaturated fatty

TABLE 32

ANALYSIS OF LINOLEIC ACID PREPARED BY FOUR DIFFERENT METHODS

No.	Iodine value[a]	T.C. value[b]	Peroxide value[c]	Percentage of conjugation					
				Diene[d]	Triene[d]	Tetraene[d]	Diene[e]	Triene[e]	Tetraene[e]
1	177.0	95.5	...	0.408	0.104	0.0262	0.393	0.236	0.0145
2	178.5	94.5	...	0.080	0.0105	0.0028	0.097	0.038	0.0018
3	180.0	...	4.0	0.0311	0.0000	0.0013	0.0056	0.0009	0.0009
4	180.2	97.0	2.7	0.0248	0.0001	0.0018	0.0050	0.0007	0.0012

[a] Wijs (1 hr.) method; theoretical iodine value, 181.03.
[b] Theoretical thiocyanogen value, 90.5; accepted empirical value, 96.7.
[c] Milliequivalents of peroxide per kilogram of acid.
[d] Calculated according to the method of Brice *et al.*[41,42]
[e] Calculated according to the method of Brode *et al.*[31]

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[41] B. A. Brice, M. L. Swain, B. B. Schaeffer, and W. C. Ault, *Oil & Soap*, **22**, 219–224 (1945).

[42] B. A. Brice and M. L. Swain, *J. Optical Soc. Am.*, **35**, 532–544 (1945).

acids. The same observation was made by McCutcheon[12] who found that unless ethyl oleate was distilled directly into evacuated Raman tubes, oxidation products were formed whose fluorescence obscured the Raman spectra.

(*4*) *Other Applications.*—Other practical applications of ultraviolet spectroscopy in the field of fat and oil chemistry include the detection of soybean oil in mixtures with cottonseed oil,[43] the determination of α-elaeostearic acid in tung oil,[44] and measurement of the rate of oxygen absorption by β-elaeostearic acid.[45]

Burr and co-workers[32,46,47] have applied ultraviolet spectroscopy to investigations of the fate of ingested fats in the animal body. They found, for example, that when elaeostearic acid is fed to rats, it is quickly changed to a new acid having a high absorption at 2350 Å. and a corresponding loss of absorption at 2700 Å. This change in absorption indicates that one double bond of the elaeostearic acid is hydrogenated or otherwise destroyed after ingestion by the animal.

Hilditch, Morton, and Riley[48] confirmed the additive nature of the alkali isomerization of the esters of linoleic and linolenic acids with respect to ultraviolet absorption spectra, and extended the method of Mitchell *et al.*[22,23] to the determination of linolenic and/or linoleic acid in the presence of elaeostearic acid. The method was applied to the determination of the unsaturated acids in sunflowerseed oil, niger seed oil, linseed oil, tung oil, and a mixture of linseed and tung oils.

The foregoing discussion of the applications of spectroscopic methods, while not all-inclusive, is sufficient to indicate the value and utility of these tools and techniques in solving many of the problems confronting the worker in the field of fats and oils. Beadle[49] has recently reviewed current developments and summarized the present status of ultraviolet spectroscopy with examples of applications in the field of fatty acids and their derivatives.

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[43] R. T. O'Connor, D. C. Heinzelman, and F. G. Dollear, *Oil & Soap*, **22**, 257–263 (1945).

[44] R. T. O'Connor, D. C. Heinzelman, A. F. Freeman, and P. C. Pack, *Ind. Eng. Chem., Anal. Ed.*, **17**, 467–470 (1945).

[45] R. W. Brauer and L. T. Steadman, *J. Am. Chem. Soc.*, **66**, 563–569 (1944).

[46] E. S. Miller, R. H. Barnes, J. P. Kass, and G. O. Burr, *Proc. Soc. Exptl. Biol. Med.*, **41**, 485–489 (1939).

[47] G. O. Burr and E. S. Miller, *Chem. Revs.*, **29**, 419–438 (1941).

[48] T. P. Hilditch, R. A. Morton, and J. P. Riley, *Analyst*, **70**, 68–74 (1945).

[49] B. W. Beadle, *Oil & Soap*, **23**, 140–145 (1946).

CHAPTER VI

THERMAL PROPERTIES

1. Introduction

The utility and applicability of a given substance is determined by its physical properties, and more often than not, by the relative value of one specific property as compared to that of other members of the same class of compounds. For example, the sodium salts of lauric, myristic, and palmitic acids find extensive employment as components of soaps because, of all the saturated fatty acids, they possess solubilities and surface-acting properties which render them most valuable as detergents. Similarly, castor oil and ricinoleic acid find many uses in the textile, petroleum, and lubrication fields because they exhibit certain viscosity behavior and surface-acting properties not found in other vegetable oils and fatty acids.

Generally speaking, as our knowledge of the physical properties of a given material increases, the applications and uses of this material likewise increase. For a long time, man had to rely almost entirely on his perceptive senses as a means of determining the nature and estimating the magnitude of the properties of matter, and consequently, such knowledge as was obtained, was purely qualitative. Gradually one means after another has been devised to measure various specific properties. These devices in their original forms were relatively simple and not highly accurate, as, for example, the chemical balance, the thermometer, and simple lenses, but with the development of more complicated and precise instruments, many new and sometimes quite abstract properties were discovered and measured with an increasing degree of accuracy. Many of these have proved to be extremely valuable both from a theoretical as well as a practical point of view.

Many organic, and especially synthetic organic, compounds have been systematically investigated with respect to a variety of physical properties, and data pertaining to them have been compiled, classified, and recorded in readily available form. This, however, has not been the case with regard to the naturally occurring higher fatty acids despite the fact that some of them have been known and have been the subject of scientific investigation for a century or more. Until very recently, such measurements as have been made were often made in an unsystematic manner and often on not very pure materials. Many of the measurements which have been reported are so scattered throughout a voluminous literature that they are located only by chance, or by the expenditure of a disproportionate amount of time and energy.

In the following pages there are brought together considerable data with reference to a number of the more important properties of the fatty acids and some of their derivatives. An effort has been made to do this in a critical manner but this has not always been possible, as in some cases only a single measurement of a given property has been reported. In other cases there is no way of judging the purity of the material used, or the accuracy of the method employed, in measuring a specific property. Many gaps occur in the data for some of the homologous series, and it is not always possible to determine the approximate value of the undetermined property by interpolation of such data as are available.

2. Heats of Formation and Combustion

(a) *Saturated Acids*

Practically all of the available information on the heats of formation and combustion of the higher fatty acids and their derivatives is due to Stohmann and co-workers.[1,2] These investigations are now more than a half century old and were carried out with products of unknown purity.

Kharasch[3] critically reviewed the literature on the heats of combustion of organic compounds and compiled a table of "best" values available up to 1929. This table includes a considerable number of saturated, unsaturated, mono- and polybasic, hydroxy, keto and other substituted aliphatic acids. The table also includes, in many cases, calculated values for heats of combustion and the experimentally determined values most nearly in agreement with the calculated value. Because of this selection, a much higher degree of correspondence is indicated between the experimental and determined values than would otherwise be expected on the basis of the probable purity of the acids generally available at the time many of the measurements were made. This is especially true of the unsaturated acids which have only recently been obtained in a relatively high state of purity. No unsaturated acid containing more than one double or one triple bond is included in the table.

The heats of combustion in Kharasch's table are expressed both in absolute kilojoules (at constant pressure) per gram molecular weight of substance *in vacuo* and in kilogram-calories at 15°C. A selected group of compounds from this table are included in a compilation contained in the

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[1] F. Stohmann, C. Kleber, H. Langbein, and P. Offenhauer, *J. prakt. Chem.*, **49**, 99–129 (1894).

[2] F. Stohmann, *Z. physik. Chem.*, **10**, 410–424 (1892).

[3] M. S. Kharasch, *Natl. Bur. Standards J. Research*, **2**, 359–430 (1929).

International Critical Tables,[4] but the heats of combustion are expressed in 1922 International Combustion Calories per gram formula weight (*in vacuo*) in the liquid state, when combustion is carried out at constant pressure of one atmosphere and at 18–20°C. to form gaseous carbon dioxide and liquid water. The heats of combustion for the saturated fatty acids from these two compilations are compared in Table 33. Heats of combustion of only a few aliphatic esters are found in either of the abovementioned compilations, and those of Kharasch,[3] which are the most extensive, are given in Table 34.

TABLE 33

HEATS OF COMBUSTION OF SATURATED FATTY ACIDS[a]

Acid	*International Critical Tables*	Kharasch Kg.-cal.$_{15°}$	
		Experimental[b]	Calculated
Formic	62.8	62.8	65.1
Acetic	209.4	209.4	208.4
Propionic	365	367.2	364.7
n-Butyric	520	524.3	521.0
n-Valeric	679	681.6	677.3
Caproic	831.0	831.0	833.6
Heptanoic	986.1	986.1	989.9
Capric	1453 (s)	1458.1	1458.8
Undecanoic	1610 (s)	1615.9	1615.1
Lauric	1772 (s)	1771.7	1771.4
Myristic	2086 (s)	2085.8	2084.0
Palmitic	2380 (s)	2398.4	2396.6
Stearic	2698 (s)	2711.8	2709.2
Arachidic	3010 (s)	3025.9	3021.8
Behenic	3338 (s)	3338.4	3334.4

[a] All values for liquid state except where indicated by (s), which indicates solid state.
[b] Selected experimental value nearest to calculated.

TABLE 34

HEATS OF COMBUSTION OF FATTY ACID ESTERS EXPRESSED IN KG.-CAL.$_{15°}$ PER MOLE IN THE LIQUID STATE EXCEPT WHERE OTHERWISE INDICATED[a]

Acid	Methyl ester		Ethyl ester		Triglyceryl ester
	Exptl.	Calcd.	Exptl.	Calcd.	Exptl.
Formic	233.1	...	391.7	...	...
Acetic	381.2	381.2	539.9	...	...
Propionic	552.3 (V)	537.5	690.8	693.8	...
Butyric	692.8	693.8	851.2	850.1	1941.1
Valeric	...	...	1017.5	1006.4	2308.6
Lauric	...	...	...	...	5706.3 (s)
Myristic	...	...	...	...	6650.3 (s)
Erucic	...	...	...	...	10264.7 (s)

[a] M. S. Kharasch, *Natl. Bur. Standards J. Research*, **2**, 359–430 (1929).

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[4] National Research Council, *International Critical Tables.* Vol. V, McGraw-Hill, New York, 1929, pp. 165–166.

(b) *Unsaturated Acids*

Data relative to the long chain unsaturated fatty acids are likewise nonextensive, as is indicated by reference to Tables 35 and 36 containing the values for the heats of combustion of several saturated acids, the corresponding *cis*- and *trans*-monoethenoid isomers, the monoethinoid acids, and the differences in the heats of combustion for the several pairs of these acids.

TABLE 35

COMPARATIVE HEATS OF COMBUSTION OF SOME SATURATED AND UNSATURATED FATTY ACIDS, KG.-CAL.$_{20°}$ PER MOLE

Acid	Formula	Experimental (solid)	Calculated (liquid)	Number of double bonds
Undecanoic	$C_{11}H_{22}O_2$	1615.9	1615.1	0
Undecenoic	$C_{11}H_{20}O_2$	1579.7	1576.0	1
Undecinoic	$C_{11}H_{18}O_2$	1537.8	1544.0	1 triple bond
Stearic	$C_{18}H_{36}O_2$	2711.8	2709.2	0
Oleic (*cis*)	$C_{18}H_{34}O_2$	2681.8 2657.0	2663.6	1
Elaidic (*trans*)	$C_{18}H_{34}O_2$	2664.2	2670.1	1
Stearolic	$C_{18}H_{32}O_2$	2628.6	2638.1	1 triple bond
Behenic	$C_{22}H_{44}O_2$	3338.4	3334.4	0
Erucic (*cis*)	$C_{22}H_{42}O_2$	3296.7	3295.3	1
Brassidic (*trans*)	$C_{22}H_{42}O_2$	3290.1	3288.8	1
Behenolic	$C_{22}H_{40}O_2$	3254.9	3263.3	1 triple bond

TABLE 36

DIFFERENCES IN HEATS OF COMBUSTION IN KG.-CAL.$_{20°}$ PER MOLE FOR PAIRS OF ACIDS SHOWN IN TABLE 35

Pairs of acids	Experimental	Calculated
Undecanoic–undecenoic	36.2	39.1
Undecanoic–undecinoic	78.1	71.1
Stearic–oleic	30.0 and 54.8	45.6
Stearic–stearolic	83.2	71.1
Behenic–erucic	41.7	39.1
Behenic–behenolic	83.5	71.1
Oleic–elaidic	17.6 and −7.2	−6.5
Erucic–brassidic	6.6	6.5

From the data in Tables 35 and 36 it is evident that both the experimental and calculated values for the heat of combustion of oleic acid are out of line with those for the related acids. Keffler[5] refers to the publications of Stohmann[1,6] wherein the heat of combustion of oleic acid was reported to be 2682.0 kg.-cal. and that of solid elaidic acid as 2664.3 kg.-cal. When these values are corrected according to the Landolt-Börnstein tables, and the value for elaidic acid calculated for the liquid state, as was done by

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[5] L. J. P. Keffler, *J. Phys. Chem.*, **34**, 1319–1325 (1930).

[6] F. Stohmann, *J. prakt. Chem.*, **31**, 273–306 (1885).

Keffler, the two values become 2680.1 kg.-cal. for oleic acid, and 2677.2 kg.-cal. for elaidic acid, or a difference of +2.9 kg.-cal. These values, although perhaps not entirely accurate, indicate that the *cis*-isomer possesses the higher heat of combustion in accordance with Stohmann's rule that the *cis*-isomer of a given pair of geometrical isomers should have the higher heat of combustion.

Keffler[5] determined the heats of combustion of oleic and elaidic acids, obtaining a mean value from four determinations of 9343 cal.$_{20°}$ per g., or 2638.9 kg.-cal. per mole, for the solid isomer. The values for oleic acid varied from 9542 cal. per g., for a two-day-old sample, to 9412 cal. per g. for the same acid after two years, with various values in between depending on the age of the sample. The heat of combustion of a sample of freshly distilled oleic acid was found to be 9473 cal. per g. when determined within two hours of preparation. This value decreased hourly to 9446 cal. per g. during the first 24 hours after preparation, or a change of 26 cal. per g. These values have been calculated to a kg.-cal. per mole basis and included in Table 37 together with other previously mentioned values for oleic acid.

TABLE 37

HEATS OF COMBUSTION OF OLEIC AND ELAIDIC ACIDS, KG.-CAL. PER MOLE

Oleic acid	Elaidic acid	Difference	Investigator
2663.6[a]	2670.1[a]	6.5	Kharasch
2681.8 2657.0	2664.1	17.7	Kharasch
2680.1	2677.2	2.9	Stohmann-Keffler
2695.1[b]	2638.9	56.2	Keffler
2668.0[c]	...	...	Keffler
2659.5[d]	...	...	Keffler

[a] Calculated.
[b] Fresh preparation.
[c] Twenty hours after preparation.
[d] Two years after preparation.

The different values for the heats of combustion of oleic and elaidic acids shown in Table 37 are not strictly comparable owing to differences in units employed in their calculations, but they are sufficiently so to indicate the fact that their heats of combustion are still not accurately known. The values obtained by different investigators reflect the difficulty of preparing and maintaining these acids in a pure state rather than a lack of precision in the experimental determination of the heats of combustion. It is significant that, with the exception of the lower value given by Kharasch,[3] the heat of combustion found for oleic acid is higher than for elaidic acid which is in accordance with other known facts concerning the relative stabilities of these two acids. It is obvious that the calculated values of the heats of combustion, if reversed, would be more nearly in accord with the experimental values.

Following the development of more rigorous methods of purifying oleic acid, Keffler[7,8] prepared a series of esters of oleic and elaidic acids and determined their heats of combustion with the results shown in Table 38. In each case the oleate was found to have the higher heat of combustion and the average isothermal heat of transition from oleate to elaidate was found to be about +1.6 kg.-cal. per mole.

TABLE 38

HEATS OF COMBUSTION OF LIQUID OLEATES AND ELAIDATES IN KG.-CAL.$_{15°}$ PER MOLE[a]

Alkyl radical	Oleate	Elaidate	Molecular heat of transformation
Methyl	2837.2	2835.7	+1.5
Ethyl	2988.2	2988.9	−0.7
Propyl	3146.2	3144.7	+1.5
Butyl	3302.3	3300.6	+1.7
Amyl	. . .	3456.5	. . .

[a] L. J. P. Keffler and J. H. McLean, *J. Soc. Chem. Ind.*, 54, 178–185T, 362–367T (1935); L. J. P. Keffler, *J. Phys. Chem.*, 41, 715–721 (1937).

(c) *Glycerides*

Few data are available for the heats of combustion of mono- and diglycerides which are especially significant with respect to the structural symmetry and stability of these compounds. Clarke and Stegeman[9] determined the heats of combustion of α- and β-monopalmitin which were found to be, respectively, 2778.78 and 2788.30 kg.-cal. per mole for the reaction at one atmosphere pressure and 25°C., or −9.52 kg.-cal. per mole for the shift from the β- to the α-position.

Stohmann and co-workers determined the heats of combustion of many fatty acids and esters among which were glyceryl dierucate, m.p. 47°C., and glyceryl dibrassidate, m.p. 67°C. These esters were prepared by Stohmann and Langbein[10] according to the method of Reimer and Will,[11] and nothing is known concerning their structural configuration or homogeneity. The heats of combustion for glyceryl dierucate and dibrassidate were found to be 6979.0 and 6953.0 kg.-cal.$_{15°}$ per mole, respectively. The glyceride of the *cis*-isomer has the higher heat of combustion which is in

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[7] L. J. P. Keffler and J. H. McLean, *J. Soc. Chem. Ind.*, **54**, 178–185T, 362–367T (1935).

[8] L. J. P. Keffler, *J. Phys. Chem.*, **41**, 715–721 (1937).

[9] T. H. Clarke and G. Stegeman, *J. Am. Chem. Soc.*, **62**, 1815–1817 (1940).

[10] F. Stohmann and H. Langbein, *J. prakt. Chem.*, **42**, 361–382 (1890).

[11] C. L. Reimer and W. Will, *Ber.*, **19**, 3320–3327 (1886).

accord with the known stability of such geometrical isomers. The classical work of Stohmann should be consulted for additional data and for more detailed information on the heats of combustion of the various compounds already mentioned, and for the natural fats, including lard, beef and mutton tallows, butter, and duck and goose fats.

3. Vapor Pressure and Related Properties

Of the various colligative properties of the higher fatty acids and esters, none is so important theoretically and practically as vapor pressure and the related properties, boiling point and heat of vaporization. It is only within the past few years that any systematic determinations have been made of these important properties of the fatty acids and much more work remains to be completed to place our knowledge of these properties on a par with that of other and much less important organic compounds.

(a) *Saturated Acids*

Lederer,[12] one of the first to determine the molecular heats of vaporization and the heat of vaporization of fatty acids at atmospheric pressure, stated, in an article published in 1930: "It appears almost incredible that, after fifty years of large-scale fatty acid distillation, data relative to these important properties are not known; at least they are not found in the literature." To this statement Lederer appended a footnote which reads: "Here might be mentioned a fact which is not without its humorous angle. A famous German equipment company, which required a knowledge of heats of vaporization of fatty acids for use in fabricating a condenser for a fatty acid still, turned to research chemists (specialists in fats and oils) for this information. One 'estimated' a heat of vaporization of 100 calories, another regretted that he could not find a value in the literature. One explained that fatty acids had in general no heats of vaporization at all, since they could not be boiled without decomposition (at atmospheric pressure)." In the fifteen-year interval since that time, our knowledge has improved considerably, but the opportunities for research in this field are far from exhausted.

Although now somewhat outmoded, and not too exact in many respects owing to the lack of reliable experimental data, portions of Lederer's work are given here as an example of the early (1930) treatment of the vapor pressure–temperature relationships of fatty acids.

Through the application of thermodynamic principles an equation can be derived for vapor pressure–temperature relation which can be brought to the form:

$$\ln p = -\frac{\lambda_0}{RT} + 1.75 \ln T - \frac{\epsilon T'}{R} + C \tag{1}$$

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[12] E. L. Lederer, *Seifensieder-Ztg.*, 57, 67–71 (1930).

where p is the vapor pressure at any optional absolute temperature T (°C. + 273), λ_0 the molecular heat of vaporization at absolute zero, R the gas constant, ϵ the temperature coefficient of the difference between specific heats in the liquid and gaseous state, and C' the so-called "conventional chemical constant." If the natural logarithm, ln, is replaced by the common logarithm, log, and there is substituted for the gas constant its numerical value (1.985 cal./°C.), equation (*1*) becomes:

$$(2) \qquad \log p = -\frac{\lambda_0}{4.571\ T} + 1.75 \log T - \frac{\epsilon}{4.571}\,T + C$$

From the data available in the literature for the boiling points of the higher fatty acids under different pressures, there can be calculated the values given in Table 39 which apply when the vapor pressure is measured in millimeters of mercury. The heat of vaporization at any absolute temperature T can be expressed approximately by the equation:

$$(3) \qquad \lambda = (\lambda_0 + 1.75\ RT - \epsilon T^2)\left(1 - \frac{p}{P}\right)$$

where the P is the critical pressure, which lies between 30 and 40 atm. for the higher fatty acids. If accurate data are not available, equation (*3*) can still be used for calculation when the pressure is not too high. At atmospheric pressure the factor in the second term of equation (*3*) has a value varying but little from unity (about 0.97), and at 100 mm. pressure it is only 0.996.

A knowledge of the three constants λ_0, ϵ, and C makes it possible to calculate over a very restricted temperature interval, the vapor pressure at a given temperature, or, what amounts to the same thing, the boiling point of the fatty acid at a given pressure. These three constants are given for a series of fatty acids in Table 39. In addition, the molecular heat of evapo-

TABLE 39

CALCULATED CONSTANTS APPLICABLE TO VAPOR PRESSURE EQUATION FOR HIGHER ALIPHATIC ACIDS[a]

Acid	λ_0	ϵ	C	λ_a	l_a	T_a	λ_a/T_a (calcd.)	Trouton
Capric	22990	0.0334	11.318	14660	85	543	27.0	22.3
Lauric	23590	0.0349	11.408	13740	68.5	574.6	23.9	22.5
Myristic	24960	0.0334	11.493	14700	67.5	601	24.5	22.8
Palmitic	26050	0.0326	11.568	15090	58.5	625	24.2	23.0
Stearic	27280	0.0317	11.636	15860	56	647	24.5	23.2
Oleic	26660	0.0304	11.340	16050	57	642	25.0	23.1
Erucic	29310	0.0264	11.458	...	...	...	...	...

[a] E. L. Lederer, *Seifensieder-Ztg.*, **57**, 67–71 (1930).

ration at atmospheric pressure, λ_a, can be calculated by means of equation (*3*). The values for λ_a are given in column 5, Table 39, and in the next column are the heats of vaporization l_a of the fatty acids at atmospheric pressure in Cal. per kg.

It should be noted that the heats of vaporization of fatty acids at pressures occurring in industrial practice are very often higher than those obtaining at atmospheric pressure. By means of equation (*3*) it is easy to calculate, for example, that lowering of the pressure from 1 atm. to 100 mm. increases the value of the heat of vaporization on the average 10 Cal. per kg. (about 20%); lowering it to 5 mm. increases this value by an average of 20 Cal. per kg. (about 40%). However, this is not important industrially because the increase in heat necessary for evaporation is small in comparison with the usual heat losses resulting from radiation, conduction, etc.

There are also given in Table 39 the absolute boiling points of the fatty acids at atmospheric pressure, T_a, as found in the literature (prior to 1930); also the proportion $\lambda_a : T_a$. This proportion should agree with the values given in the last column of Table 39 which were calculated on the basis of the Trouton-Nernst rule. From the fact that the value of this proportion is always greater than that calculated by the Trouton-Nernst rule, it may be concluded that the fatty acids in the liquid state are fairly completely associated, while in the vapor state the vapor density corresponds to their normal molecular weight.

With the aid of the data given in Table 39, the vapor pressures of the various acids at definite temperatures have been calculated and compared in Table 40 with the values given in the Landholt-Börnstein tables. Since the constants are derived from the data at atmospheric pressure and at 100 mm. pressure, it is self-evident that the calculated and experimental values will agree at both these points. Their inclusion in Table 40 is, therefore, unnecessary. For oleic acid, pressures of 100 mm. and of 10 mm. were used for purposes of computation for lack of accurate data at atmospheric pressure. Because of the good agreement between the calculated and the experimentally determined values, equation (*3*) was assumed to be reliable for use in calculating the boiling point, using the constants given by Lederer. It should be borne in mind, however, that at the time (1930) very few data were available in the literature by which this equation could be checked.

It is evident from Table 39 that the values of the constants for the various fatty acids do not differ greatly, and this is especially true of the temperature coefficient of specific heat, ϵ. It is evident that in equation (*2*) the terms, with the exception of the first and last, are merely correction factors, and it can be assumed therefore that the difference in the specific heats of the fatty acids in the liquid and vapor states is almost independent of temperature. Consequently, equation (*2*) may be written in a much simpler form, or a graphical method may be used in its place, thus obviating the necessity for calculations in many cases.

Inspection of equation (*2*) indicates that if both middle terms are disregarded, and the reciprocal values of the absolute temperatures be plotted as abscissas against the logarithms of the vapor pressures (in mm.) as ordinates, the result will be a straight line. If the middle terms are not disregarded, the plot of the data will depart slightly from a straight line as is indicated in Figure 35. On the other hand, it can be assumed that, because of the small differences in the critical pressures of the fatty acids, their boiling points comprise corresponding states.[12a,12b] This is also the case at any temperature at which the quotient of the absolute boiling point and the temperature in question is the same; and the desired data for any fatty acid whatever can be read from such a graphical plot, at least with accuracy sufficient for engineering calculation, when only the boiling point

Table 40

VAPOR PRESSURE AT VARIOUS TEMPERATURES FOR SEVERAL FATTY ACIDS ACCORDING TO LEDERER[a]

Acid	Temperature, °K.	Vapor pressure, mm.	
		Calcd.	Found
Capric	458	45	50
	439	19.4	21
	426	10	10
Lauric	484	55	50
	472	32	35
	465	27	27
	462	23	24
	451	14.4	13.2
Myristic	506	54.6	50
	497	38.8	40
	493.7	34.8	35
	490.4	30.5	30
	486.2	25.9	25
	480.6	20.6	20
	467.7	11.9	12
	463.8	10	10
Palmitic	498	19.1	22.1
	493	15.8	15.7
	488	13.0	15
Stearic	505	8.7	15
Oleic	537	49	50
	523	29.5	30
	506	15.2	15

[a] E. L. Lederer, *Seifensieder-Ztg.*, **57**, 67–71 (1930).

[12a] G. van Iterson, *Z. physik. Chem.*, **53**, 633–640 (1905).
[12b] J. H. Hildebrand, *J. Am. Chem. Soc.*, **37**, 970–978 (1915).

at atmospheric pressure (or eventually at any other given pressure) is known.

The two curves reproduced in Figure 35 were obtained by plotting as abscissas, the quotients of the absolute boiling points at atmospheric pressure divided by the observed temperatures at any other pressure (T_a/T) and plotting as ordinates the corresponding pressures in mm. The ordinates at the right (pressure in mm.) and the abscissas at the bottom (atmospheric boiling points divided by the required temperatures) are read from the solid line, the ordinates at the left and the abscissas at the upper edge are read from the broken line; the solid line is drawn over a pressure range of from 600 to 3 mm. of mercury, the broken line over a range from 4 to 0.01 mm. of mercury. The value and use of this graph are best illustrated by a few practical examples, as follows: At what temperature does stearic acid boil at a pressure of 20 mm. taking T_a = 647°K. (374°C.) from Table 39? By reference to the solid line it is found that a pressure of 20 mm. corresponds to an abscissa of 1.25; T_a divided by 1.25 gives 517°K. or 244°C. As another example, it might be desired to know the pressure at which

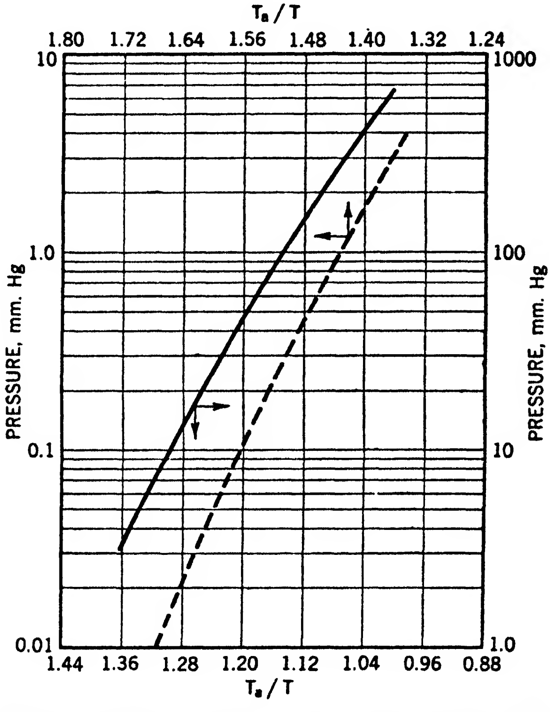

Fig. 35. Relation between vapor pressure and boiling points of the fatty acids.[12]

myristic acid would boil at a temperature of 228°C. (501°K.), $T_a = 601$°K. (328°C.). T_a divided by 501°K. gives 1.20, for which abscissa the corresponding pressure is found to be 47 mm.

For problems occurring in industry, the solid line will be generally used in dry distillation, but for steam distillation involving the determination of the boiling point at a given pressure, or the vapor pressure at a given temperature, frequent use must be made of the broken line. In the case of steam distillation other data are necessary, namely, the proportion by weight of steam used for distillation to the amount of acid to be distilled. However, both pressure and temperature may be given and the problem may be to determine the proportion by weight of steam and fatty acid.

For steam distillation, Dalton's Law of Partial Pressure can be applied as a good approximation. If the total pressure is p, the partial pressure of the fatty acid is x, the molecular weight of the fatty acid is M (that of steam is 18), and the proportion by weight of steam to fatty acid is v, then, with an accuracy sufficient for industrial use, $v = 18(p-x)/Mx$. The method of calculation may be illustrated by the following: At what temperature does palmitic acid boil at 100 mm. pressure when the proportion by weight of steam to acid is 1:1 ($v = 1$)? Here, $p = 100$, $M = 256$, and since $v = 1$, it can be calculated by means of the equation just given that $x = 6.6$ mm. At this ordinate (solid line) it is found that the abscissa is 1.318 and, therefore, the temperature sought ($T_a = 625$) is 625 divided by 1.318 = 475°K. = 202°C.

It may be desired to know, for example, what pressure should be used to distill oleic acid ($M = 282$) at a temperature of 187°C. or 460°K., with twice the amount of steam ($v = 2$). $T_a = 642$, and 642 divided by 460 = 1.39. This abscissa corresponds to a partial pressure, $x = 1.9$ mm. on the dotted line. By means of the above equation the desired total pressure p can be calculated as 61.4 mm. Another example might be to determine what proportion of water by weight should be used to distill stearic acid ($M = 284$) at a total pressure of 30 mm. and a temperature of 157°C. or 430°K. T_a divided by 430 = 1.50. At this abscissa it is found from the broken line that the partial pressure is 0.3 mm.; therefore:

$$v = (18 \times 29.7)/(284 \times 0.3) = 6.2$$

therefore, more than six times as much water as fatty acid must be used.

Although sometimes desirable as a laboratory operation, distillation of a single pure fatty acid is very seldom conducted on an industrial scale, whereas distillation of mixtures of fatty acids is an important operation on both scales. In general, mixtures of fatty acids can be fractionated until a maximum boiling point is reached. At this temperature the mixture exhibits a constant boiling point and further separation by means of fractional distillation cannot be achieved.

Since Lederer published his article, additional data have become available with respect to the boiling points and vapor pressures of the fatty acids and their derivatives which may be applied as he has indicated in the solution of practical problems.

Gensecke[13] investigated the vapor pressure–temperature relations of the fatty acids from acetic to docosanoic over a limited pressure range (2 to 100 mm.) employing steam distillation under vacuum. The curves obtained by this means are reproduced in Figure 36 in which the temperatures in °C. are plotted as abscissas against the logarithms of the vapor pressures as ordinates. The vapor pressure curves obtained in this manner, although not as accurate as those obtained by the use of dry distillation, are nevertheless useful in cases where more accurate data are not available.

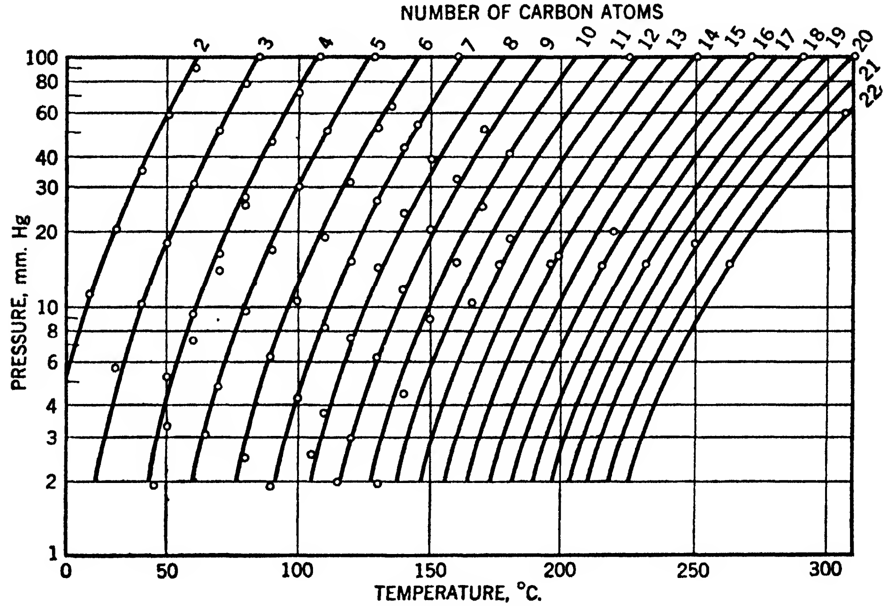

Fig. 36. Boiling points of the fatty acids under conditions of vacuum-steam distillation.[13]

The most accurate determination of the vapor pressure–temperature relationships for the fatty acids and their derivatives has been made by Ralston and co-workers. Pool and Ralston[14] determined the boiling points of the *n*-alkyl acids from C_6 to C_{18} over a range of pressures from 1 to 760 mm. and computed the data required to construct the corresponding vapor pressure–temperature curves which are reproduced in Figure 37.

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[13] W. Gensecke, in *Chemie und Technologie der Fette und Fettprodukte.* Vol. II, G. Hefter and H. Schönfeld, eds., Springer, Vienna, 1937, p. 508.

[14] W. O. Pool and A. W. Ralston, *Ind. Eng. Chem.*, **34**, 1104–1105 (1942).

Cramer[15] determined the vapor pressures of the even-numbered fatty acids from caproic to stearic by the static method of Smith and Menzies[16] with the results shown in Figure 37a. By means of the equation:

$$\frac{d \ln p}{d(1/T)} = -\frac{W}{R}$$

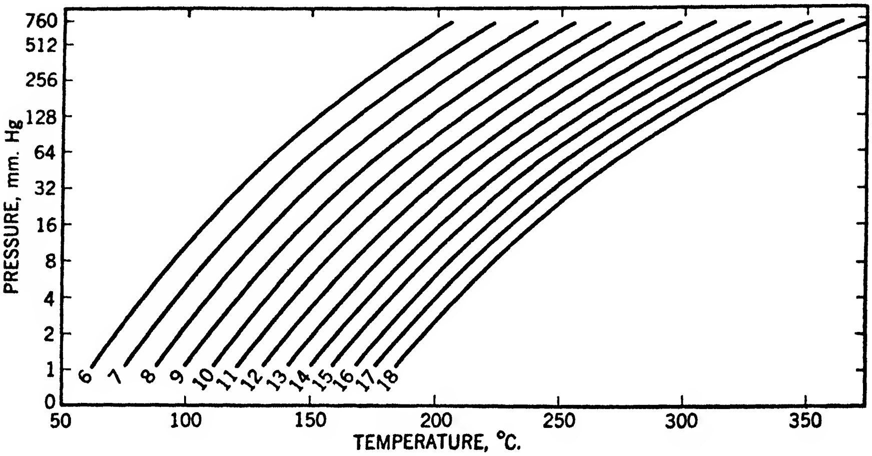

Fig. 37. Vapor pressure curves of the n-alkyl acids containing from 6 to 18 carbon atoms.[14]

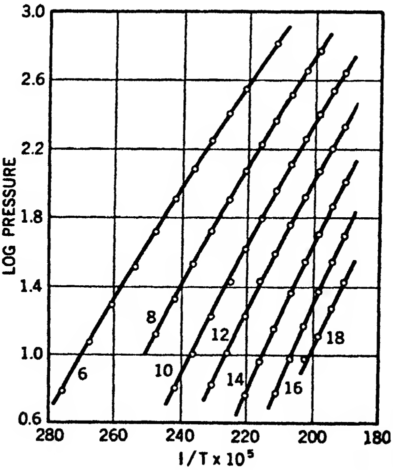

Fig. 37a. Relation between vapor pressure in millimeters and temperature of saturated fatty acids. Numbers refer to number of carbon atoms in acid.[15]

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[15] J. S. N. Cramer, *Rec. trav. chim.*, **62**, 606–610 (1943).

[16] A. Smith and A. W. C. Menzies, *J. Am. Chem. Soc.*, **32**, 1412–1434 (1910).

where W is the heat of vaporization per gram mole, T the absolute temperature, and R the gas constant, he calculated the heats of vaporization of the acids at the temperatures shown in Table 41.

TABLE 41

CALCULATED HEATS OF VAPORIZATION OF SATURATED ACIDS AT VARIOUS TEMPERATURES[a]

Acid	Temperature, °C.	Heats of vaporization, cal./g.
Caproic	94	133
	135	129
	190	113
Caprylic	134	116
	172	108
	224	97
Capric	145	99
	187	99
	246	85
Lauric	164	97
	247	77
Myristic	182	93
	209	87
	243	75
Palmitic	202	84
	244	76
Stearic	242	67

[a] J. S. N. Cramer, *Rec. trav. chim.*, **62**, 606–610 (1943).

The foregoing data relative to the experimental and calculated values for the boiling points and heats of vaporization, while still lacking in completeness, nevertheless represent a very great improvement in our knowledge of these properties of the saturated fatty acids in comparison to that available fifteen years ago.

(b) *Alkyl Esters of the Saturated Acids*

The boiling points at atmospheric pressure of the alkyl esters of the lower molecular weight fatty acids are well known as indicated by the compilation of Reid[17] which is reproduced in Table 42. Recently, Althouse

TABLE 42

BOILING POINTS IN DEGREES CENTIGRADE AT ATMOSPHERIC PRESSURE OF ALKYL ESTERS OF LOWER MOLECULAR WEIGHT ALIPHATIC ACIDS

Alkyl radical	Formates	Acetates	Propionates	Butyrates	Valerates	Hexoates	Heptoates	Octoates
Methyl	31.8	57.1	79.9	102.3	127.3	149.5	172.5	192.9
Ethyl	54.3	77.1	99.1	121.3	145.5	166.6	187.5	205.8
Propyl	81.3	101.6	123.4	143.0	167.5	185.5	206.4	224.7
Butyl	106.8	126.5	145.4	164.4	185.6	204.3	225.1	240.5
Amyl	130.4	147.6	...	184.8	203.7	222.2	...	...
Hexyl	153.6	169.3	...	205.1	223.8	...	...	...
Heptyl	176.7	191.5	208.1	225.2	243.6	259.4	274.0	289.8
Octyl	198.1	210.1	226.4	244.5	260.2	268.2	290.4	305.9

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[17] E. E. Reid, *College Organic Chemistry.* Van Nostrand, New York, 1929.

and Triebold[18] determined the boiling points of the methyl esters of the even-numbered, saturated acids from caproic to stearic, over the pressure range of 2 to 40 mm. as shown in Table 43. Vapor pressures for each ester were determined by the dynamic method of Ramsay and Young[19] and the corresponding vapor pressure curves were constructed by plotting the reciprocal of the absolute temperature × 1000 against the logarithm of the pressure in millimeters of mercury. The curves, thus constructed, were extrapolated to 760 mm. pressure as shown in Figure 38. These authors also determined the decomposition pressures and temperatures of the same series of esters as shown in Table 44.

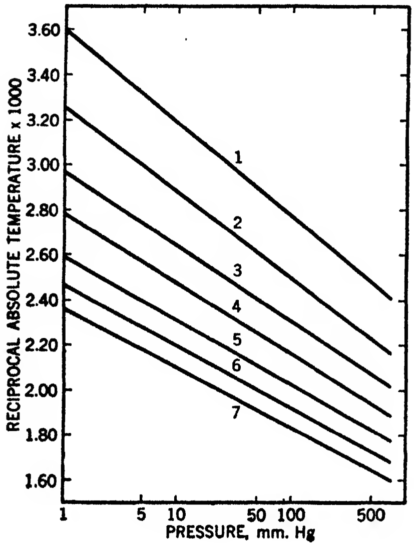

Fig. 38. Vapor pressure curves of methyl esters of the even-numbered fatty acids from caproic to stearic[18]: (1) methyl caproate; (2) methyl caprylate; (3) methyl caprate; (4) methyl laurate; (5) methyl myristate; (6) methyl palmitate; (7) methyl stearate.

Subsequently, Norris and Terry[20] published the results of their determinations of the boiling points of the methyl esters of myristic, palmitic, stearic, oleic, and linoleic acids over the pressure range of 1 to 20 mm. (Table 45). The corresponding heats of evaporation were calculated by application of the Clausius-Clapeyron equation and compared

TABLE 43

BOILING POINTS IN DEGREES CENTIGRADE OF METHYL ESTERS AT VARIOUS PRESSURES[a]

Ester	Pressure in millimeters of mercury						
	2	4	6	8	10	20	40
Methyl caproate	15	26	33	38	42	55	70
Methyl caprylate	45	58	65	71	76	89	106
Methyl caprate	77	89	97	103	108	123	139
Methyl laurate	100	113	121	128	134	149	166
Methyl myristate	127	141	150	157	162	177	197
Methyl palmitate	148	162	172	177	184	202	[b]
Methyl stearate	166	181	191	199	204	[b]	[b]

[a] P. M. Althouse and H. O. Triebold, *Ind. Eng. Chem., Anal. Ed.*, **16**, 605–606 (1944).
[b] Decomposes.

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[18] P. M. Althouse and H. O. Triebold, *Ind. Eng. Chem., Anal. Ed.*, **16**, 605–606 (1944).
[19] W. Ramsay and S. Young, *J. Chem. Soc.*, **47**, 42–45 (1885).
[20] F. A. Norris and D. E. Terry, *Oil & Soap*, **22**, 41–46 (1945).

with those of the corresponding acids. Reference to these data in Table 46 indicates that the latent heats of vaporization of myristic, palmitic, and stearic acids are 3200 to 3800 cal. per mole greater than those of the corresponding methyl esters.

TABLE 44

DECOMPOSITION PRESSURES AND TEMPERATURES OF METHYL ESTERS OF FATTY ACIDS[a]

Ester	Pressure in millimeters of mercury	Temperature, °C.
Methyl caproate	>760	>150
Methyl caprylate	>760	>193
Methyl caprate	>760	>224
Methyl laurate	160	204
Methyl myristate	60	205
Methyl palmitate	25	151
Methyl stearate	18	221
Methyl oleate	16	217
Methyl linoleate	11	208

[a] P. M. Althouse and H. O. Triebold, *Ind. Eng. Chem., Anal. Ed.*, **16**, 605–606 (1944).

TABLE 45

BOILING POINTS IN DEGREES CENTIGRADE OF METHYL ESTERS AT VARIOUS PRESSURES[a]

Methyl	Pressure in millimeters of mercury				
	1	2	5	10	20
Myristate	114	125	143.5	157.5	172.5
Palmitate	136	149	166.5	180.5	196.5
Stearate	155.5	170	189.5	204.5	222
Oleate	152.5	166.5	186	201	218.5
Linoleate	149.5	163	182.5	198	215

[a] F. A. Norris and D. E. Terry, *Oil & Soap*, **22**, 41–46 (1945).

TABLE 46

HEATS OF VAPORIZATION FOR METHYL ESTERS AND FATTY ACIDS[a]

Methyl	L_v, cal./mole	Acids	L_v, cal./mole
Myristate	17,550	Myristic	20,800[b]
Palmitate	18,900	Palmitic	22,100[b]
Stearate	19,000	Stearic	22,800[b]
Oleate	18,900	. . .	. . .
Linoleate	18,750	. . .	. . .

[a] F. A. Norris and D. E. Terry, *Oil & Soap*, **22**, 41–46 (1945).
[b] Calculated from data of Pool and Ralston.

(c) *Unsaturated Acids and Esters*

Except for oleic acid and the methyl esters of oleic, linoleic, and linolenic acids, few data are available relative to the vapor pressure–temperature relationships of the unsaturated fatty acids and esters.

Boiling points for oleic acid have been reported, among others, by Lederer[12] and by Brown and Shinowara,[21] and for methyl oleate by Althouse and Triebold[18] and by Norris and Terry[20] as indicated in the compilation in Table 47.

TABLE 47

BOILING POINTS OF OLEIC ACID AND METHYL OLEATE

Oleic acid				Methyl oleate		
Pressure, mm.		B.p., °C.	Ref. No.	Pressure, mm.	B.p., °C.	Ref. No.
Obs.	Calcd.					
1.2	..	200	21	1	152.5	20
5.0	..	215	21	2	166.5	20
					166.2	18
10.0	..	225	21	4	182	18
15.0	..	234	21	5	186	20
15.2	15	233	12	6	192	18
29.5	30	250	12	8	201	20
					199.5	18
				10	205.3	18
49	50	264	12	20	218.5	20

TABLE 48

BOILING POINTS OF METHYL LINOLEATE AND METHYL LINOLENATE

Pressure, mm.	Methyl linoleate, °C.	Ref. No.	Methyl linolenate,^{d} °C.	Ref. No.
1	149.5	20	...	23
2	166.5	18	...	
	163	22	...	
2.5	175	22	174	
4	182.4	18	184	
4.5	187.5	20	...	
5	182.5	20	...	
6	193.0	18	...	
	193.5	22	...	
6.5	...		198	
8	199.9	18	...	
10	206.0	18	...	
	198	20	...	
11	...		211	
12	212	22	...	
15	...		218	
17	224	22	...	
20	215	20	...	

Owing to the thermal instability of the higher polyethenoid acids, accurate boiling point determinations can be made only over a limited tempera-

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[21] J. B. Brown and G. Y. Shinowara, *J. Am. Chem. Soc.*, **59**, 6–8 (1937).
[22] J. W. McCutcheon, *Can. J. Research*, **B16**, 158–175 (1938).
[23] J. W. McCutcheon, *Can. J. Research*, **B18**, 231–239 (1940).

ture–pressure range. Boiling point determinations have been reported for methyl linoleate by Norris and Terry,[20] Althouse and Triebold,[18] and by McCutcheon,[22] and for methyl linolenate by McCutcheon,[23] as shown in Table 48. While in general the boiling points of methyl linoleate shown in Table 48 are fairly consistent, some inconsistencies are noted, especially at the higher temperatures and pressures where partial decomposition may have occurred.

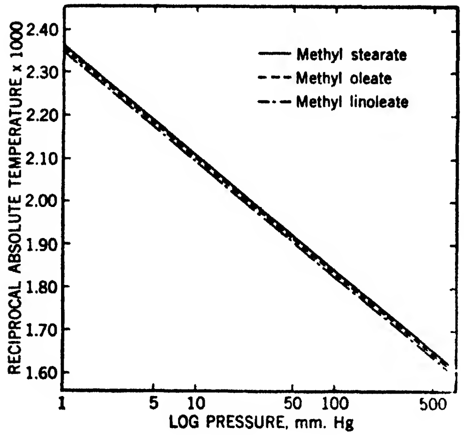

Fig. 39. Vapor pressure curves of methyl stearate, methyl oleate, and methyl linoleate according to Althouse and Triebold.[18]

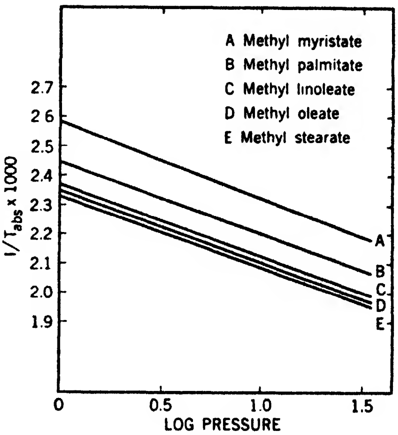

Fig. 39a. Vapor pressure curves of saturated and unsaturated methyl esters according to Norris and Terry.[20]

Althouse and Triebold[18] and Norris and Terry[20] determined the vapor pressures of methyl oleate and methyl linoleate and constructed the vapor pressure curves shown in Figures 39 and 39a. It is apparent from inspection of the vapor pressure curves of the saturated esters that the lower members should be readily separable by distillation and that, as the series is ascended, this type of separation should become increasingly difficult. Comparison of the vapor pressure curves of methyl stearate, methyl oleate, and methyl linoleate indicates that their separation by distillation should be very difficult.

Furthermore, comparison of the data of Althouse and Triebold with that of Norris and Terry reveals several inconsistencies, principally in the relative positions of the vapor pressure curves for the methyl esters of the three C_{18}-acids. Althouse and Triebold found them to be in descending order stearate–oleate–linoleate, whereas Norris and Terry found them to be linoleate–oleate–stearate. According to the latter authors, these discrepancies are due to inaccuracies in the data of Althouse and Triebold. In substantiation of this view, they state that the order of Althouse and Triebold's vapor pressure curves is contrary to practical experience since they obtained 95% methyl oleate in the first fractions from the distillation of a methyl oleate–methyl stearate mixture and some concentration of methyl linoleate in the first fractions from the distillation of a methyl linoleate–methyl oleate mixture.

Table 49

BOILING POINTS OF SOME UNSATURATED FATTY ACIDS AND METHYL ESTERS[a]

Acid	Acid b.p., °C.	Methyl ester b.p., °C.	Acid	Acid b.p., °C.	Methyl ester b.p., °C.
$\Delta^{9,10}$-Decenoic	142^{4}	$115\text{–}16^{12}$	Erucic	281^{30}	225^{5}, $169\text{-}70^{1}$
Dodecenoic	...	$89\text{–}90^{1}$	Ricinoleic	...	225^{10}
$\Delta^{5,6}$-Tetradecenoic	...	$110\text{–}11^{1}$	Hydnocarpic	...	203^{20}
Myristoleic	...	$108\text{–}109^{1}$	Chaulmoogric	248^{20}	227^{20}
Palmitoleic	...	$134\text{–}35^{1}$	Gorlic	...	219^{12}
Elaidic	...	150^{1}	Elaeostearic	235^{12}	...
Petroselinic	...	150^{1}	Arachidonic	...	$160\text{–}65^{1}$
Eicosenoic	...	160^{1}	Clupanodonic	...	$170\text{–}75^{1}$

[a] Superscripts refer to pressures in millimeters of mercury.

The discrepancies between the results of these two groups of workers attest to the difficulties encountered in the separation by distillation of the higher fatty acids and esters of the same chain length. See Chapter XXII for further treatment of this subject.

Only a few scattered values for the boiling points have been reported for other than the three previously mentioned unsaturated acids. Typical of these data are the values collected in Table 49 which represent, for the most part, observations made during fractional distillation of mixtures of fatty acids or esters containing the specific compound as the principal product.

CHAPTER VII

SOLUBILITY OF FATTY ACIDS AND SOLUTION PROPERTIES

1. Introduction

A solution may be defined as a homogeneous mixture of various molecular species or as a one-phase system consisting of two or more molecular species. Pairs of substances which are capable of forming solutions when brought in contact, do so to very different degrees, depending on the nature of the two substances and the conditions under which they are mixed. For example, at some specified temperature water and acetic acid may be miscible in all proportions, whereas water and stearic acid may be almost immiscible.

When two substances are mixed to form a solution, one component is referred to as the solvent and the other as the solute. In the case of solutions of two liquids either component may be considered as the solvent. For example, at −3°C. a mixture of water and butyric acid will contain 39.5% of butyric acid and the water may be considered as the solvent, whereas a mixture of caproic acid and water at 46°C. will contain 9.7% of water and caproic acid may be considered as the solvent.

Solutions in general, and so-called ideal solutions in particular, exhibit the same interrelationships between colligative properties—vapor pressure, boiling points, freezing points, etc.—as are exhibited by pure liquids, and they are amenable to the same type of thermodynamic treatment, although the effect of changing concentrations complicates their quantitative treatment. Besides colligative properties, solutions possess other properties such as refractive index, viscosity, conductivity, etc., which are of importance in evaluating or utilizing the systems comprising such mixtures. In the act of mixing two substances, physical phenomena involving changes in heat content, volume, density, etc., occur which may be of considerable magnitude and importance, especially when such processes are carried out on a large scale.

The investigation of the solubility relationships and the properties of solutions forms one of the most important fields of physical chemical research, and one which has received a vast amount of attention over a period of many years. However, but little of the work in this field has been directed toward the fatty acids, and particularly toward the higher fatty acids. This is probably due in part to the relatively low solubility of these substances in water and the fact that organic solutions are more difficult to investigate than are aqueous types. Only in the past few years, and primarily through the efforts of a single group of workers, has our knowledge of the solubilities of the fatty acids and related compounds (alcohols, ketones, amines, amine salt, anilides, and diphenylamides) been placed in a comparable position with other and less important homologous series of organic compounds.

The data with reference to solubility determinations may be expressed in several ways and the choice of the mode of expression is generally dependent on the use which is to be made of the results. Data collected in solubility tables are generally expressed as grams of solute in one hundred milliliters of solvent at a specified temperature, usually 20°C. Since different solvents possess different densities, solubility properties are not readily comparable on this basis; therefore, it is often preferable to express the composition on a weight per cent basis, *i. e.*, on the basis of the number of grams of solute which are soluble in one hundred grams of solvent. Although the latter method is preferable in many instances, it is not convenient for use in investigations of the colligative properties of solutions which are dependent on the relative number of molecules present in the solution rather than the relative weights of the substances present. In this case it is necessary to express composition in terms of gram molecular weights or mole fractions, *i. e.*, in moles, equivalents, or formula weights per liter of solution or per one thousand grams of solvent.

2. Miscible Aqueous Systems

(*a*) *Solutions of Fatty Acids and Water*

The fact that the normal fatty acids exhibit appreciable solubilities in water compared to the corresponding hydrocarbons is due to the presence in the former of the polar or hydrophilic carboxyl group. The lowest molecular weight hydrocarbons are slightly soluble in water at room temperature but their solubility decreases rapidly as the carbon chain increases and above C_8H_{18} they are practically insoluble. In contrast to the hydrocarbons the first four members of the saturated fatty acid series are miscible with water in all proportions at room temperature and even valeric acid, C_4H_9-COOH, is soluble to the extent of 3.7 g. per 100 g. water.

These relations are emphasized by the solubility values for the first seven normal hydrocarbons and those of the corresponding acids shown in Table 50. It is evident, from the data in Table 50 that, as the hydrocarbon chain increases, the ability of the carboxyl group to bring about solubility of the acid in water becomes decreasingly effective. As will be shown later, its ultimate effect will be merely to orient the fatty acid with respect to a water surface.

Ralston and Hoerr[1] reported the results of a systematic investigation of the solubility in water of the normal fatty acids from caproic to stearic at various temperatures between 0° and 60°C. Their results are reproduced in Table 51. Ralston and his co-workers[2] also determined the effect of the addition of water on the depression of the freezing point of the same series of fatty acids with the results shown in Figure 40. Reference to the curves of Figure 40 indicates that the maximum depression for any given acid is greater than that of the next higher member of the series; also that the maximum lowering of the freezing point varies from approximately 2°C. in the case of caproic acid containing 2.2% of water to approximately 0.5°C. for stearic acid saturated with water.

TABLE 50

SOLUBILITY OF NORMAL HYDROCARBONS AND CORRESPONDING FATTY ACIDS IN WATER AT 20°C. (EXCEPT AS OTHERWISE INDICATED)

Hydrocarbon			Acid		
Name	Formula	g./100 g.	Name	Formula	g./100 g.
Ethane	CH_3CH_3	470	Acetic	CH_3COOH	∞
Propane	$CH_3CH_2CH_3$	650^{18}	Propionic	CH_3CH_2COOH	∞
Butane	$CH_3(CH_2)_2CH_3$	1500^{17}_{772}	Butyric	$CH_3(CH_2)_2COOH$	∞
Pentane	$CH_3(CH_2)_3CH_3$	0.036^{16}	Valeric	$CH_3(CH_2)_3COOH$	3.7
Hexane	$CH_3(CH_2)_4CH_3$	0.0138^{15}	Caproic	$CH_3(CH_2)_4COOH$	0.9
Heptane	$CH_3(CH_2)_5CH_3$	0.005^{15}	Heptanoic	$CH_3(CH_2)_5COOH$	0.24
Octane	$CH_3(CH_2)_6CH_3$	0.001_{16}	Caprylic	$CH_3(CH_2)_6COOH$	0.07

TABLE 51

SOLUBILITIES OF FATTY ACIDS IN WATER[a]

Acid	Grams acid per 100 grams water				
	0.0°C.	20.0°C.	30.0°C.	45.0°C.	60.0°C.
Caproic	0.864	0.968	1.019	1.095	1.171
Heptanoic	0.190	0.244	0.271	0.311	0.353
Caprylic	0.044	0.068	0.079	0.095	0.113
Nonanoic	0.014	0.026	0.032	0.041	0.051
Capric	0.0095	0.015	0.018	0.023	0.027
Undecanoic	0.0063	0.0093	0.011	0.013	0.015
Lauric	0.0037	0.0055	0.0063	0.0075	0.0087
Tridecanoic	0.0021	0.0033	0.0038	0.0044	0.0054
Myristic	0.0013	0.0020	0.0024	0.0029	0.0034
Pentadecanoic	0.00076	0.0012	0.0014	0.0017	0.0020
Palmitic	0.00046	0.00072	0.00083	0.0010	0.0012
Heptadecanoic	0.00028	0.00042	0.00055	0.00069	0.00081
Stearic	0.00018	0.00029	0.00034	0.00042	0.00050

[a] A. W. Ralston and C. W. Hoerr, *J. Org. Chem.*, **7**, 546–555 (1942).

These authors also determined the approximate solubilities of water in fatty acids at various temperatures and computed those of the undeter-

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[1] A. W. Ralston and C. W. Hoerr, *J. Org. Chem.*, **7**, 546–555 (1942).

[2] C. W. Hoerr, W. O. Pool, and A. W. Ralston, *Oil & Soap*, **19**, 126–128 (1942).

TABLE 52

APPROXIMATE SOLUBILITIES OF WATER IN SATURATED FATTY ACIDS AT VARIOUS TEMPERATURES[a]

Acid	Temp., °C.	Water, %	Acid	Temp., °C.	Water, %
Caproic	−5.4	2.21	Lauric	42.7	2.35
	12.3	4.73		75.0	2.70
	31.7	7.57		90.5	2.85
	46.3	9.70	Tridecanoic	40.8	2.00
Heptanoic	−8.3	2.98	Myristic	53.2	1.70
	42.5	8.98	Pentadecanoic	51.8	1.46
Caprylic	14.4	3.88		90.0	1.62
Nonanoic	10.5	3.45	Palmitic	61.8	1.25
Capric	29.4	3.12	Heptadecanoic	60.4	1.06
Undecanoic	26.8	2.72	Stearic	68.7	0.92
	57.5	4.21		92.4	1.02

[a] C. W. Hoerr, W. O. Pool, and A. W. Ralston, *Oil & Soap*, **19**, 126–128 (1942).

mined systems with the results shown in Table 52. From the data in this table it may be seen that increasing the temperature increases the solubility of water in the acids of low molecular weight, but in the case of the higher members it has only a very small effect.

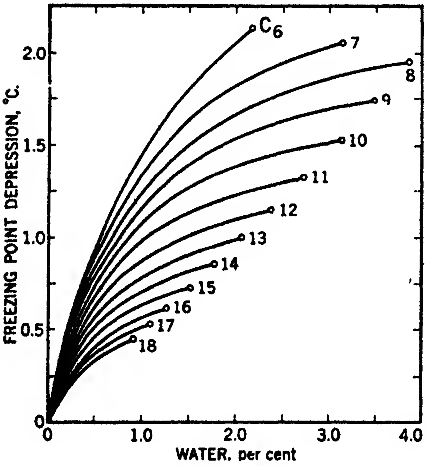

Fig. 40. Effect of addition of water on the freezing point[2] of the fatty acids from C_6 to C_{18}.

(*b*) *Dissociation and Electrical Conductance*

Solution of a fatty acid in water is accompanied by dissociation of the molecule into ions in a manner analogous to inorganic acids. The acidic properties, or the ionizable hydrogen of all the fatty acids, have their origin in the same portion of the molecule, namely, the carboxyl group. While the hydrogen of the carboxyl group is as replaceable by metals as that of inorganic acids, dissociation of fatty acids in aqueous solution occurs to a much smaller degree than is the case with strong mineral acids.

The degree of dissociation of an acid and its relative strength is expressed as the dissociation constant. This constant, which is derived from the dilution law, relates the degree of dissociation of a weak acid and its dilution. If, in the case of the fatty acids which are dissociated as follows:

$$C_nH_{2n+1}COOH \rightleftharpoons C_nH_{2n+1}COO^- + H^+$$

it is assumed that one gram mole of acid is dissolved in y liters of water, and x gram mole is dissociated, then the concentration of ions is x/y and that of the undissociated acid $(1 - x)/y$, and from the law of mass action under equilibrium conditions:

$$\frac{[H]^+[C_nH_{2n+1}COO]^-}{[C_nH_{2n+1}COOH]} = \frac{x^2/y^2}{(1-x)/y} = k = \frac{x^2}{y(1-x)}$$

The values of k for the normal fatty acids have been determined only for the series formic to nonanoic, because the solubility of the acids in water is very slight with chain lengths above C_9.

Closely related to the dissociation of fatty acids into ions, is the electrical conductance of their solutions. In fact, the conductance of such solutions serves as a measure of the degree of dissociation of the dissolved acids.[3] These relationships are emphasized by the values for the dissociation constants and equivalent conductances of the acids shown in Table 53.

Table 53

DISSOCIATION CONSTANTS AND EQUIVALENT CONDUCTANCES FOR NORMAL FATTY ACIDS IN AQUEOUS SOLUTIONS AT 25°C.[a]

Acid	Dissociation constant, $k \times 10^5$	Equivalent conductance, Λ_0
Formic	21.0	404
Acetic	1.813	390.8
Propionic	1.32	386
Butyric	1.50	383
Valeric	1.56	381
Caproic	1.40	379
Heptanoic	1.30	378
Caprylic	1.41	377
Nonanoic	1.1	377

[a] J. Kendall, in *International Critical Tables*. Vol. VI, McGraw-Hill, New York, 1929, pp. 259–304.

From this table it is seen that formic acid undergoes dissociation to an extent about ten times greater than acetic acid. Acetic acid has a dissociation constant of 1.8×10^{-5} and is, therefore, a weak and sparingly dissociated acid. A 1 M aqueous solution is dissociated only to the extent of 0.4% compared to the strong mineral acids which are completely ionized in dilute solutions. Tenth normal acetic acid is only about one-hundredth as much dissociated as 0.1 N hydrochloric acid, that is—it is only one-hundredth as strong as hydrochloric acid.

Propionic acid is even more feebly ionized and as the series is ascended the dissociation constants and equivalent conductances decrease but

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[3] J. Kendall, "Electrical Conductivity and Ionization Constants of Weak Electrolytes in Aqueous Solution," in *International Critical Tables*. Vol. VI, McGraw-Hill, New York, 1929, pp. 259–304.

slightly. Although all of these acids are feebly acidic, they are stronger than carbonic acid ($k_1 = 3.4 \times 10^{-7}$). The relative dissociation constants of the fatty acids indicate that they will be liberated from their alkali salts by hydrochloric acid, and that they in turn will liberate carbonic acid from sodium bicarbonate.

The degree of dissociation is often affected appreciably by temperature, but in the case of the fatty acids variation of the value of the dissociation constant is small.

The alkali salts of the very weakly dissociated higher fatty acids are always considerably hydrolyzed in aqueous solution, and as a result their solutions react alkaline as indicated by the equation:

$$C_nH_{2n+1}COONa + HOH \rightleftharpoons C_nH_{2n+1}COOH + NaOH$$

The normal aliphatic acids, or at least the lower members which have been investigated, are strongly associated, and at temperatures just above their boiling points have molecular weights twice the molecular weight corresponding to their empirical formulas. Because of the tendency of the fatty acids to exist as dimers they are capable of forming salts of the formula: $C_nH_{2n+1}COONa \cdot C_nH_{2n+1}COOH$.

Substitution of various substituents, especially halogens and hydroxyls, for hydrogen in the methylene chain markedly affects the dissociation constant of the resultant acid. The most marked effect occurs when the substitution takes place in the methylene group nearest the carboxyl, and decreases with increasing distance from this group. The effect of substitution of various atoms and radicals on the dissociation constant of fatty acids is illustrated in Table 54.

TABLE 54

EFFECT OF SUBSTITUTION AND POSITION OF SUBSTITUENT ON VALUE OF DISSOCIATION CONSTANT ($k \times 10^5$) OF FATTY ACIDS

Substituent	Acetic	Propionic		Butyric			Valeric
	α	α	β	α	β	γ	δ
None	1.85	1.32	1.32	1.53	1.53	1.53	1.59
CH_3	1.32	1.48	1.53	1.69	1.67	1.59	1.46
Cl	147.0	160.0	8.59	140.0	8.85	2.96	2.0
Br	132.0	106.0	9.3	102.0	...	2.61	1.88
I	70.0	...	8.6	...	...	2.26	1.68
OH	15.0	13.6	3.07	31.0	...	1.90	1.32
SH	22.5	...	...	...	...	...	...

The α,ω-dibasic acids are both more soluble and more extensively dissociated than the corresponding monobasic acids. Since the dibasic acids contain two carboxyl groups, both of which yield hydrogen ions, they have two dissociation constants, k_1 and k_2, of which the former is very much greater than the latter.

3. Immiscible Aqueous Systems

It was mentioned previously that the solubility of the normal fatty acids in water resulted primarily from the presence of the carboxyl group in the otherwise insoluble or slightly soluble hydrocarbon chain of these compounds. It was also mentioned that, as the hydrocarbon chain increased in length, the effectiveness of the carboxyl group in producing solubility of the acids diminished almost to the vanishing point. It will now be seen that even when the carboxyl group is relatively incapable of effecting solution it may still influence the behavior of a water–acid interface to produce oriented mono- and polymolecular films.

(a) *Monomolecular Films*

Nature of Monomolecular Films.—When a drop of an *immiscible* animal or vegetable oil, fatty acid, oxidized paraffin hydrocarbon, fatty acid ester, higher alcohol, ketone, nitrile, amide, or other polar or semipolar substance is placed on water it spreads to form a thin uniform layer. Investigation of the properties of these films by means of the film balance has led to important discoveries concerning the forces between the molecules, the cross-section area of packed molecules, orientation of surfaces, and other related properties.

Several theories have been advanced relative to the spreading of oil films on water. The theory of Langmuir[4] is perhaps the simplest and most applicable to the naturally occurring fats and oils and their derived products. According to Langmuir's theory, nonpolar liquids, such as the hydrocarbons, do not spread on water, but if the molecules contain a polar or *hydrophilic* group and a nonpolar or *hydrophobic* group, the liquid will spread. Furthermore, most of the films formed in this manner are only one molecule thick and for any given substance have all their molecules similarly oriented, often simply perpendicular to the surface and parallel to each other.

Investigation has revealed the fact that the molecules of these oriented films are arranged so that their polar (hydrophilic) portions, which possess an affinity for water, go into solution while the insoluble (hydrophobic) portion tends to float above the surface of the water. Oriented films of this type exhibit various properties which can be qualitatively observed and quantitatively measured. For example, they are subject to mechanical compression which produces several readily observable effects. A thin film of colorless mineral oil such as Nujol when placed on a clean surface of water does not spread, but if the oil is first slightly oxidized it spreads as a uniform polymolecular film. If the expanded film is subjected to compression by a movable barrier, it will exhibit a series of colors (yellow, gold, red-purple,

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[4] I. Langmuir, *J. Am. Chem. Soc.*, **39**, 1848–1906 (1917).

blue, and green) as the compression is increased. On further compression the color spectrum will be repeated four or more times until a limiting compression value is reached when the film again becomes colorless.

Measurement of Monomolecular Films.—The effect of this compression can be measured quantitatively by means of the film or hydrophil balance. The film balance is a relatively simple device by means of which considerable quantitative information can be obtained concerning the nature of the material composing the film. One type of film balance (Fig. 41), developed by Detroit Edison Company for determining the film-forming characteristics of oils, consists of a metal tray 65 cm. long, 14 cm. wide, and 1.5 cm. deep. A support which spans the tray carries a measuring device consisting of a torsion wire secured at both ends in torsion heads, each of which is driven by a worm gear arrangement which permits very precise adjustment.

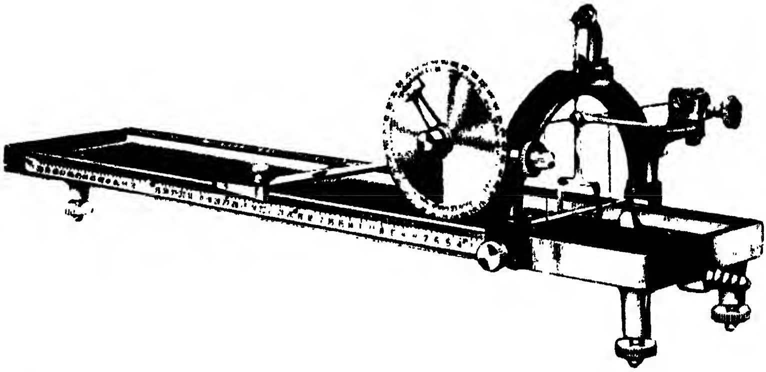

Fig. 41. Film or hydrophil balance (courtesy *Central Scientific Company*).

The forward torsion head extends through a circular plate provided with a scale graduated from 0° to 360° and a vernier which permits readings to be made to 0.1°. This mechanism is attached to a mica float which rests lightly on the liquid medium. Any force exerted by the film on the mica float can be accurately measured by the torsion mechanism. The trough is graduated along its long dimension and is provided with a movable straight edge which permits changes to be made in the surface area of the film and makes possible the determination of any particular area of the oily film which is formed by movement of the barrier. The film balance is applied in determining the force exerted against the float when the film is compressed to any corresponding area. The force is measured in dynes per centimeter and the area in square centimeters. Other types of film-pressure measuring devices have been described by Adam[5] as well as by others.

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[5] N. K. Adam, *Proc. Roy. Soc. London*, A101, 452–472 (1922).

Various methods may be used in producing the film to be investigated. A drop of liquid may be placed directly on the distilled water surface or the substance may be dissolved in a volatile solvent and the solution dropped on the water. On evaporation of the solvent, the film of the solute remains. In some cases a solid may be placed on the surface and allowed to spread. The long chain fatty acids, higher alcohols, ethyl esters, glycerides, and natural oils have been extensively investigated with respect to their film-forming characteristics by means of various types of film balances.

Monomolecular Films of Saturated Fatty Acids on Distilled Water.—Adam[6] made many quantitative measurements of the properties of monomolecular films including those formed by the even- and odd-numbered carbon acids from C_{12} to C_{26}. When spread on the surface of distilled water at a constant temperature of 20°C., all of the saturated fatty acids were found to exhibit essentially similar behavior with respect to the compressibility of their films. This behavior is illustrated by the force–area curve reproduced[6a] in Figure 42, from which it is seen that at areas greater than about 21×10^{-16} sq. cm. per molecule there is little or no measurable resistance to pressure. At this point there is observed a sudden opposition to further contraction, and the compressing force increases practically linearly with decreasing area up to the point at which the film collapses due to piling up of the molecules of the film.

These results may be interpreted as evidence that when the area of a film of saturated fatty acids has been reduced to the extent where the molecules are closely packed together, the area occupied per molecule is 21×10^{-16} sq. cm. and is independent of the length of the carbon chain. The fact that the molecules occupy the same area independent of the length of the carbon chain, and the fact that the area formed (21×10^{-16} sq. cm.) is the area of the cross section of a CH_2 group determined in other ways, is conclusive proof of the orientation of the molecules of fatty acids producing the film. It is evident, therefore, that because of the affinity of the hydrocarbon portion of the molecules for each other, the molecules spread on the surface of the water only far enough for their heads or hydrophilic parts to come in contact with water. The surface tension of the water, therefore, is not decreased unless enough fatty acid is added to cover the surface completely with a monomolecular film. By measuring the volume of fatty acid required to form a monomolecular film covering a given area, the thickness of the film can be calculated. Also, by placing a known number of molecules on the surface and measuring the area to which the

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[6] N. K. Adam, *Proc. Roy. Soc. London*, **A99**, 336–351 (1921); **A101**, 516–531 (1922); **A103**, 676–687, 687–695 (1923); see **A106**, 694–709 (1924); **A110**, 423–441 (1926).

[6a] Data from H. S. Taylor, ed., *A Treatise on Physical Chemistry.* Vol. I, Van Nostrand, New York, 1925, p. 137.

film spreads before the surface tension becomes that of pure water, the area per molecule can be measured.

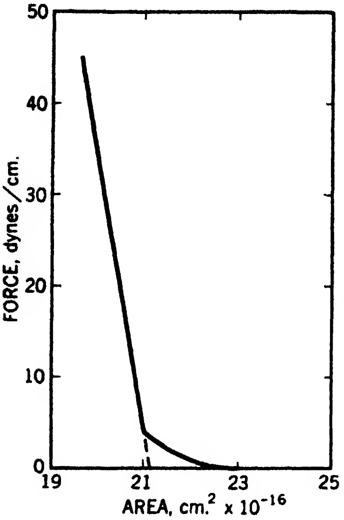

Fig. 42. Force–area curve for monomolecular films of saturated fatty acids on distilled water at 20°C.[6a]

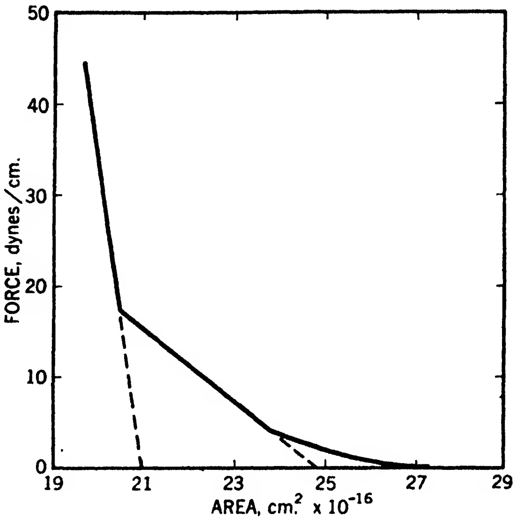

Fig. 43. Force–area curve for monomolecular films of saturated fatty acids on 0.01 *N* hydrochloric acid solution.[6a]

Monomolecular Films of Saturated Fatty Acids on Dilute Acid Solutions.—Adam also measured the compressibility of the films formed with the saturated fatty acids on water at different *p*H values. When 0.01 *N* hydrochloric acid solutions were used, the force–area curves were found to differ from those obtained with pure distilled water as may be seen by reference to Figure 43.[6a] With areas greater than about 25 × 10^{-16} sq. cm. per molecule, little or no resistance to compression is observed, after which the compression force increases linearly to an area of 21 × 10^{-16} sq. cm. The slope of the curve changes sharply at this compression value and resembles that obtained with water up to the point where the film collapses.

This behavior of saturated fatty acid films is explained by the fact that the head of the molecule, *i. e.*, the carboxyl group, occupies a greater area than the cross section of the chain. When the film is spread over distilled water the cross section of the chain gives the effective area, because of the different depths to which alternate molecules enter into the water. When the *p*H of the water is increased, as in the case of 0.01 *N* hydrochloric acid solution, the attraction of the carboxyl group for the water decreases and forces all these groups to the same level.

The area, 25 × 10^{-16} sq. cm. per molecule, therefore, corresponds to the cross section of the polar (COOH) group, and the area, 21 × 10^{-16} sq. cm. per molecule, observed on compression to the point where the heads of the molecules have all been forced to the level at which all the carbon chains are again in close contact, corresponds to the cross section of the methylene (CH_2) group.

Effect of Temperature on Monomolecular Films.—Another observation made by Adam relates to the effect of temperature on the compressibility of saturated fatty acid films. This effect is illustrated by the curve in Figure 44 for a monomolecular film of palmitic acid on 0.01 *N* hydrochloric acid in which the temperature in °C. is plotted against the area in sq. cm. × 10^{-16} under a constant force of 1.4 dynes per cm. It may be seen from this figure that when the force is maintained at 1.4 dynes per cm. and the temperature is raised, the area remains constant at 25.1 × 10^{-16} sq. cm. per molecule from 0° to about 28°C. As the temperature is increased above 28° a sharp expansion of the area occurs which continues to about 35°C. after which the expansion likewise continues but at a very diminished rate. The expansion coefficient above 35°C. was found to correspond in magnitude to the thermal expansion coefficient of a gas and it was considered that a change in state occurred, analogous to the change of a solid to a gas.

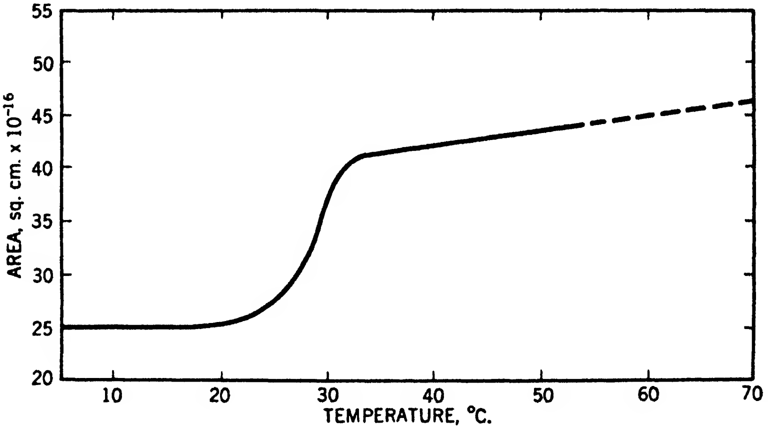

Fig. 44. Effect of temperature on compressibility of a monomolecular film of palmitic acid on 0.01 *N* hydrochloric acid under a constant force of 1.4 dynes per cm.[65]

It was found by Adam that, the longer the carbon chain, the higher was the observed temperature at which the expansion was observed. This

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[65] Data from N. K. Adam, *Proc. Roy. Soc. London*, **A101**, 519 (1922).

change appears to be due to a separation of the molecules from one another at the surface, brought about by the thermal agitation becoming so violent that the lateral attractions of the molecules for each other are overcome. Films in this state are referred to as *expanded films* in contrast to *condensed films* where the molecules are in close contact at low temperatures. Expanded films may be described as being formed from close-packed condensed films by a rise in temperature, the change being complete in a few degrees at constant pressure, and being similar in nature irrespective of the substance.

Monomolecular Films of Other Long Chain Acids.—Adam and Jessop[7] examined the films formed by the dibasic acids containing 16, 20, 24, and 32 methylene groups, and the diethyl esters containing 10, 11, 16, 20, and 32 methylene groups and the monoethyl ester, $COOH(CH_2)_{16}COOC_2H_5$. All of the diethyl esters, $C_2H_5OOC(CH)_nCOOC_2H_5$, were observed to form monomolecular films. The dibasic acids formed similar films attached to the water surface by one carboxyl group only. The films were, however, rather unstable and tended to collapse under compression.

Adam also examined films formed on 0.01 N hydrochloric acid by a number of unsaturated acids, including $\Delta^{2,3}$-oleic, $\Delta^{9,10}$-oleic, elaidic, erucic, and brassidic acids. All of these acids produced films in the expanded state. The presence of double bonds in the middle of the chain caused the films to expand more easily than films with saturated chains of similar length. Since unsaturated hydrocarbons behave similarly, it is assumed that the double bond attracts water more than a saturated linkage. *Cis*- and *trans*-acids behave somewhat differently. The *cis*-form is more strongly attracted to the water than the *trans*-form. A double bond near the carboxyl group, as in $\Delta^{2,3}$-oleic acid, lowers the expansion of the film compared with that observed when the double bond is near the middle of the chain.

Fatty acids and glycerides having two or more double bonds exhibit interesting behaviors. If the double bonds are remote from the end group, expanded films are formed in which the limiting area increases with the number of double bonds in the molecule. Stearolic acid with a triple bond, elaeostearic acid with three conjugated double bonds, triricinolein containing three double bonds and three hydroxyl groups, exhibit characteristic film-forming properties.[8-11] Many other lipids, including sterols, phosphatides, ketones, alcohols, amides, nitriles, etc., have been examined with respect to their film-forming properties.

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[7] N. K. Adam and G. Jessop, *Proc. Roy. Soc. London*, **A112, 362–375, 376–380 (1926).**

[8] A. H. Hughes and E. K. Rideal, *Proc. Roy. Soc. London*, **A140, 253–269 (1933).**

[9] G. Gee and E. K. Rideal, *Proc. Roy. Soc. London*, **A153, 116–128 (1935).**

[10] G. Gee and E. K. Rideal, *Proc. Roy. Soc. London*, **A153, 129–141 (1935);** *Trans. Faraday Soc.*, **32, 187–195 (1936).**

[11] N. K. Adam, *Proc. Roy. Soc. London*, **A140, 223–226 (1933).**

The data obtained by measurement of the properties of the monomolecular films of the long chain fatty acids and related compounds have been used for calculating certain molecular dimensions of these compounds, *e. g.*, cross-section areas, chain length, etc., as shown in Table 55. The values thus obtained are generally smaller than those obtained by x-ray measurements which would indicate these compounds are more closely packed in monomolecular films than in crystals and are comparable with the actual dimensions of the molecule.

For a more detailed treatment of the above-mentioned work on monomolecular films, the reader is referred to Adam's general work[12] on surface films and to Harkins' thermodynamic treatment[13] of film formation and the effect of compression on surface films of fatty acids, alcohols, and esters.

TABLE 55

MOLECULAR DIMENSIONS OF LONG CHAIN ALIPHATIC ACIDS AND RELATED COMPOUNDS CALCULATED FROM MONOMOLECULAR FILM MEASUREMENTS

Substance	Number of carbon atoms	Head group	Cross sections, Å. (as packed in films)		Approx. length, Å.
			Chain	Head	
Myristic acid	14	$—CH_2—CH_2—COOH$	21.0	25.1	21.1
Pentadecanoic acid	15	$—CH_2—CH_2—COOH$	21.0	25.1	22.4
Stearic acid	18	$—CH_2—CH_2—COOH$	21.0	25.1	26.2
Behenic acid	22	$—CH_2—CH_2—COOH$	21.0	25.1	31.4
Iso-oleic acid	18	$-CH{=}CH—COOH$	21.0	28.7	26.2
Octadecyl urea	19	$—NH—CO—NH_2$	21.0	26.3	28.8
Stearic amide	18	$—CONH_2$	21.0	Not greater than 21.5	26.1
Ethyl palmitate	18	$—COOC_2H_5$	21.0	22.3	26.1
Ethyl behenate	24	$—COOC_2H_5$	21.0	22.3	34.0
Cetyl alcohol	16	$—CH_2OH$	21.0	21.7	22.4
Stearic nitrile	18	$—CH_2CN$	21.0	27.5	..

Monomolecular Films of Glycerides.—Long and co-workers[14] applied a modified Langmuir film balance in measuring the force–area values of monomolecular films of stearic and oleic acids and the corresponding mono-, di-, and triglycerides as well as a number of other esters and salts with the results shown in Table 56.

The cross-section area of stearic acid found by Adam, Langmuir, and Long *et al.* from monomolecular film measurements are in good agreement with one another, namely, 21.0, 22.0, and 22.5 $\text{cm.}^2 \times 10^{-16}$. Comparative values for oleic acid, triolein, and tristearin found by Langmuir and by

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[12] N. K. Adam, *The Physics and Chemistry of Surfaces.* 3rd ed., Oxford Univ. London, 1941.

[13] W. D. Harkins, *Chem. Revs.*, **29**, 385–417 (1941).

[14] J. S. Long, W. W. Kittelberger, L. K. Scott, and W. S. Egge, *Ind. Eng. Chem.*, **21**, 950–955 (1929).

Long *et al.* are 52 and 52, 126 and 127, and 66 and 72 cm.^{2} × 10^{-16}, respectively.

Long *et al.* also examined films produced with a number of oxidized and bodied linseed oils, and found that oxidation and heat bodying resulted in appreciable change in the force–area of these oils compared with untreated oils. The changes in area, and in the shape of the force–area curves, were found to be a function of the time and temperature of "blowing" as indicated in Figure 45. The changes in these curves were found to be of sufficient magnitude to permit the use of the method as a means of following variations occurring during heat bodying of linseed oil.

TABLE 56

FORCE–AREA AND RELATED DATA FROM MONOMOLECULAR FILM MEASUREMENTS OF LINSEED OIL ACIDS AND ESTERS[a]

Compound	Refractive index	Mol. wt.	Area, cm.^{2} × 10^{-16} cm.	Molecule length, cm. × 10^{-8}	Area per mol. at point of collapse, cm.^{2} × cm. 10^{-16}	Force at point of collapse, dynes/cm.
Stearic acid	....	284.3	22.5	21.9	18	60
Oleic acid	1.4606	282.3	52	10.2	28	28
Mixed acids[b]	1.4728	280	67	8.2	28	28
Oleic monoglyceride	1.4605	356	47	12.8	25	29
Oleic diglyceride	1.4661	621	86	12.7	63	16.7
Oleic triglyceride	1.4709	885	127	12.3	100	12.3
Stearic monoglyceride	....	358	27	20.6	20	55
Stearic diglyceride	....	625	49	21.3	41	56
Stearic triglyceride	....	891	72	21.5	...	..
Mixed monoglyceride	1.4788	354	61	10.3	35	25
Mixed diglyceride	1.4811	617	103	10.3	73	15
Mixed triglyceride	1.4832	879	143	10.7	110	12
Lead oleate	....	767	100	10.5	47	27
Manganese linoleate	....	615	125	7.46	57	26.5
Ethylene glycol ester[b]	1.4779	586	98	10.9	72	14
Dimannitol ester[b]	1.4880	706	105	11.5	75	15
Diethylene glycol ester[b]	1.4777	630	110	10.2	73	18.4
Tetramannitol ester[b]	1.4880	1230	176	12.1	147	8.2

[a] J. S. Long, W. W. Kittelberger, L. K. Scott, and W. S. Egge, *Ind. Eng. Chem.*, 21, 950–955 (1929).
[b] Chilled, filtered, and distilled fatty acids of linseed oil.

(*b*) *Polymolecular Films*

In contrast to monomolecular films formed by long chain fatty acids and their derivatives on the surface of water, polymolecular films can be built up on metals by the Langmuir-Blodgett[15] method. These polymolecular films, or layers of molecules, are formed by transferring any number of monomolecular films to a metallic block having a highly polished surface

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[15] K. B. Blodgett, *J. Am. Chem. Soc.*, 57, 1007-1022 (1935).

or to foils of transparent Resoglaz, by dipping them through a monomolecular film on a water surface. By minor variations in the technique of preparation it is possible to deposit either an even or an odd number of monolayers to produce a polylayer of any desired thickness, or to deposit layers of different polymorphic forms of the same substance.

Polymolecular films thus formed can be examined by means of electron diffraction using reflection methods if produced on metals and transmission methods if produced on transparent Resoglaz. When a beam of electrons is permitted to fall on deposited films of these types, the electrons are diffracted like light waves and the diffraction pattern thus produced can be recorded on a photographic plate just as in the case of x-ray diffraction. Analysis of the diffraction pattern thus produced makes possible the determination of the arrangement of the molecules forming the multimolecular layer.[16]

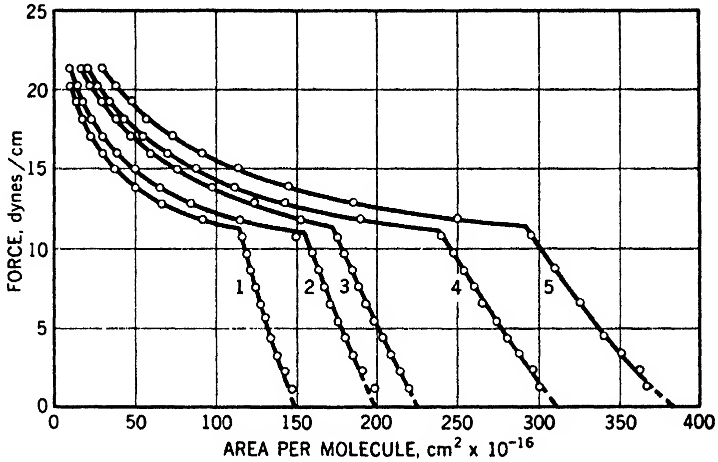

Fig. 45. Effect of heat bodying at 293°C. on the force–area curves of monomolecular films of refrigerated linseed oil with 0.028% cobalt as linoleate.[14]

Curve	Time of testing, hrs.	Molecular weight
1	0.75	960
2	2.25	1332
3	3.00	1510
4	4.50	2223
5	5.50	2500

Germer and Storks[17] examined, by means of electron diffraction patterns, various long chain fatty acids and their barium soaps using both reflec-

[16] L. H. Germer, in *Recent Advances in Surface Chemistry and Chemical Physics*. F. R. Moulton, ed., Am. Assoc. Advancement Sci., Pub. No. 7. Science Press, Lancaster, Pa., 1939, pp. 47–53.

[17] L. H. Germer and K. H. Storks, *J. Chem. Phys.*, 6, 280–293 (1938).

tion and transmission methods. They found that the hydrocarbon chains of barium stearate molecules formed hexagonal arrays with their axes normal to the supporting surface and separated by distances of 4.85 Å. Stearic acid molecules formed monoclinic crystals having the dimensions $a = 8.27$ Å., $b = 4.96$ Å., $\beta = 70°$, the a and b axes lying in the plane of the supporting surface. These dimensions are somewhat greater than those obtained by Müller[18] from x-ray measurements of the crystal, which are: $a = 5.54$ Å., $b = 7.38$ Å., $\beta = 63° 38'$.

Stenhagen[19] prepared and examined a large number of built-up films of fatty acid monoesters and di- and triglycerides. He found that the molecules in these films in the crystal state can be arranged in four different ways, *i. e.*, the lattice planes can be separated by one or two, inclined or vertically oriented molecules. Built-up films of fatty acids and their barium, calcium, magnesium, copper, and lead salts have been examined by x-ray[20–23] and by electron diffraction methods.[24]

4. Solutions of Fatty Acids in Nonaqueous Solvents

(a) *Solubility of Fatty Acids at Ordinary and Elevated Temperatures*

The solubility behavior of the fatty acids, especially the higher fatty acids, and their derivatives in organic solvents is of considerable theoretical and industrial importance. Solubility data for the lowest members of the series in a wide variety of organic solvents are available and complete phase diagrams for many of these systems have been constructed. Numerous investigations dealing with systems composed of one or more of the first six members (formic to caproic) of the fatty acid series and various organic solvents have been reported and the data therefrom have been compiled by Seidell.[25]

Data with respect to the solubilities of the organic solvent–fatty acid systems from caprylic to stearic acid are due almost entirely to the efforts of Ralston and co-workers.[26,27] These investigators determined the solubilities of eleven fatty acids in fifteen different organic solvents, including hydrocarbons, chlorinated hydrocarbons, alcohols, ketones, glacial acetic acid, esters, and nitrogen-containing solvents. Owing to the wide utility of these data, they are reproduced in tabular form in Tables 57 to 71, and,

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[18] A. Müller, *Proc. Roy. Soc. London*, A114, 542–561 (1927).
[19] E. Stenhagen, *Trans. Faraday Soc.*, 34, 1328–1338 (1938).
[20] C. Holley and S. Bernstein, *Phys. Rev.*, 52, 525 (1937); see 53, 534–537 (1938).
[21] S. Bernstein, *J. Am. Chem. Soc.*, 60, 1511 (1938); 62, 374–378 (1940).
[22] J. J. Bikerman and J. H. Schulman, *Phys. Rev.*, 53, 909 (1938).
[23] I. Fankuchen, *Phys. Rev.*, 53, 909 (1938).
[24] E. Havinga and J. de Wael, *Chem. Weekblad*, 34, 694–701 (1937).
[25] A. Seidell, *Solubilities of Organic Compounds.* Vol. II, 3rd ed., Van Nostrand, New York, 1941.
[26] A. W. Ralston and C. W. Hoerr, *J. Org. Chem.*, 7, 546–555 (1942).
[27] C. W. Hoerr and A. W. Ralston, *J. Org. Chem.*, 9, 329–337 (1944).

in the case of eleven of the solvents, in graphic form in Figures 46 to 56. The numbers in the tables and on the curves refer to the total number of

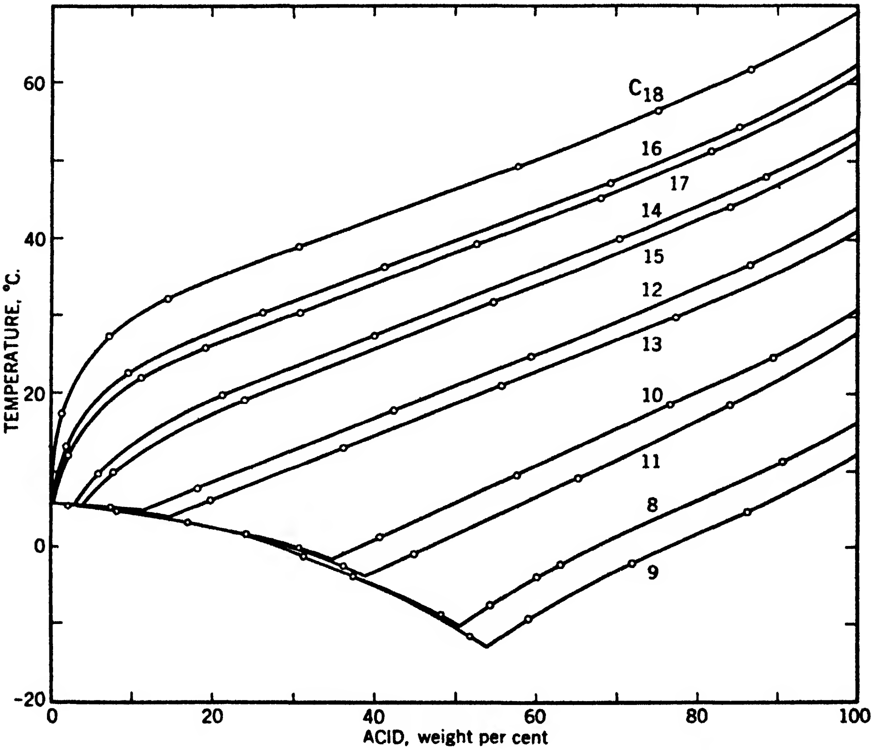

Fig. 46. Solubilities of fatty acids in anhydrous benzene.[26]

Table 57

SOLUBILITIES OF FATTY ACIDS IN BENZENE[a]

Number of C atoms	Grams acid per 100 g. benzene					
	10°C.	20°C.	30°C.	40°C.	50°C.	60°C.
8	770	∞	∞	∞	∞	∞
9	2680	∞	∞	∞	∞	∞
10	145	398	8230	∞	∞	∞
11	208	663	∞	∞	∞	∞
12	32.3	93.6	260	1390	∞	∞
13	42.4	117	354	7600	∞	∞
14	6.95	29.2	87.4	239	1290	∞
15	8.84	36.2	103	295	2280	∞
16	1.04	7.30	34.8	105	306	2170
17	1.52	9.23	42.1	121	369	5450
18	0.24	2.46	12.4	51.0	145	468

[a] A. W. Ralston and C. W. Hoerr, *J. Org. Chem.*, 7, 546–555 (1942).

carbon atoms in each acid investigated. The acids used in the solubility determinations were of relatively high purity judged by their freezing

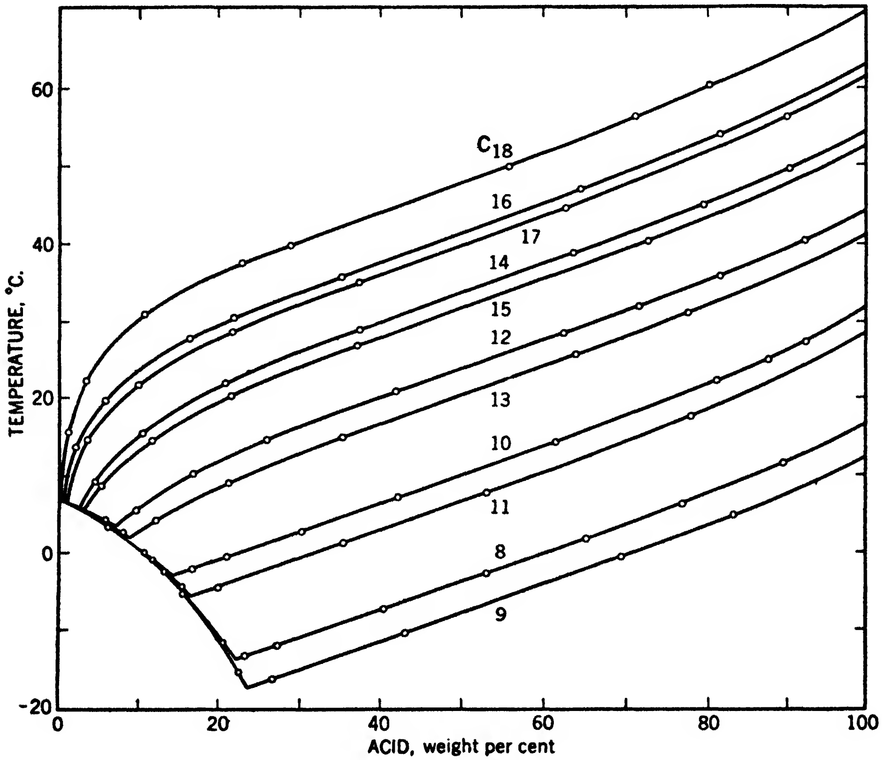

Fig. 47. Solubilities of fatty acids in cyclohexane.[27]

Table 58

SOLUBILITIES OF FATTY ACIDS IN CYCLOHEXANE[a]

Number of C atoms	Grams acid per 100 g. cyclohexane					
	10.0°C.	20.0°C.	30.0°C.	40.0°C.	50.0°C.	60.0°C.
8	670	∞	∞	∞	∞	∞
9	2340	∞	∞	∞	∞	∞
10	103	342	7600	∞	∞	∞
11	150	525	∞	∞	∞	∞
12	19.8	68	215	1310	∞	∞
13	31.0	100	330	8200	∞	∞
14	5.3	21.5	72	217	1310	∞
15	6.8	27.1	88	277	2460	∞
16	0.9	6.5	27.4	92	285	2530
17	1.5	8.4	34.0	108	365	7600
18	0.2	2.4	10.5	43.8	133	450

[a] C. W. Hoerr and A. W. Ralston, *J. Org. Chem.*, **9**, 329–337 (1944).

points which are included in Table 26 in Chapter IV (page 114). The solubilities were generally measured either from 0°C. or from the freezing

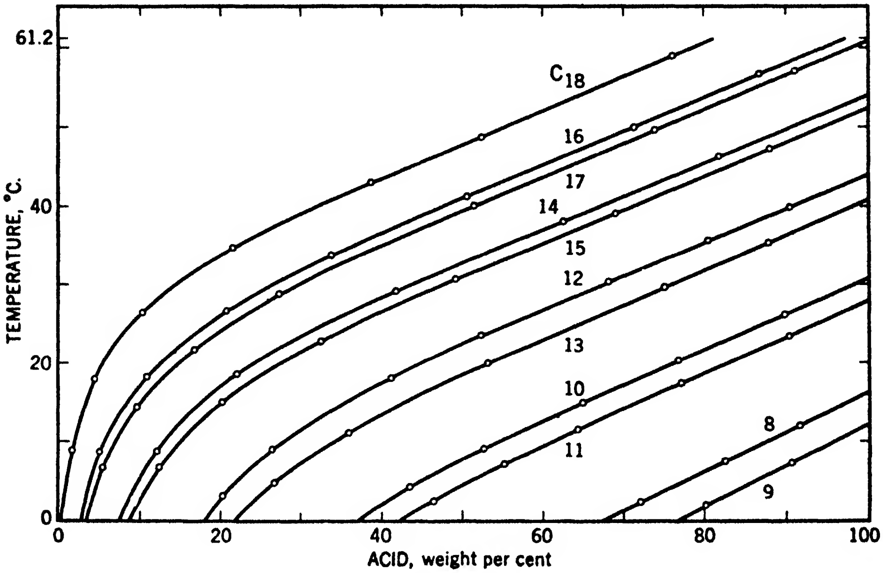

Fig. 48. Solubilities of fatty acids in trichloromethane.[27]

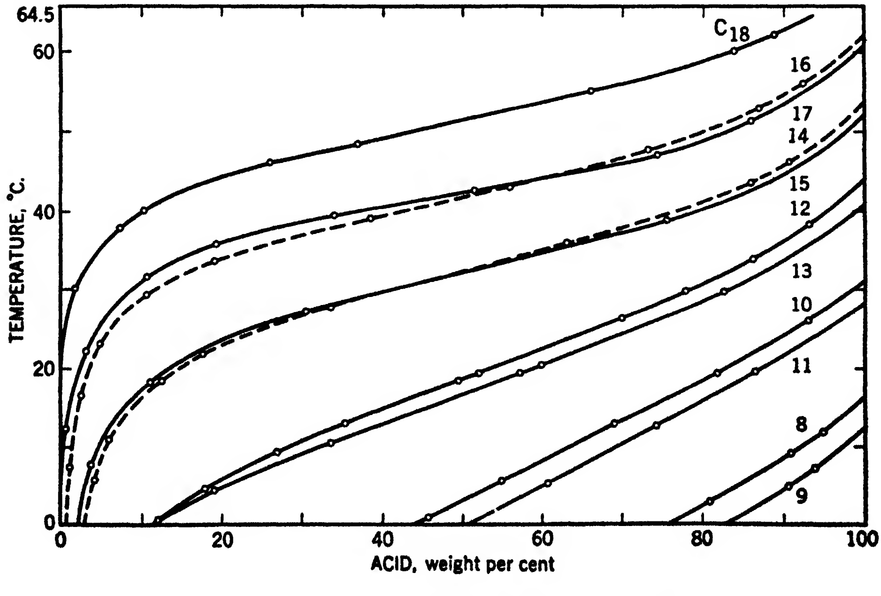

Fig. 49. Solubilities of fatty acids in methanol.[27]

TABLE 59

SOLUBILITIES OF FATTY ACIDS IN TRICHLOROMETHANE[a]

Number of C atoms	Grams acid per 100 g. trichloromethane						
	0.0°C.	10.0°C.	20.0°C.	30.0°C.	40.0°C.	50.0°C.	60.0°C.
8	213	720	∞	∞	∞	∞	∞
9	336	2340	∞	∞	∞	∞	∞
10	61	122	326	6550	∞	∞	∞
11	74	161	485	∞	∞	∞	∞
12	22.4	39.1	83	207	2120	∞	∞
13	28.4	53	116	315	6550	∞	∞
14	8.1	15.1	32.5	78	205	1000	∞
15	9.5	17.7	38.1	91	246	1750	∞
16	2.9	6.0	15.1	36.4	91	250	1820
17	3.6	7.5	17.8	42.6	106	297	5000
18	0.4	2.0	6.0	17.5	48.7	124	365

[a] C. W. Hoerr and A. W. Ralston, *J. Org. Chem.*, **9**, 329–337 (1944).

TABLE 60

SOLUBILITIES OF FATTY ACIDS IN TETRACHLOROMETHANE[a]

Number of C atoms	Grams acid per 100 g. tetrachloromethane						
	0.0°C.	10.0°C.	20.0°C.	30.0°C.	40.0°C.	50.0°C.	60.0°C.
8	115	370	∞	∞	∞	∞	∞
9	158	1150	∞	∞	∞	∞	∞
10	27.0	64	210	4650	∞	∞	∞
11	35.1	88	318	∞	∞	∞	∞
12	9.2	20.5	53	160	835	∞	∞
13	11.3	26.9	75	240	5450	∞	∞
14	3.2	6.8	17.6	55	166	870	∞
15	3.8	8.4	22.2	69	208	1560	∞
16	0.6	1.8	5.8	21.5	72	212	1590
17	0.7	2.0	6.8	25.1	83	250	4650
18	...	0.2	2.4	10.7	36.4	108	325

[a] C. W. Hoerr and A. W. Ralston, *J. Org. Chem.*, **9**, 329–337 (1944).

TABLE 61

SOLUBILITIES OF FATTY ACIDS IN METHANOL[a]

Number of C atoms	Grams acid per 100 g. methanol						
	0.0°C.	10.0°C.	20.0°C.	30.0°C.	40.0°C.	50.0°C.	60.0°C.
8	330	1300	∞	∞	∞	∞	∞
9	510	4650	∞	∞	∞	∞	∞
10	80	180	510	9900	∞	∞	∞
11	105	235	740	∞	∞	∞	∞
12	12.7	41.1	120	383	2250	∞	∞
13	12.6	48.5	148	515	14000	∞	∞
14	2.8	5.8	17.3	75	350	2670	∞
15	2.2	5.0	16.4	75	400	4400	∞
16	0.8	1.3	3.7	13.4	77	420	4650
17	0.1	0.7	2.5	9.9	62	500	12000
18	...	...	0.1	1.8	11.7	78	520

[a] C. W. Hoerr and A. W. Ralston, *J. Org. Chem.*, **9**, 329–337 (1944).

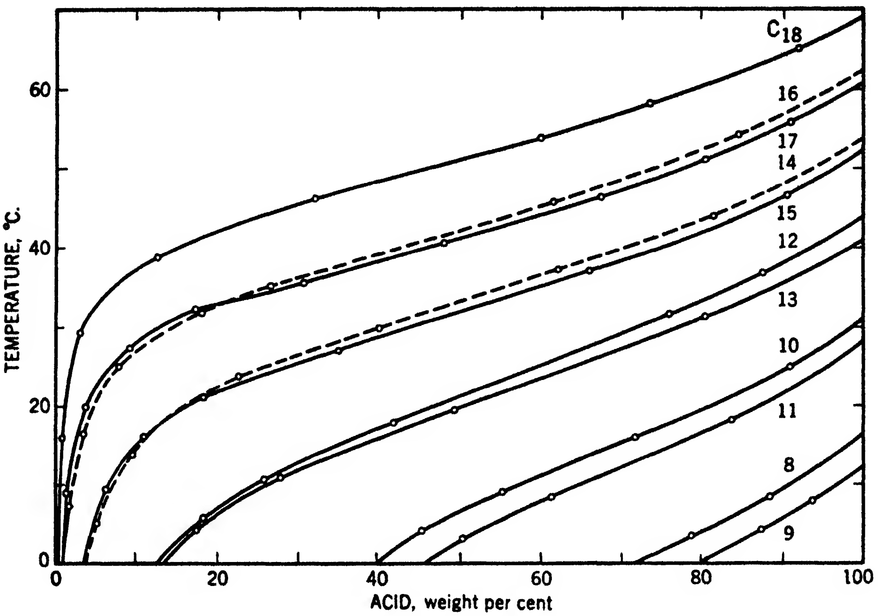

Fig. 50. Solubilities of fatty acids in ethanol (95.0% by weight).[26]

TABLE 62

SOLUBILITIES OF FATTY ACIDS IN ETHANOL[a]

Ethanol per cent by wt.	Number of C atoms	Grams acid per 100 g. solvent						
		0°C.	10°C.	20°C.	30°C.	40°C.	50°C.	60°C.
99.4	12	20.4	41.6	105	292	1540	∞	∞
	14	7.07	9.77	23.9	84.7	263	1560	∞
	16	1.89	3.20	7.21	23.9	94.2	320	2600
	17	2.04	2.98	6.62	22.2	110	388	8230
	18	0.42	1.09	2.25	5.42	22.7	105	400
95.0	8	262	1035	∞	∞	∞	∞	∞
	9	393	3230	∞	∞	∞	∞	∞
	10	60.6	93.5	440	8980	∞	∞	∞
	11	85.2	190	706	∞	∞	∞	∞
	12	15.2	34.0	91.2	260	1410	∞	∞
	13	15.5	34.5	104	336	6560	∞	∞
	14	3.86	7.64	18.9	68.7	238	1485	∞
	15	3.82	7.18	19.5	78.5	295	2460	∞
	16	0.85	2.10	4.93	16.7	73.4	287	2280
	17	1.03	1.68	4.17	15.3	84.2	344	6560
	18	0.24	0.65	1.13	3.42	17.1	83.9	365
91.1	16	0.76	1.94	4.60	15.3	. . .	. . .	. . .
	18	0.13	0.35	0.66	2.30	13.5	68.7	. . .
80.8	18	*ca.* 0.06	0.10	0.20	0.81	3.20	50.8	238

[a] A. W. Ralston and C. W. Hoerr, *J. Org. Chem.*, **7**, 546–555 (1942).

point of the solution to 100° C. in the case of solvents boiling above this temperature.

Two striking phenomena may be noted in the results of the work of Ralston *et al.*[26,27] on the organic solvent–fatty acid systems, namely, the tendency toward pairing of the solubility curves and the formation of eutectics between some of the solvents and fatty acids. Eutectic formation with benzene, cyclohexane, and acetic acid was observed in the case of all the acids investigated. The composition of these eutectics and the corresponding eutectic temperatures have been assembled in Table 72.

Table 63

SOLUBILITIES OF FATTY ACIDS IN ISOPROPANOL[a]

Number of C atoms	Grams acid per 100 g. isopropanol						
	0.0°C.	10.0°C.	20.0°C.	30.0°C.	40.0°C.	50.0°C.	60.0°C.
8	280	900	∞	∞	∞	∞	∞
9	422	2920	∞	∞	∞	∞	∞
10	67	140	360	5750	∞	∞	∞
11	82	182	540	∞	∞	∞	∞
12	21.5	44.1	100	253	1270	∞	∞
13	22.1	52	125	340	6550	∞	∞
14	7.2	13.6	31.6	82	230	1210	∞
15	6.2	13.3	34.4	95	272	2070	∞
16	2.4	4.6	10.9	32.3	94	270	2460
17	1.2	3.0	10.8	37.9	108	345	6550
18	≈0.1	0.4	2.0	10.0	38.1	118	422

[a] C. W. Hoerr and A. W. Ralston, *J. Org. Chem.*, **9**, 329–337 (1944).

The peculiar pairing of the solubility curves for the odd- and even-numbered acids is readily discernible by inspection of Figures 46 to 56. Without exception, the solubility curve of the even-numbered carbon acid lies above the curve of the next higher odd-numbered carbon acid throughout all, or a considerable part of the temperature range, *e. g.*, myristic acid is generally less soluble than pentadecanoic acid, and palmitic acid is generally less soluble than margaric (heptadecanoic) acid in the same solvent at any given temperature. The even- and odd-numbered acids, therefore, form two distinct solubility series in which the differences in spacing intervals between the curves produce the pairing observed in Figures 46 to 56.

On the basis of the solubility data assembled in Tables 57 to 71 and Figures 46 to 56, Ralston concluded that the normal saturated fatty acids are generally *more* soluble in trichloromethane and *less* soluble in nitroethane and acetonitrile than in any of the fifteen organic solvents investigated. The solubility curves for tetrachloromethane and trichloromethane, and for cyclohexane and benzene, exhibit a similar type of pairing, *i. e.*, the next higher odd-numbered homolog is the more soluble of the pair.

In the other solvents, all of which are more polar than trichloromethane, the adjacent homologs are also paired but the solubility curves intersect at moderate dilutions. Thus, the next higher odd-numbered homolog is the less soluble of each pair at temperatures below the intersection, and the solubilities of the acids decrease without alternation as the series is ascended. In the less polar solvents, this intersection of the paired solubility curves

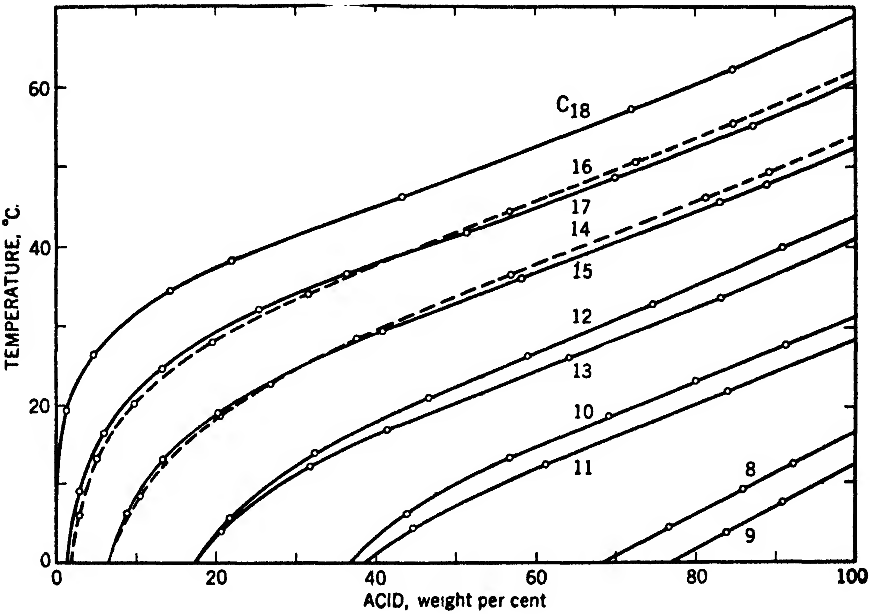

Fig. 51. Solubilities of fatty acids in *n*-butanol.[27]

TABLE 64

SOLUBILITIES OF FATTY ACIDS IN *n*-BUTANOL[a]

Number of C atoms	Grams acid per 100 g. *n*-butanol						
	0.0°C.	10.0°C.	20.0°C.	30.0°C.	40.0°C.	50.0°C.	60.0°C.
8	225	750	∞	∞	∞	∞	∞
9	355	2530	∞	∞	∞	∞	∞
10	59	103	280	4650	∞	∞	∞
11	64	131	415	∞	∞	∞	∞
12	21.4	37.2	83	217	1070	∞	∞
13	21.5	39.8	100	295	5750	∞	∞
14	7.3	13.1	28.7	71	194	980	∞
15	7.1	12.5	28.4	74	220	1680	∞
16	1.9	4.2	10.5	30.0	84	243	1960
17	1.6	3.6	9.5	27.4	85	274	4900
18	. . .	0.2	1.6	9.0	36.2	111	370

[a] C. W. Hoerr and A. W. Ralston, *J. Org. Chem.*, 9, 329–337 (1944).

occurs above lauric acid at ordinary temperatures, while in the more polar solvents it occurs also in the lower acids.

The solubilities of the fatty acids in ethyl and butyl acetates are qualitatively similar to those observed with acetone and 2-butanone, whose polarities approximate those of the acetates. The acids are, in general, more soluble in methanol than in n-butanol at higher temperatures, while at lower temperatures the order is reversed. They are somewhat more solu-

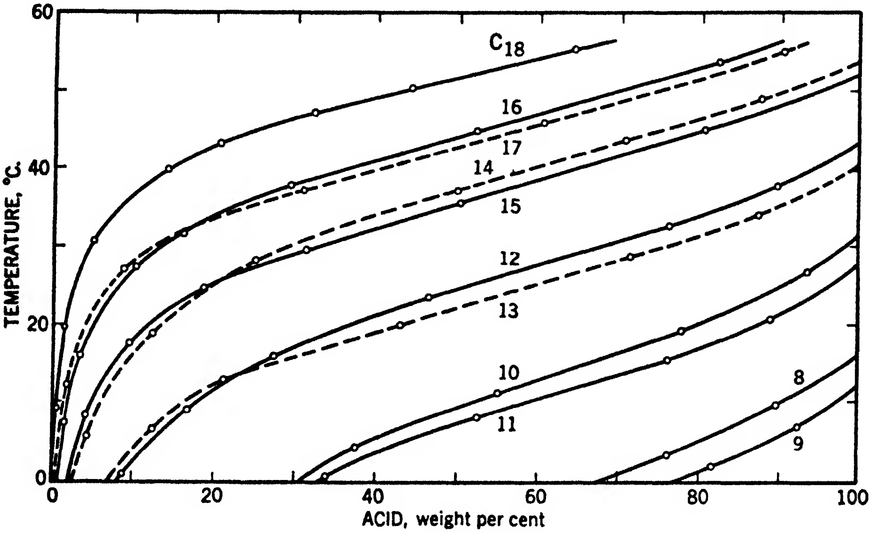

Fig. 52. Solubilities of fatty acids in acetone.[26]

Table 65

SOLUBILITIES OF FATTY ACIDS IN ACETONE[a]

Number of C atoms	Grams acid per 100 g. acetone					
	0°C.	10°C.	20°C.	30°C.	40°C.	56.5°C.
8	221	975	∞	∞	∞	∞
9	356	3740	∞	∞	∞	∞
10	45.3	112	407	4660	∞	∞
11	50.2	149	706	∞	∞	∞
12	8.95	21.9	60.5	218	1590	∞
13	7.52	20.2	78.6	316	8230	∞
14	2.75	6.50	15.9	42.5	149	∞
15	2.20	5.27	13.8	49.3	183	∞
16	0.60	1.94	5.38	15.6	58.0	880
17	0.40	1.50	4.28	14.6	67.5	1330
18	0.21	0.80	1.54	4.93	17.0	220

[a] A. W. Ralston and C. W. Hoerr, *J. Org. Chem.*, 7, 546–555 (1942).

ble in the lower alcohols than in any of the other solvents investigated with the exception of trichloromethane.

Except for their solubilities in the alcohols, the normal saturated fatty acids show a marked correlation between their solubilities and the polarities of the solvents. In the nonpolar solvents, the solubilities of the acids are almost linearly dependent upon temperature, but as the polarity of the solvent increases, the relation between concentration and temperature deviates considerably from linearity.

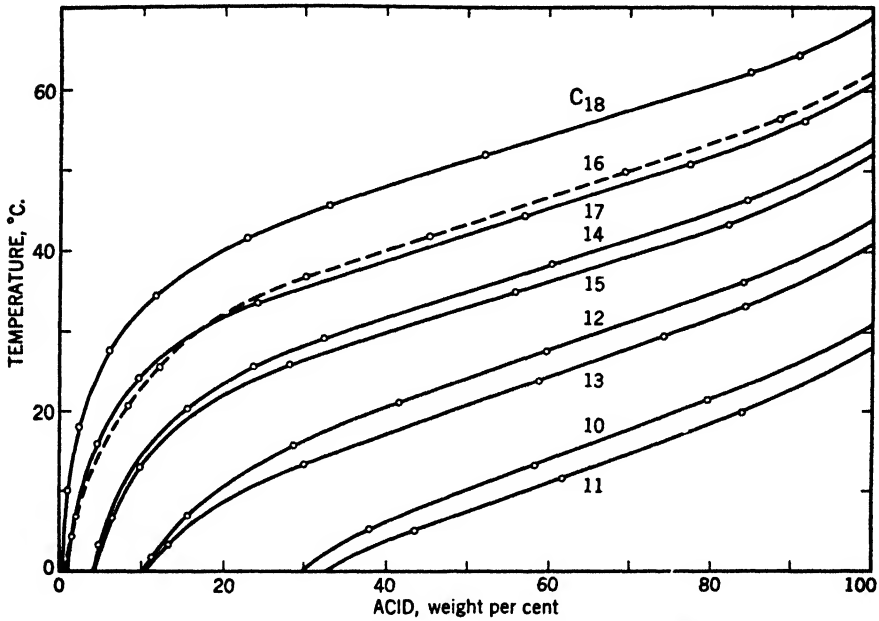

Fig. 53. Solubilities of fatty acids in 2-butanone.[26]

Table 66

SOLUBILITIES OF FATTY ACIDS IN 2-BUTANONE[a]

Number of C atoms	Grams acid per 100 g. 2-butanone						
	0°C.	10°C.	20°C.	30°C.	40°C.	50°C.	60°C.
10	42.4	100	318	7040	∞	∞	∞
11	47.9	139	521	∞	∞	∞	∞
12	11.5	24.7	64.7	202	1825	∞	∞
13	11.9	29.5	95.0	315	8230	∞	∞
14	4.28	8.46	18.5	54.3	189	1230	∞
15	4.28	8.70	20.2	70.4	257	2530	∞
16	0.90	3.09	8.57	20.6	66.1	228	2390
17	0.71	2.88	7.41	20.3	77.7	288	6560
18	0.25	1.01	2.99	8.34	24.8	84.7	344

[a] A. W. Ralston and C. W. Hoerr, *J. Org. Chem.*, **7**, 546–555 (1942).

TABLE 67

SOLUBILITIES OF FATTY ACIDS IN GLACIAL ACETIC ACID[a]

Number of C atoms	Grams acid per 100 g. glacial acetic acid				
	20°C.	30°C.	40°C.	50°C.	60°C.
10	567	8230	∞	∞	∞
11	800	∞	∞	∞	∞
12	81.8	297	1480	∞	∞
13	96.8	395	8230	∞	∞
14	10.2	51.1	289	1410	∞
15	8.76	62.0	350	2600	∞
16	2.14	8.11	51.7	313	2280
17	1.27	6.52	61.0	384	6560
18	0.12	1.68	7.58	74.8	485

[a] A. W. Ralston and C. W. Hoerr, *J. Org. Chem.*, **7**, 546–555 (1942).

TABLE 68

SOLUBILITIES OF FATTY ACIDS IN ETHYL ACETATE[a]

Number of C atoms	Grams acid per 100 g. ethyl acetate						
	0.0°C.	10.0°C.	20.0°C.	30.0°C.	40.0°C.	50.0°C.	60.0°C.
8	161	610	∞	∞	∞	∞	∞
9	250	2020	∞	∞	∞	∞	∞
10	34.2	90	289	7850	∞	∞	∞
11	38.7	114	425	∞	∞	∞	∞
12	9.4	18.5	52	250	1250	∞	∞
13	10.1	22.5	70	281	8200	∞	∞
14	3.4	6.6	15.3	44.7	164	1350	∞
15	2.8	6.2	15.4	51	208	2370	∞
16	0.8	2.2	6.1	17.6	53	203	2340
17	0.4	1.6	5.3	16.8	59	242	6000
18	...	...	0.5	5.2	21.6	78	348

[a] C. W. Hoerr and A. W. Ralston, *J. Org. Chem.*, **9**, 329–337 (1944).

TABLE 69

SOLUBILITIES OF FATTY ACIDS IN BUTYL ACETATE[a]

Number of C atoms	Grams acid per 100 g. butyl acetate						
	0.0°C.	10.0°C.	20.0°C.	30.0°C.	40.0°C.	50.0°C.	60.0°C
8	206	700	∞	∞	∞	∞	∞
9	316	2340	∞	∞	∞	∞	∞
10	44.6	111	330	8230	∞	∞	∞
11	55	145	515	∞	∞	∞	∞
12	13.0	26.8	68	212	1350	∞	∞
13	14.5	33.0	95	322	9000	∞	∞
14	4.8	9.9	21.6	61	208	1370	∞
15	4.5	9.7	22.3	66	253	2460	∞
16	1.5	3.8	8.9	23.4	69	226	2330
17	1.2	3.5	8.7	24.0	75	269	6350
18	<0.1	0.2	1.6	8.1	28.7	97	350

[a] C. W. Hoerr and A. W. Ralston, *J. Org. Chem.*, **9**, 329–337 (1944).

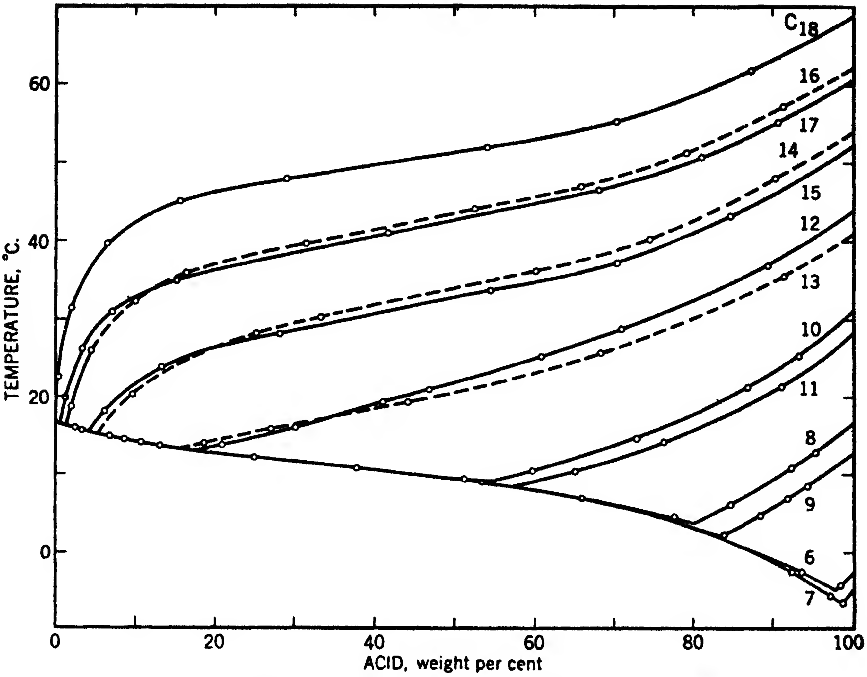

Fig. 54. Solubilities of fatty acids in glacial acetic acid.[26]

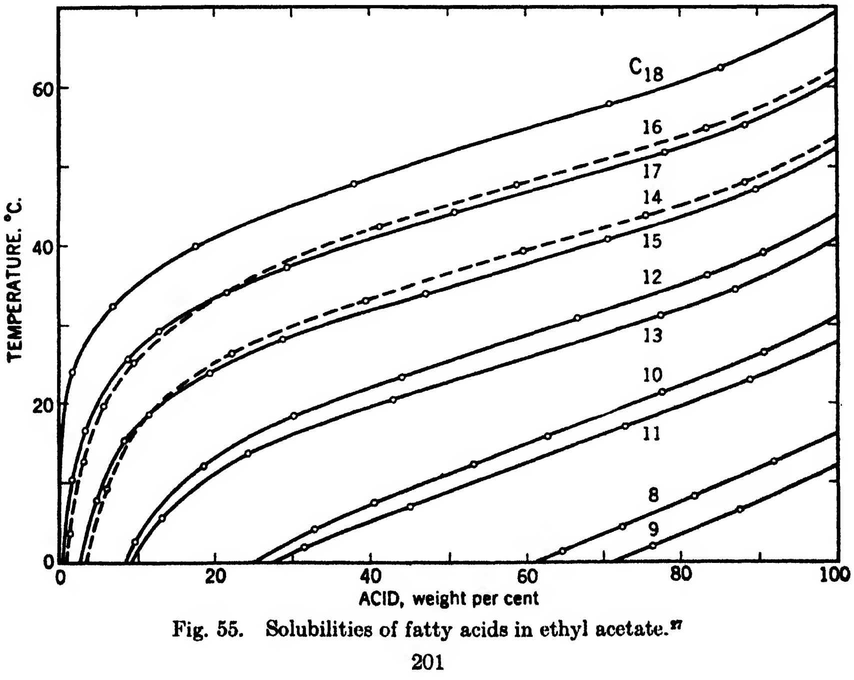

Fig. 55. Solubilities of fatty acids in ethyl acetate.[27]

Recently, Hoerr, Sedgwick, and Ralston[27a] extended their investigations to include the solubilities of the acids from caprylic to stearic in toluene, *o*-xylene, chlorobenzene, nitrobenzene, 1,4-dioxane, furfural, 1,2-dichloroethane, and nitroethane.

TABLE 70

SOLUBILITIES OF FATTY ACIDS IN NITROETHANE[a]

Number of C atoms	Grams acid per 100 g. nitroethane						
	0.0°C.	10.0°C.	20.0°C.	30.0°C.	40.0°C.	50.0°C.	60.0°C.
8	25.2	790	∞	∞	∞	∞	∞
9	45.0	2340	∞	∞	∞	∞	∞
10	9.2	12.5	55	7000	∞	∞	∞
11	8.1	13.2	131	∞	∞	∞	∞
12	1.9	2.8	5.4	16.3	1460	∞	∞
13	1.4	2.1	4.5	17.3	9000	∞	∞
14	0.3	0.5	1.2	3.3	10.7	1180	∞
15	0.1	0.2	0.7	2.4	10.2	2460	∞
16	...	...	<0.1	0.7	2.6	10.0	1650
17	...	...	...	0.2	1.9	9.6	4250
18	...	...	...	...	0.3	2.7	14.0

[a] C. W. Hoerr and A. W. Ralston, *J. Org. Chem.*, **9**, 329–337 (1944).

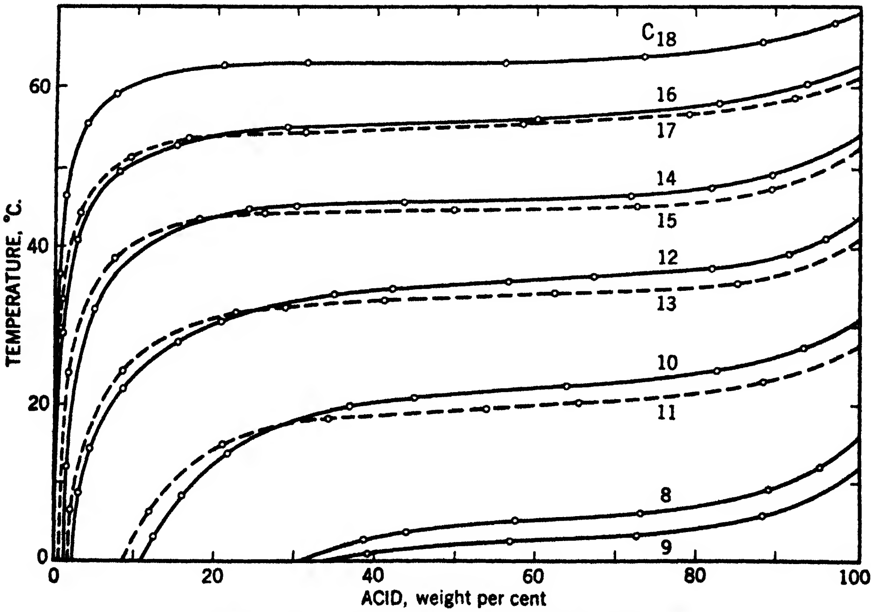

Fig. 56. Solubilities of fatty acids in acetonitrile.[27]

[27a] C. W. Hoerr, R. S. Sedgwick, and A. W. Ralston, *J. Org. Chem.*, **11**, 603–609 (1946).

TABLE 71

SOLUBILITIES OF FATTY ACIDS IN ACETONITRILE[a]

Number of C atoms	Grams acid per 100 g. acetonitrile						
	0.0°C.	10.0°C.	20.0°C.	30.0°C.	40.0°C.	50.0°C.	60.0°C.
8	44.5	1020	∞	∞	∞	∞	∞
9	51	3470	∞	∞	∞	∞	∞
10	11.8	21.0	66	7600	∞	∞	∞
11	8.7	17.3	185	∞	∞	∞	∞
12	2.1	2.8	7.3	24.4	1540	∞	∞
13	1.4	2.0	5.8	21.4	8600	∞	∞
14	0.7	0.9	1.8	4.1	13.0	1210	∞
15	0.4	0.5	1.1	2.9	10.5	2460	∞
16	<0.1	0.2	0.4	1.0	2.8	9.9	1200
17	...	<0.1	0.2	0.6	1.9	8.3	3600
18	...	...	<0.1	0.3	0.8	2.0	10.3

[a] C. W. Hoerr and A. W. Ralston, *J. Org. Chem.*, **9**, 329–337 (1944).

TABLE 72

EUTECTIC COMPOSITIONS OF SATURATED FATTY ACIDS WITH VARIOUS ORGANIC SOLVENTS

Acid	Eutectic with benzene		Eutectic with cyclohexane		Eutectic with acetic acid	
	Fatty acid, % by wt.	Temperature, °C.	Fatty acid, % by wt.	Temperature, °C.	Fatty acid, % by wt.	Temperature, °C.
Caproic	...	...	...	...	97.7	−5.4
Heptanoic	...	...	...	...	98.8	−6.5
Caprylic	50.4	−10.5	22.0	−14.0	80.0	3.1
Nonanoic	54.0	−13.1	23.9	−17.5	83.6	1.6
Capric	34.5	− 2.0	14.1	− 3.2	55.1	8.6
Undecanoic	38.9	− 4.0	16.2	− 5.9	57.5	8.0
Lauric	11.2	4.5	6.8	+ 3.2	17.3	12.8
Tridecanoic	14.6	3.7	8.6	1.9	15.9	13.1
Myristic	2.88	5.20	2.4	5.6	5.3	15.18
Pentadecanoic	3.65	5.15	2.9	5.4	4.3	15.40
Palmitic	0.19	5.40	0.4	6.4	1.23	16.17
Heptadecanoic	0.42	5.35	0.7	6.3	0.58	16.34
Stearic	0.015	5.50	<0.1	≈ 6.6	0.03	16.48

(*b*) *Solubility of Fatty Acids at Low Temperatures*

Owing to the utility of low-temperature-solvent crystallization processes for laboratory and technical preparation of fatty acids and esters, Foreman and Brown[28] investigated the solubility behavior of a number of higher fatty acids in several solvents over the temperature range +10° to −70°C. The solubility of all of the even-numbered saturated acids from C_{12} to C_{22} and three unsaturated acids, namely, oleic, linoleic, and eicosenoic, were determined in Skellysolve B, methanol, and acetone over the temperature ranges shown in Figures 57 to 59.

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[28] H. D. Foreman and J. B. Brown, *Oil & Soap*, **21**, 183–187 (1944).

Because of the long time required to establish equilibrium at the lower temperatures, the solid and solvent were stirred for an arbitrary period of ten hours at the selected temperature prior to determining the solubility.

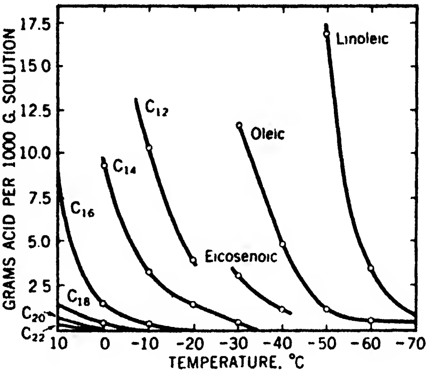
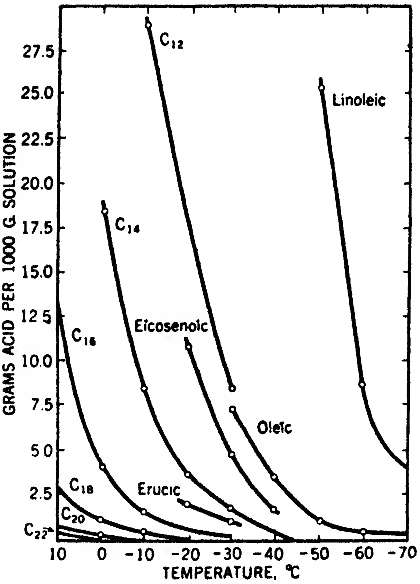


Fig. 57. Solubilities of fatty acids in Skellysolve B.[28]



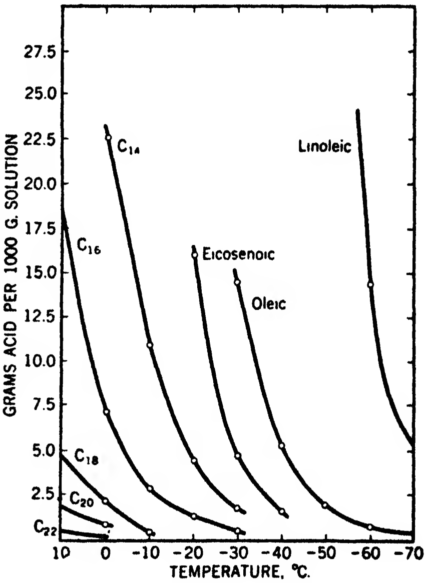


Fig. 58. Solubilities of fatty acids in methanol.[28]

Fig. 59. Solubilities of fatty acids in acetone.[28]

Solubility values obtained by approaching the selected temperature from the warm side were found to be approximately 10% higher than those obtained by approaching it from the cold side. However, in low-temperature crystallization, a solution of fatty acids is generally cooled to effect separation of a specific component, consequently the determinations were made in this manner rather than by warming to a higher temperature.

In addition to the data reproduced in graphic form, Foreman and Brown[28] determined the solubility ratios of several pairs of fatty acids in various solvents which are reproduced in Table 73. These data are especially useful in selecting conditions for separating mixtures of these acids by means of low-temperature fractional crystallization.

TABLE 73

SOLUBILITY RATIOS OF FATTY ACIDS UNDER VARIOUS CONDITIONS[a]

Solvent	Temp., °C.	Oleic	Palmitic	Ratio: oleic/palmitic
Methyl acetate	−25	10.0	0.74	14.7:1
Acetone	−30	14.2	0.48	30.0:1
Methanol	−30	7.08	0.20	35.4:1
Butanol	−25	62.8	1.32	47.6:1
Ethylidene dichloride	−25	26.8	3.24	82.7:1
Skellysolve B	−30	11.8	0.09	130.0:1
Carbon disulfide	−30	15.7	<0.1	>157.0:1
Toluene	−30	50.2	<0.1	>500.0:1
Ethyl ether	−40	43.7	<0.1	>450.0:1
Solvent	**Temp.**	**Linoleic**	**Oleic**	**Ratio: linoleic/oleic**
Skellysolve B	−70	0.60	0.24	2.5:1
Carbon disulfide	−62	4.12	0.398	10.3:1
Methanol	−70	3.94	0.32	12.3:1
Acetone	−70	5.19	0.40	13.0:1

[a] H. D. Foreman and J. B. Brown, *Oil & Soap*, **21**, 183–187 (1944). Solubilities expressed in g. per 1000 g. solution.

(c) *Anomalous Solubility and Association*

The mutual solubility effect of one acid on another is of very common occurrence and of extreme practical importance, but it has received little attention. This phenomenon is responsible for the difficulty and sometimes impossibility of obtaining a pure component by crystallization of a mixture of several fatty acids; and also for the failure of small amounts of hexabromostearic acid to separate from a large amount of tetra- and dibromostearic acid, or of small amounts of tetrabromostearic acid to separate from large amounts of dibromostearic acid. It is also responsible for the separation during crystallization of palmitic–stearic acid mixtures having the properties of margaric acid. This phenomenon is the cause of the inability to prepare absolutely pure unsaturated acids from mixtures of unsaturated acids by low-temperature crystallization.

The mutual solubility effect of one acid on another in certain solvents may be very large as was shown by Waentig and Pescheck[29] who found that the solubility of palmitic acid in carbon tetrachloride was increased 250% by the presence of lauric acid. These authors found that the mutual solubility effect decreased with increased concentration of the second component and ultimately approached a limiting concentration. An explanation of this anomalous solubility effect was sought in the hypothesis that compound formation occurred between two acids and that the compound thus formed was more soluble than the pure acid.

Various workers[26, 29–35] have found by means of ebullioscopic and cryoscopic determinations of molecular weights of fatty acids in solution that these compounds are associated in certain solvents, *e. g.*, benzene, acetic acid, cyclohexane, quinoline, pyridine, etc. Ralston and Hoerr[26] showed that at the freezing point, the ratio of apparent to true molecular weight (M/M_0) for caprylic acid in benzene approaches a value of 2 at about 0.5 molal, indicating association in solution. In solutions of lauric acid in benzene, the values of M/M_0 approach 2 at 0.3 molal. Other investigators[30–32] have found that the values of M/M_0 for various fatty acids in benzene approach limits somewhat less than 2, and their limiting value is approached in relatively higher concentrations.

Ralston and Hoerr[26] also found from freezing point data that the values of M/M_0 for lauric acid in acetic acid approach 1.65 at about 0.2 molal.

It has already been shown in the chapter on crystal properties, that compound formation occurs between fatty acids in the solid state. Lederer[36] found that the value of the ratio of molecular heat of evaporation to the absolute boiling point, λ_a/T_a, of fatty acids at atmospheric pressure is always higher than the ratio calculated according to the Trouton-Nernst rule which he interpreted as indicating that fatty acids in the liquid state are fairly completely associated while in the vapor state their density indicates they are monomolecular.

Waentig and Pescheck[29] postulate the occurrence of three such compounds in a solution of two fatty acids which are capable of associating in a given solvent in accordance with the following equation: $(L)_2 + (P)_2 \rightleftharpoons 2(PL)$; and presupposes that each of the compounds would exert a mutual solubility effect. On this assumption a mutual solubility effect should not be observed in solvents in which association of the acids does not occur, and they claim this to be the case. Thus, mutual solubility effects were ob-

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[29] P. Waentig and G. Pescheck, *Z. physik. Chem.*, **93**, 529–569 (1919).
[30] J. Meisenheimer and O. Dorner, *Ann.*, **523**, 299–301 (1936).
[31] K. Hrynakowski and A. Zochowski, *Ber.*, **70**, 1739–1743 (1937).
[32] H. Dunken, *Z. physik. Chem.*, **B45**, 201–215 (1940).
[33] G. Broughton, *Trans. Faraday Soc.*, **30**, 367–372 (1934).
[34] P. Matavulj, *Bull. soc. chim. roy. Yougoslav.*, **10**, 25–33 (1939).
[35] P. Matavulj and J. Khojnian, *Bull soc. chim. roy. Yougoslav.*, **10**, 43–49 (1939).
[36] E. L. Lederer, *Seifensieder-Ztg.*, **57**, 67–71 (1930).

served with solvents such as carbon tetrachloride, chloroform, benzene, toluene, and nitrobenzene, in which the fatty acids are dimolecularly associated, but not with ethyl alcohol, ethyl ether, ethyl acetate, and benzaldehyde, in which the fatty acids are monomolecular.

These authors further concluded that the mutual solubility effect is independent of temperature but that it is markedly affected by even traces of moisture. It has also been emphasized by Waentig and Pescheck that a determination of the temperature at which a definite amount of fatty acid just dissolves in a definite amount of solvent affords an extraordinarily precise determination of the purity of the fatty acid; more so than the determination of the melting point.

Ralston and Hoerr[36a] do not agree with the explanation offered by Waentig and Pescheck for the mutual solubility influence of one fatty acid on another. According to the former authors, the determination of the degree of association of the higher aliphatic compounds by cryoscopic and ebullioscopic measurements, upon which Waentig and Pescheck based their conclusions, tends toward erroneous results, and the more recent concept of hydrogen bonding indicates that the fatty acids (at least the lower homologs) exist as double molecules in all states, even in solution.

Ralston and Hoerr determined the solubility of various binary mixtures of palmitic and stearic acids in benzene, acetone, chloroform, and ethyl acetate. They also determined the solubility of various mixtures of palmitic acid and hepadecane in 2-butanone. In the case of the palmitic–stearic acid mixture the greatest solubility was found to correspond to the 70:30 palmitic–stearic acid eutectic rather than to the 50:50 compound. As a matter of fact the most soluble mixture was found to correspond to the minimum melting point composition of the palmitic–stearic acid system. The temperature–solubility curves of Ralston and Hoerr indicate that the chief factor which apparently governs the solubility of a given mixture is the melting point rather than the proportion of bimolecular complex present in the mixture. This observation is considered to be thermodynamically sound since solubility is a function of the latent heat of fusion of a solute according to interpretation of Raoult's law. Furthermore, the solubility relationships were not appreciably altered by change of solvent; benzene (nonpolar), chloroform (slightly polar), ethyl acetate (moderately polar), and acetone (highly polar) gave temperature–solubility curves which exhibited remarkable uniformity.

Solubility of Fatty Acids in Liquid Propane.—The hydrocarbon, propane, $CH_3CH_2CH_3$, boils at −42.4°C. but can be liquefied at ordinary temperatures and can, therefore, serve as a solvent for fatty acids similarly to the higher boiling hydrocarbons. The specific gravity of liquid propane

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[36a] A. W. Ralston and C. W. Hoerr, *J. Org. Chem.*, **10**, 170–174 (1945).

in the region of its boiling point is 0.5824 or somewhat lower than *n*-hexane, $0.6594^{20°}$, which is widely used as a solvent for fats and fatty acids.

The availability of propane in large quantities has led to its application in solvent refining (dewaxing) of lubricating oils and has attracted the attention of various workers as a possible medium for solvent refining of vegetable oils and for the fractionation of fatty acids.

Hixson and co-workers[36b–36d] investigated the various binary and ternary systems composed of liquid propane and fatty acids, monoesters, triglycerides, and vegetable oils. These systems included: propane–oleic acid[36b]; propane–refined cottonseed oil, propane–oleic acid–refined cottonseed oil, propane–tristearin, propane–tripalmitin, propane–tricaprylin[36c]; propane–stearic acid, propane–oleic acid, propane–cetyl stearate, and propane–stearic acid–palmitic acid.[36d]

The binary systems of liquid propane and fatty acids and esters exhibited typical U-shaped phase diagrams having critical solution temperatures as follows: oleic acid 91.1°C., stearic acid 91.4°, palmitic acid 96.9°, cetyl stearate 95.2°, tristearin 69.2°, tripalmitin 73.5°, tricaprylin 100.5°. A plot of the critical solution temperatures against effective molecular weight indicated that the free acids were associated in bimolecular form.

The solubility curves for the binary saturated acid and binary monoester systems with liquid propane indicated complete miscibility in all proportions from the melting point of the acid or ester up to the critical solution temperature, which is near the critical temperature of propane. The solubility data for the propane–palmitic acid–stearic acid system show that separation of these two acids in liquid propane is impractical.

(*d*) *Solubilities of Other Long Chain Compounds*

In addition to the organic solvent–fatty acid systems previously discussed, Ralston and co-workers investigated a number of other related systems, including the higher aliphatic hydrocarbons,[37] symmetrical ketones,[38] primary alcohols,[39] primary amines,[40] amine hydrochlorides and acetates,[41] secondary amines,[42] tertiary amines,[43] nitriles,[44] amides,[45] anilides[45] and *N,N*-diphenylamides.[45]

[36b] A. W. Hixson and A. N. Hixson, *Trans. Am. Inst. Chem. Engrs.*, **37**, 927–954 (1941).

[36c] A. W. Hixson and J. B. Bockelmann, *Trans. Am. Inst. Chem. Engrs.*, **38**, 891–930 (1942).

[36d] D. A. Drew and A. N. Hixson, *Trans. Am. Inst. Chem. Engrs.*, **40**, 675–694 (1944).

[37] A. W. Ralston, C. W. Hoerr, and L. T. Crews, *J. Org. Chem.*, **9**, 319–328 (1944).

[38] F. M. Garland, C. W. Hoerr, W. O. Pool, and A. W. Ralston, *J. Org. Chem.*, **8**, 344–357 (1943).

[39] C. W. Hoerr, H. J. Harwood, and A. W. Ralston, *J. Org. Chem.*, **9**, 267–280 (1944).

[40] A. W. Ralston, C. W. Hoerr, W. O. Pool, and H. J. Harwood, *J. Org. Chem.*, **9**, 102–112 (1944).

[41] H. J. Harwood, A. W. Ralston, and W. M. Selby, *J. Am. Chem. Soc.*, **63**, 1916–1920 (1941).

[42] C. W. Hoerr, H. J. Harwood, and A. W. Ralston, *J. Org. Chem.*, **9**, 201–210 (1944).

[43] A. W. Ralston, C. W. Hoerr, and P. L. DuBrow, *J. Org. Chem.*, **9**, 259–266 (1944).

Seidell[25] has brought together in his solubility tables, data with reference to other fatty acid systems whose discussion has been omitted here. The most extensive series of these systems have ethanol as the solvent and a fatty acid (behenic, lignoceric, oleic, elaidic, erucic, and elaeostearic) or fatty acid ester (cetyl palmitate, cetyl stearate, dicaprin, dilaurin, dimyristin, dipalmitin, tricaprylin, tricaprin, trilaurin, trimyristin, tripalmitin, and tristearin) as solute. However, many of the systems, especially those with reference to the fatty acid esters, are comprised of solvents other than alcohol, principally petroleum ether, benzene, diethyl ether, chloroform, and carbon disulfide. The solubility of hexabromostearic acid has been reported for twenty-eight different solvents.

[44] C. W. Hoerr, E. F. Binkerd, W. O. Pool, and A. W. Ralston, *J. Org. Chem.*, **9**, 68–80 (1944).

[45] A. W. Ralston, C. W. Hoerr, and W. O. Pool, *J. Org. Chem.*, **8**, 473–488 (1943).

CHAPTER VIII

PROPERTIES OF THE FATTY ACIDS IN THE LIQUID STATE

1. Introduction

In addition to the colligative properties which have been discussed previously, fatty acids possess other properties which are not only of theoretical interest but also of considerable practical importance. These properties, which are of particular importance in the liquid state, include density, molar volume, viscosity, surface tension, refractivity, etc. They are dependent upon the kind, number, or position of atoms in the molecule, and upon the attractive or repulsive forces which one molecule exerts on another. This is true also of some of the other properties which have been discussed, such as optical rotation, melting point, etc.

Some of these specific properties can be expressed on a molar basis, as, for example, molar volume and molar refractivity, while others exhibit no molar relationships and may be expressed by arbitrarily defined terms, *e.g.*, dielectric constant.

2. Density, Molar Volume, and Dilation

The density, d, of any substance is the mass per unit volume, dm/dv, where m is the mass and v the volume. Density, which is expressed in grams per cubic centimeter, is sometimes referred to as absolute density to distinguish it from relative density or specific gravity, which is the ratio of the mass of a substance to the mass of an equal volume of water at 4°C. or at some other specified temperature, ordinarily denoted as $d_{t_1}^{t_2}$.

Molar volume is the volume occupied by one mole of a substance, and is derived by dividing the molecular weight by the density of the substance. Specific volume is the reciprocal of the absolute density.

When a substance is heated or cooled, it expands or contracts, *i. e.*, it undergoes a change in volume and, therefore, in density. In the case of liquids, expansion or contraction usually can be expressed as some simple function of the temperature, but in the case of solids the change in volume may be complicated by changes in the crystalline state, *i. e.*, from one polymorphic form to another, and in such cases it is not possible to relate in any simple manner, the volume at one temperature to that at another.

The factor which relates the volume of a liquid at one temperature to that at another temperature is known as the *coefficient of volume expansion*, and it is defined as the ratio of the change in volume per degree to the volume at 0°C., if the substance is liquid at this temperature. The value of the coefficient varies with temperature. The general equation for the magnitude m_t (length or volume) at a temperature t, where m_0 is the magnitude at 0°C., is $m_t = m_0 (1 + at + bt^2 + ct^3 \ldots)$ where a, b, c, etc., are empirically determined coefficients. The volume expansion of liquids can be expressed as $V_t = V_0(1 + bt)$.

The above-mentioned properties and relationships are of considerable utility in their application to the fatty acids and derived products. They have, however, received little systematic attention and such data as are available are in some cases not too useful and others are of questionable accuracy. Although various isolated values for the densities or specific gravities of an appreciable number of the fatty acids and esters can be found in the literature, they are quite often not comparable owing to the different temperatures employed in determining them. Also, in some cases it is not certain whether the value reported refers to density or specific gravity.

TABLE 74

SPECIFIC GRAVITIES OF NORMAL FATTY ACIDS AND METHYL AND ETHYL ESTERS[a]

Acid		Methyl ester	Ethyl ester
Formic	1.220	0.975	0.906
Acetic	1.049	0.933	0.899
Propionic	0.992	0.917	0.891
Butyric	0.959	0.898	0.879
Valeric	0.942	0.910^{0}	0.877
Caproic	0.929	0.904^{0}_{0}	0.875^{15}_{4}
Heptanoic	0.922	0.881^{15}_{5}	0.872^{15}_{4}
Caprylic	0.910	0.887	0.878^{17}
Nonanoic	0.907	$0.877^{17.5}$	$0.866^{17.5}$
Capric	0.895^{30}	. . .	0.862
Undecanoic	. . .	. . .	. . .
Lauric	0.883	. . .	0.868^{13}_{4}
Tridecanoic	. . .	. . .	. . .
Myristic	0.858^{60}_{4}	. . .	. . .
Pentadecanoic	. . .	. . .	. . .
Palmitic	0.853^{62}_{4}	. . .	. . .
Margaric	0.853^{60}	. . .	. . .
Stearic	$0.847^{69.3}$	. . .	. . .

[a] The superscripts refer to the temperatures at which the determinations were made and the subscripts refer to the temperatures of comparison substances; where no sub- and superscripts are given the values are for 20°/4°C.

(a) *Densities and Specific Volumes of Saturated Fatty Acids*

A compilation of specific gravities, typical of those found in the literature for the saturated fatty acids and methyl and ethyl esters are given in Table 74.

Garner and Ryder[1] determined the densities and specific volumes of the saturated fatty acids from caprylic to lauric, by the so-called air thermometer method. Two measurements were made for each state, solid and liquid, and from these data the temperature coefficients per degree Centigrade were calculated with the results shown in Table 75. They also determined the densities of the same acids in the liquid state by the pycnometer method at two temperatures, one of which was as close as possible to the melting point. The densities and calculated temperature coefficients for the liquid state are given in Table 76.

Following the work of Garner and Ryder few systematic investigations of the densities of the saturated fatty acids were reported until Dorinson, McCorkle, and Ralston[2] determined the densities of the homologous series

TABLE 75

DENSITIES, SPECIFIC VOLUMES, AND TEMPERATURE COEFFICIENTS OF FATTY ACIDS FROM C_8 TO C_{12} BY THE AIR THERMOMETER METHOD

Acid	Temperature, °C.	Density, g./cc.	Specific volume, 1/*d*	Temp. coeff. per °C.
Caprylic	10.0	1.0326	0.9685	0.00098
	15	1.0274	0.9733	...
	20	0.9109	1.0979	0.00046
	25	0.9090	1.1002	...
Nonanoic	5.0	0.9952	1.0048	0.00074
	10	0.9916	1.0085	...
	15	0.9097	1.0993	0.00104
	25	0.9011	1.1097	...
Capric	15.0	1.0266	0.9741	0.00085
	25	1.0176	0.9827	...
	35	0.8927	1.1202	0.00128
	40	0.8876	1.1266	...
Undecanoic	0.12	1.0431	0.9587	0.00054
	10.0	1.0373	0.9640	...
	20	0.9948	1.0052	0.00079
	25	0.9905	1.0096	...
	30	0.8907	1.1227	0.00093
	35	0.8871	1.1273	...
Lauric	35.0	1.0099	0.9902	0.00087
	40	1.0055	0.9945	...
	45	0.8767	1.1406	0.00142
	50	0.8713	1.1477	...

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[1] W. E. Garner and E. A. Ryder, *J. Chem. Soc.*, 127, 720–730 (1925).

[2] A. Dorinson, M. R. McCorkle, and A. W. Ralston, *J. Am. Chem. Soc.*, 64, 2739–2741 (1942).

TABLE 76

DENSITIES AND TEMPERATURE COEFFICIENTS OF FATTY ACIDS FROM C_8 TO C_{12} IN THE LIQUID STATE BY THE PYCNOMETER METHOD

Acid	Temperature, °C.	Density, g./cc.	Temp. coeff. per °C.
Caprylic	50.27	0.8862	0.00099
	20.02	0.9101	...
Nonanoic	50.17	0.8813	0.00097
	15.00	0.9087	...
Capric	50.17	0.8773	0.00095
	35.05	0.8884	...
Undecanoic	50.15	0.8741	0.00095
	30.00	0.8889	...
Lauric	50.25	0.8707	0.00095
	45.10	0.8744	...

TABLE 77

DENSITIES OF NORMAL FATTY ACIDS FROM C_6 TO C_{18} AT 80°C.[a]

Acid	Density	Acid	Density
Caproic	0.8751	Tridecanoic	0.8458
Heptanoic	0.8670	Myristic	0.8439
Caprylic	0.8615	Pentadecanoic	0.8423
Nonanoic	0.8570	Palmitic	0.8414
Capric	0.8531	Margaric	0.8396
Undecanoic	0.8505	Stearic	0.8390
Lauric	0.8477		

[a] A. Dorinson, M. R. McCorkle, and A. W. Ralston, *J. Am. Chem. Soc.*, **64**, 2739–2741 (1942).

of acids from caproic to stearic. The determinations were made in a modified Ostwald pycnometer at a temperature of 80 ± 0.05°C., and all weighings were corrected for the buoyancy of air. The values for the densities found by Dorinson *et al.* are given in Table 77.

(*b*) *Molar Volumes of Saturated Fatty Acids*

As previously mentioned, the molar volume of a substance in the liquid state may be ascertained by dividing the molecular weight of the substance by its density. In the case of the solid state, the molar volume is also related to the cross-section area of the unit cell of the crystal for any given polymorphic form. If, for example, the molar volume in the solid state is known and the length of the unit cell is determined, *e. g.*, by x-ray measurement, then the cross-section area of the unit cell of the crystal can be calculated.

Prior to the work of Garner and Ryder[1] in 1925 no calculations had been made of the molar volumes of the higher aliphatic acids in the solid state and data for the acids in the liquid state were far from complete as indicated by the compilation of Pauly.[3] Garner and Ryder calculated the molar volumes of the fatty acids from caprylic to lauric in the solid state at 15°C. and in the liquid state at 50°C. Their results, together with those previously reported by Pauly, are given in Table 78.

TABLE 78

MOLAR VOLUMES IN CUBIC CENTIMETERS PER GRAM MOLE OF FATTY ACIDS IN SOLID AND LIQUID STATES

Acid	Liquid			Solid at 15°C.	
	Pauly[a]	Garner and Ryder[b]	Increment	Garner and Ryder	Increment
Formic	41.2	...		...	
			22.6		...
Acetic	63.8	...		...	
			22.0		...
Propionic	85.8	...		...	
			22.4		...
Butyric	108.2	...		...	
			21.7		...
Valeric	129.9	...		...	
			22.7		...
Caproic	152.6	...		...	
			21.6		...
Heptanoic	174.2	...		...	
			23.4		...
Caprylic	197.6	162.61		140.2	
			16.8		19.9
Nonanoic	...	179.43		160.1	
			16.8		17.7
Capric	...	196.20		167.8	
			16.8		18.7
Undecanoic, α-form	...	212.95		186.5	
					18.7
Undecanoic, β-form	...	...		180.0	
			16.9		15.2
Lauric	...	229.84		195.2	

[a] Temperature not specified.
[b] At 50°C.

According to the data of Pauly, the molar volumes of the lower members of the series increase by an average of 22.3 cc. per gram mole in the liquid state for each CH_2 group added to the chain while Garner and Ryder found

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[3] H. Pauly, *Z. anorg. allgem. Chem.*, 119, 271–291 (1921).

this increment to be 16.8 cc. per gram mole in the liquid state. In the solid state alternation occurred as the series was ascended. On the basis of the data for the solid state and the values for the chain length obtained by x-ray measurements, Garner and Ryder calculated the cross section of a single molecule in the crystal to be 23.8 Å. This cross section was found to be a nonalternating property, therefore changes in molecular volume must be due entirely to changes in chain length.

TABLE 79

MOLAR VOLUMES OF SATURATED FATTY ACIDS[a]

Acid	V_m at 20°C.		V_m at 80°C.	
	Exptl.	Calcd.	Exptl.	Calcd.
Formic	37.71	40.51	...	...
Acetic	57.21	57.40	61.11	63.38
Propionic	74.55	74.29	79.68	80.63
Butyric	91.93	91.18	97.95	97.88
Valeric	108.69	108.07	115.33	115.13
Caproic	125.04	124.96	132.67	132.38
Heptanoic	141.89	141.85	150.07	149.63
Caprylic	158.57	158.74	167.30	166.88
Nonanoic	174.53	175.63	184.50	184.13
Capric	...	...	201.80	201.38
Undecanoic	...	...	218.90	218.63
Lauric	...	...	236.29	235.88
Tridecanoic	...	..	253.27	253.13
Myristic	...	...	270.41	270.38
Pentadecanoic	...	...	287.61	287.63
Palmitic	...	...	304.56	304.88
Margaric	...	...	321.90	322.13
Stearic	...	...	338.85	339.38

[a] A. Dorinson, M. R. McCorkle, and A. W. Ralston, *J. Am. Chem. Soc.*, **64**, 2739–2741 (1942).

Using the values for the densities of the fatty acids given in Table 77, and additional values found in the literature, Dorinson, McCorkle, and Ralston calculated, by means of an empirical equation, the molar volumes at 20° and 80°C. for the normal fatty acids from formic to stearic. The calculations were predicated on the fact that the densities of the saturated fatty acids are linear functions of the temperature.

The calculated and experimental values for the molar volumes of the saturated fatty acids according to Dorinson *et al.* are given in Table 79. These authors found that at 20°C. the molar volumes of the acids from acetic to pelargonic (nonanoic) could be expressed by the equation $V_m = 16.89\,n + 23.62$, where n is the number of carbon atoms in the chain; and at 80°C. the molar volumes of the acids from butyric to stearic could be expressed by the equation $V_m = 17.25\,n + 28.88$. Only the first three acids of the series deviated appreciably from linearity as expressed by the latter equation.

(*c*) *Specific Gravities, Densities, and Molar Volumes of Unsaturated Acids and Esters*

As in the case of most other properties of the unsaturated fatty acids, few data are available with respect to the specific gravity, density, and molar volume of these compounds. Values for the specific gravity of a few unsaturated acids and esters are assembled in Table 80.

TABLE 80

SPECIFIC GRAVITIES OF SOME UNSATURATED ACIDS AND ESTERS[a]

Acid		Methyl ester	Ethyl ester
Petroselinic	0.868^{40}	. . .	. . .
Oleic	$0.895^{17.7}$	. . .	. . .
Erucic	$0.860_4^{57.1}$	0.870	0.865
Linoleic	0.903	. . .	$0.8846_4^{15.4}$, 0.8776_4^{25}
Linolenic	0.914	. . .	$0.8959_4^{15.4}$, 0.8890_4^{25}

[a] The superscripts refer to the temperatures at which the determinations were made and the subscripts refer to the temperatures of comparison substances; where no sub- and superscripts are given the values are for 20°/4°C.

TABLE 81

DENSITIES OF OLEIC ACID AND ALKYL OLEATES[a]

Temperature, °C.	Oleic acid	Methyl oleate	Ethyl oleate	Propyl oleate	Butyl oleate
15	0.8939	0.8774	0.8724	0.8708	0.8704
20	0.8905	0.8738	0.8687	0.8673	0.8669
25	0.8870	0.8702	0.8651	0.8637	0.8634
30	0.8835	0.8666	0.8613	0.8601	0.8599
60	0.8634	0.8450	0.8400	0.8389	0.8390
90	0.8429	0.8234	0.8183	0.8175	0.8178

[a] L. Keffler and J. H. McLean, *J. Soc. Chem. Ind.*, **54,** 178–185T (1935).

The most extensive and painstaking investigation of the densities of oleic acid and its methyl, ethyl, propyl, and butyl esters was made by Keffler and McLean.[4] Highly purified oleic acid and alcohols were used in the preparation of the esters and measurements were made over a temperature range from 15° to 90°C. as indicated in Table 81. On the basis of the values of the densities for the temperature range 30° to 90°C., the calculated temperature coefficients of density were found to be: oleic acid

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[4] L. Keffler and J. H. McLean, *J. Soc. Chem. Ind.*, **54,** 178–185T (1935).

0.00068, methyl oleate 0.00072, propyl oleate 0.00071, and butyl oleate 0.00070.

Keffler and McLean, using the density values in Table 81, calculated the molar volumes and increments in molar volume of oleic acid and the alkyl oleates, corresponding to temperatures of 30°, 60°, and 90°C. as shown in Table 82.

TABLE 82

MOLAR VOLUMES AND INCREMENTS IN MOLAR VOLUMES FOR OLEIC ACID AND ALKYL OLEATES[a]

Compound	Molar volume at 30°C.	Increment	Molar volume at 60°C.	Increment	Molar volume at 90°C.	Increment
Oleic acid	319.5	...	326.9	...	334.9	...
Methyl oleate	341.9	22.4	350.6	23.7	359.8	24.9
Ethyl oleate	360.3	18.4	369.4	18.8	379.2	19.4
Propyl oleate	377.1	16.8	386.6	17.2	396.7	17.5
Butyl oleate	393.5	16.4	403.3	16.7	413.7	17.0

[a] L. Keffler and J. H. McLean, *J. Soc. Chem. Ind.*, 54, 178–185T (1935).

(*d*) *Dilation of Fatty Acids*

As has been previously mentioned, all substances undergo a change in volume on heating, the magnitude of which is generally determined by measurement of the density of the substance at various temperatures. It is difficult and, in many cases, impossible to follow changes in density by direct measurement over a wide range of temperatures, but such changes can be determined with comparative ease and simplicity by means of the dilatometer. Furthermore, the use of a dilatometer permits continuous observation or measurement of the change in volume of a substance in both the solid and liquid states, and, in addition, reveals other useful information, such as changes from one polymorphic form to another, or from solid to liquid. The melting point can be very accurately determined by use of the dilatometer and in the case of fats is the only method by which this can be done with a high degree of accuracy.

In principle the dilatometer is not unlike a thermometer and consists essentially of a reservoir, which is filled with the substance whose change in volume it is desired to measure and a confining liquid, attached to a U-shaped capillary graduated or otherwise provided with a means of observing the change of volume as a function of change in temperature of the system.

Various types of dilatometers and the methods of applying them in investigations of fatty acids and natural fats have been described by

Normann,[5] van Roon,[6] Jensen,[7] Reinders, Doppler, and Oberg,[8] Coffey and Spannuth,[9] Hofgaard,[10] and Bailey and co-workers.[11-14]

The Dilatometer.—Although not as yet applied to the measurement of the dilation of fatty acids, the dilatometers described by Bailey and Kraemer[11] represent improvements in construction over those used by Normann,[5] Hofgaard,[10] and others, and they are described here in prefer-

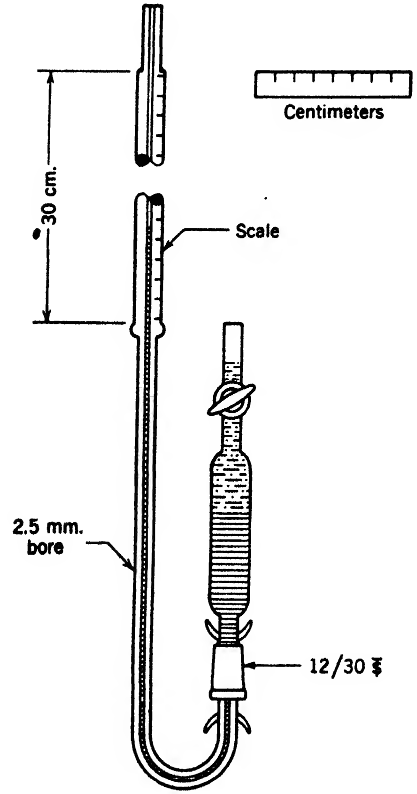

Fig. 60. Type *A* or volumetric type of dilatometer.[11]

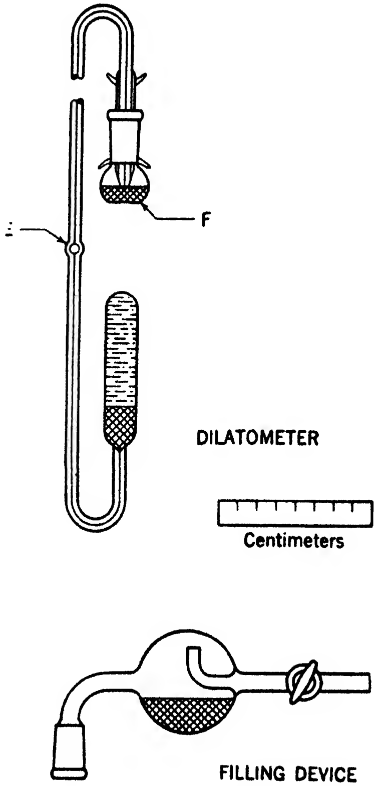

Fig. 61. Dilatometer and filling device—type *B* or gravimetric type.[11]

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[5] W. Normann, *Chem. Umschau Fette Öle Wachse Harze*, **38**, 17–22 (1931).

[6] J. D. van Roon, *Chem. Weekblad*, **27**, 498–502 (1930).

[7] H. R. Jensen, *The Chemistry, Flavouring and Manufacture of Chocolate Confectionery and Cocoa.* Blakiston, Philadelphia, 1931.

[8] W. Reinders, C. L. Doppler, and E. L. Oberg, *Rec. trav. chim.*, **51**, 917–939 (1932).

[9] C. A. Coffey and H. T. Spannuth, *Oil & Soap*, **17**, 41–42 (1940).

[10] K. Hofgaard, *Dilatometriske Fedtstof-Undersøgelser*, Dissertation, Danmarks Tekniske Højskole. G. E. C. Gad Forlag, Copenhagen, 1938.

[11] A. E. Bailey and E. A. Kraemer, *Oil & Soap*, **21**, 251–253 (1944).

[12] E. A. Kraemer and A. E. Bailey, *Oil & Soap*, **21**, 254–256 (1944).

[13] A. E. Bailey and W. S. Singleton, *Oil & Soap*, **22**, 265–271 (1945).

[14] W. S. Singleton and A. E. Bailey, *Oil & Soap*, **22**, 295–299 (1945).

ence to older types. The dilatometers of Bailey and Kraemer are of two types, the constructions of which are illustrated in Figures 60 and 61.

Type *A* (Fig. 60) is of the usual volumetric variety, not essentially different from that first described by Normann. Its novel features consist of the introduction of a ground-glass joint between the bulb and the side arm, to facilitate filling and cleaning, and the provision of a scale of new design. The scale is made from a section of a 50-ml. burette, and is attached permanently to the side arm. The capillary must of course be calibrated. In this dilatometer water is usually employed as the confining liquid, although mercury may also be used. It is useful chiefly for the examination of fats of relatively low melting points, in cases where extreme accuracy in the measurements is not required.

In filling this dilatometer, complete displacement of air is effected by permitting the confining fluid to enter through the side arm and force a small portion of the sample out through the stopcock. The weight of the fat actually retained in this bulb is determined at the conclusion of the experiment by washing out the interior of the bulb through the ground-glass joint, weighing the bulb plus the fat retained in the outlet tube and stopcock bore, and subtracting the weight of this fat from the weight of the original sample. The weight of the confining fluid must also be determined, so that the total observed expansion can be properly distributed between sample and confining fluid.

Dilatometer *B* (Fig. 61) is of the gravimetric type, and may be considered a modification of the instrument described by Burlew.[15] In this dilatometer mercury is used as the confining liquid; the mercury thread in the capillary side arm communicates with a reservoir of mercury in the small flask, *F*. Volume changes in the fat cause mercury to be expelled into the reservoir or withdrawn therefrom. Readings are made by detaching and weighing the flask and its contents. In the event of formation of an air bubble in the capillary as a result of detaching the flask for weighing, the bubble may be eliminated by raising the dilatometer from the bath a sufficient distance to expose expansion bulb *E*, and by gently warming the bulb.

After the sample is placed in the bulb, the side arm is sealed on by fusion. The filling device illustrated in Figure 61 is provided for filling the dilatometer with mercury. The dilatometer containing the sample is connected to the filling device by means of the ground-glass joint provided for the purpose, and the sample is melted and degassed under vacuum. The assembly of dilatometer and filling device is then tilted, to bring the mercury in the latter over the tip of the capillary, and the stopcock is turned to shut off the vacuum and admit air which forces mercury into the dilatometer.

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[15] J. S. Burlew, *J. Am. Chem. Soc.*, **62**, 690–695 (1940).

Manipulation of the assembly is simplified if the fat is chilled until pasty before the mercury is admitted to the system. A high vacuum should be employed, to completely eliminate air bubbles in the bulb.

Before the reservoir flask is attached, lubricant should be removed from the male joint on the end of the capillary, to insure constant weight of the flask and to permit the joint to pass sufficient air to avoid building up pressure in the flask as the mercury expands.

This latter type of dilatometer is recommended for all precise work, and particularly for use with highly saturated fats, which must be carried to relatively high temperatures, and which are inclined to undergo very slow polymorphic transformations. Since the instrument is sealed to form one solid, all-glass apparatus the possibility of leakage is eliminated. Ordinarily mercury can be weighed with greater accuracy than its volume can be measured; hence smaller volume changes can be detected with this dilatometer than with those of the usual type. The use of mercury as the confining fluid eliminates slight inaccuracies due to the appreciable solubility of water in fats.

Method of Determining the Expansion of Fatty Acids.—The dilatometer has found increasing application in the investigation of fats and fat products, especially in the past few years, but it has found little application in the examination of the fatty acids and none at all in the case of the monoesters. Normann[5] appears to be one of the first to apply dilatometry to the investigation of the expansibility of fats and oils and their derived fatty acids. He used a simple type of dilatometer consisting of a calibrated cylinder of approximately 15 ml. capacity, closed with a ground-glass stopper, and having attached at the lowest point, a vertical, graduated capillary side arm which was closed at the upper end with a rubber bulb from a dropping bottle.

In using the dilatometer in investigating the expansibility of fatty acids it was weighed, filled with boiled water to the desired point, *i. e.*, to a point one-third to two-thirds the height of the anticipated maximum expansion, and then weighed again. It was then warmed and while warm filled with melted, air-free fatty acid, and then closed, cooled, and weighed again. The filled dilatometer was placed in a thermostatically controlled water bath and allowed to remain 15 to 20 minutes, after which the temperature and height of the water in the capillary were read. The temperature of the bath was raised by increments, and after 20 minutes the temperature and capillary height were again recorded. This sequence of operations was repeated throughout the desired temperature range, and up to approximately 10°C. above the melting point of the fatty acids.

The calculations were made from the known weights of the dilatometer, water, and fat. Since the expansion of water per gram per degree rise in temperature was known, the total expansion of the contents of the dilatometer was read on the graduated capillary, and from these data the expansion due to the fatty acid was calculated. From these values the expansions per gram, or per one hundred grams of fatty acid were calculated and the results plotted in the form of graphs. As pointed out by Normann, these values represent apparent expansions in glass and are related to the original volume rather than the original weight of the fatty acid. By making use of the specific gravity of the acid, the specific volume expansions could be calculated, but these too are apparent values in glass and not absolute values.

Normann determined the expansibility over a limited temperature range, and the melting dilation of stearic and elaidic acids by the method and apparatus just described. The results are reproduced in Table 83 and graphically in Figure 62. It is evident from the curves in Figure 62 that the melting point of the sample of elaidic acid used by Normann is relatively sharp while that of the stearic acid is anything but sharp, thus indicating the effect of impurities in the commercial acid used in making these measurements. Also, it may be noted that the expansion of elaidic acid between 17° and 30°C. is practically zero which is probably due to the balancing of two thermal changes.

TABLE 83

RELATIVE EXPANSIONS OF STEARIC AND ELAIDIC ACIDS BY THE NORMANN DILATOMETER METHOD[a]

Stearic acid (m.p. 68–70°C.)		Elaidic acid (m.p. 44°C.)	
Temperature, °C.	Relative expansion	Temperature, °C.	Relative expansion
48.2	. . .	16.9	. . .
52.3	465	20.7	0.0
57.3	1155	27.5	54
59.8	1455	32.7	181
62.2	1956	37.2	435
64.4	3100	41.0	1030
67.3	3705	43.9	6490
71.8	15450	46.4	15540
75.3	16650	49.0	15800
78.1	17280	52.2	16150
81.2	17550	55.6	16500
		60 0	16950

[a] W. Normann, *Chem. Umschau Fette Öle Wachse Harze*, **38**, 17–22 (1931).

Normann also determined the expansion of oleic acid over a series of temperature ranges, namely, 20° to 72°C., 0° to 15.5°, 0° to 77°, −21° to 81° and −12° to 39.0°. When these data were plotted in graphic form, it was found that all of the curves were parallel above 20°C. but below this temperature the various samples appeared to behave anomalously and it was, therefore, concluded that the oleic acid used was impure. Although the sample of oleic acid was probably impure as stated by Normann, nevertheless part of the apparent anomaly was due in the lower temperature region to unrecognized transitions from one polymorphic form to another. It is now known[10–14] that the prior history of the sample is an all-important consideration in interpreting the results of dilatometric measurements. Normann recognized this to some extent in the observation that the original temperature in the solid state affected the subsequent expansion, and he recommended that, in the examination of commercial fats, they all be brought to an arbitrary minimum temperature of 20°C. However, this temperature is well above many of the transitions occurring in various fats, fatty acids, and fatty acid derivatives, consequently these materials must be cooled to relatively low temperatures and tempered to produce the most stable modification. Unfortunately, the more refined methods of dilatometry described by Hofgaard[10] and Bailey and coworkers[11–14] have not yet been applied to the measurement of the dilation of fatty acids and monoesters.

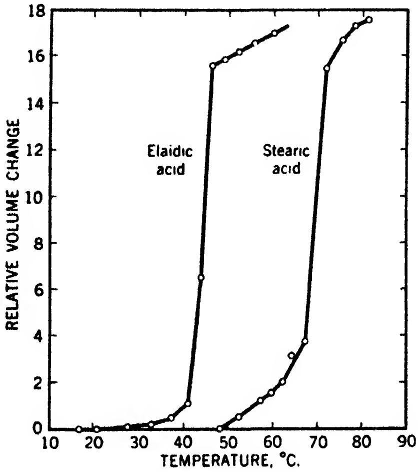

Fig. 62. Expansibility and melting dilation of stearic and elaidic acids according to Normann.[5]

3. Viscosity

According to Bridgman[16] viscosity is perhaps the most significant *non-thermodynamic* property of a liquid, and this is certainly true of the fatty acids, esters, and natural fats. This property is especially important wherever movement through or by these substances occurs in the liquid state.

A liquid offers no permanent resistance to forces tending to change its shape, yielding steadily to the slightest deforming force. However, different liquids yield at different rates or offer different resistances to deformation. This resistance is termed *internal friction* or *viscosity*. Some liquids, like glycerol or oleic acid, flow much more slowly down an inclined plane or tube than does water. Such flow consists in a continuous change in shape of each part of the liquid.

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[16] P. W. Bridgman, *Proc. Am. Acad. Arts Sci.*, **61**, 57–99 (1926).

In flow down an inclined plane, the motion is greater near the surface than at the bottom; hence a shearing stress is created; and the ratio of this shearing stress to the rate of shear is a constant for a given liquid, but differs for different liquids. The constant ratio of the shearing stress in a liquid to its rate of shear is called the *coefficient of viscosity*. In other words, if a fluid is flowing in a plane *ab* with a velocity *v* it exerts on an adjacent plane a tangential drag equal to $\eta(dv/dx)$ per unit of area. η is called the *viscosity*, *coefficient of viscosity*, or *coefficient of internal friction*.

The unit used to express viscosity is denoted a *poise*. If the tangential force per unit area, which one layer of a fluid exerts on an adjacent one, is one dyne when the space rate of variation of the tangential velocity from layer to layer is unity, the viscosity of the fluid is one poise, or 1.00 g. per cm. per second. The 1/100th part of this unit, or the *centipoise* (0.01 poise = 1 centipoise), is quite often used in practice. The absolute viscosity of water at 20.20°C. is 1.000 centipoise, and at 20°C. is 1.0050 centipoise. Reference is also often made to *kinematic viscosity* which is the ratio of the viscosity in poises to the density of a fluid in grams per cubic centimeter.

Various methods have been devised for measuring both *absolute* and *relative viscosities*. The most common of these methods involves the measurement of flow through a tube of very small bore. With colloidal solutions the method of the falling sphere is preferable. Descriptions of the various methods and viscometers used in determining viscosity are given by Reilly and Rae.[17] Cannon and Fenske[18] devised a modified viscosity pipette which permits the determination of *kinematic viscosity* with a high degree of precision.

Perhaps the best instrument available for accurately determining the *absolute viscosity* of liquids over a wide range (0.65 to 100,000 centipoises) at temperatures up to 50°C. is the Hoeppler viscometer, which has been adopted by the International Standards Committee on Viscosimetry. Bingham and Jackson[19] have described in detail methods for standardizing viscometers and the preparation of standard reference liquids.

(*a*) *Viscosities of the Saturated Fatty Acids*

The investigation of the relations between viscosity of liquids and their chemical nature by Thorpe and co-workers[20] is classical in scope and thoroughness. These workers included in their investigation the lower

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[17] J. Reilly and W. N. Rae, *Physico-chemical Methods*. 3rd ed., 2 vols., Van Nostrand, New York, 1940.

[18] M. R. Cannon and M. R. Fenske, *Ind. Eng. Chem., Anal. Ed.*, **10**, 297–301 (1938); **13**, 299–300 (1941).

[19] E. C. Bingham and R. F. Jackson, *Bull. Natl. Bur. Standards*, **14**, 59–86 (1918).

[20] T. E. Thorpe and J. W. Rodger, *Phil. Trans. Roy. Soc. London*, **A185**, 397–710 (1894); **A189**, 71–107 (1896).

members of the aliphatic series of acids and most of their analogs, including the corresponding anhydrides, alcohols, ethers, monoesters, hydrocarbons, and halides. The viscosities of these compounds were generally determined over their entire liquid range and the data reported in both tabular and graphic form, together with the calculated values for the *molecular viscosity work, i. e.*, viscosity times the specific molecular volume of the liquid. Unfortunately, the series of acids was restricted to the first four members as indicated by the data reproduced in Table 84 which gives the coefficients of viscosity in dynes per sq. cm. as a function of temperature in °C. Determinations of the viscosities of the remainder of the fatty acid series up to and including stearic acid were reported by Dunstan and co-workers,[21-23] but the temperature range was relatively narrow, generally from the point of liquefaction to about 95°C. A similar series of viscosity measurements was reported by Gartenmeister[24] for the acids from acetic to caprylic.

TABLE 84

VISCOSITIES IN DYNES PER SQUARE CENTIMETER OF FIRST FOUR MEMBERS OF FATTY ACID SERIES[a]

Temperature, °C.	Formic acid	Acetic acid	Propionic acid	Butyric acid
0	Solid	Solid	0.01519	0.02284
10	0.02245	Solid	0.01286	0.01849
20	0.01782	0.01219	0.01099	0.01538
30	0.01457	0.01036	0.00956	0.01301
40	0.012155	0.00901	0.00841	0.011175
50	0.010315	0.00791	0.00747	0.009715
60	0.00887	0.00700	0.006685	0.008535
70	0.00775	0.00625	0.006015	0.00756
80	0.00682	0.00560	0.005445	0.00674
90	0.00606	0.00505	0.00495	0.006045
100	0.00542	0.004575	0.00452	0.00545
110	..	0.004165	0.004135	0.00494
120	..	..	0.003795	0.004495
130	..	..	0.003495	0.00409
140	..	..	0.003215	0.00374
150	..	..	..	0.00343
160	..	..	..	0.00314

[a] T. E. Thorpe and J. W. Rodger, *Phil. Trans. Roy. Soc. London*, **A185**, 397–710 (1894); **A189**, 71–107 (1896).

Owing to the differences in solidification points it is not possible to compare the viscosities of an extended series of fatty acids at temperatures be-

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[21] A. E. Dunstan, T. P. Hilditch, and F. B. Thole, *J. Chem. Soc.*, **103**, 133–144 (1913).
[22] A. E. Dunstan, F. B. Thole, and P. Benson, *J. Chem. Soc.*, **105**, 782–795 (1914).
[23] A. E. Dunstan, *J. Chem. Soc.*, **107**, 667–672 (1915).
[24] R. Gartenmeister, *Z. physik. Chem.*, **6**, 524–551 (1890).

low 70°C. Comparisons at several selected temperatures are made in Table 85 and graphically over an extended temperature range in Figure 63. Comparison of the data in Table 84 for acetic, propionic, and butyric acids would indicate that viscosity was an alternating property of the fatty acids, but no alternation is evident in the temperature–viscosity curves of Figure 63 for the acids from C_6 to C_9.

TABLE 85

VISCOSITIES OF SATURATED FATTY ACIDS AT SEVERAL SELECTED TEMPERATURES[a]

Acid	Temperature, °C.	Viscosity, centipoises[b]
Formic	20.0	1.782
Acetic	20.0	1.219 (1.234)
Propionic	20.0	1.099 (1.109)
Butyric	20.0	1.538 (1.599)
Valeric	20.0	2.30 (2.23)
Caproic	20.0	3.23 (3.19)
Heptanoic	20.0	4.33 (4.35)
Caprylic	20.0 (50.0)	5.74 (2.62)
Nonanoic	20.0 (50.0)	8.08 (3.79)
Capric	50.0 (70.0)	4.34 (2.88)
Undecanoic	50.0	7.30
Lauric	50.0 (70.0)	7.3 (4.43)
Myristic	70.0	5.83 (6.76)
Palmitic	70.0	7.8
Stearic	70.0	9.87 (9.4)

[a] Water at 20.20°C. = 1.000 centipoises.
[b] Where two values are reported for only one temperature, both appear equally creditable.

From Figure 63 it is seen that the viscosity decreases with increased temperature but the change is not linear. However, it has been shown by Dunstan, Hilditch, and Thole,[21] and later confirmed by Dunstan, Thole, and Benson[22] and by Dunstan,[23] that the curves connecting the *logarithms of the viscosities* with molecular weights are approximately linear for the normal fatty acids and the methyl, ethyl, and certain other alkyl esters This linearity does not appear to hold for the first two acids (formic and acetic) of the series. The curves also depart considerably from strict linearity at the upper end of the series. This departure in the linear relationship may be the result of differences in association of the various liquids at the particular temperatures at which their viscosities were measured.

Dunstan[23] observed that the series of fatty acids presented several marked peculiarities. The viscosities of formic and acetic acids are much higher relatively than those of the succeeding members, formic acid being more viscous than acetic acid. The average value of the homologous increment throughout the series was found to be considerably in excess of that obtaining in such series as the esters, ethers, paraffins, and ketones, where agreement between the various CH_2 group differences is relatively good.

(b) *Viscosities of Alkyl Esters of Saturated Acids*

Data with reference to the viscosities of the methyl and ethyl esters of the saturated fatty acids are considerably less extensive than for the corresponding acids. Except for the first three members[20,24] most of the determinations have been reported for single temperatures, and the series is relatively incomplete, as is evident by reference to Table 86. Dunstan, Thole, and Benson[22] determined the viscosities of a number of the fatty acid esters of the higher alcohols, and more recently Gill and Dexter[25] prepared the methyl, ethyl, propyl, butyl, and amyl esters of the acids from acetic to caproic and determined their viscosities at 25°C. The latter authors plotted the logarithms of the viscosities in poises against the number of carbon atoms in the ester and found the points were scattered about a straight line, but it is difficult to conclude anything of significance from the plot of these data.

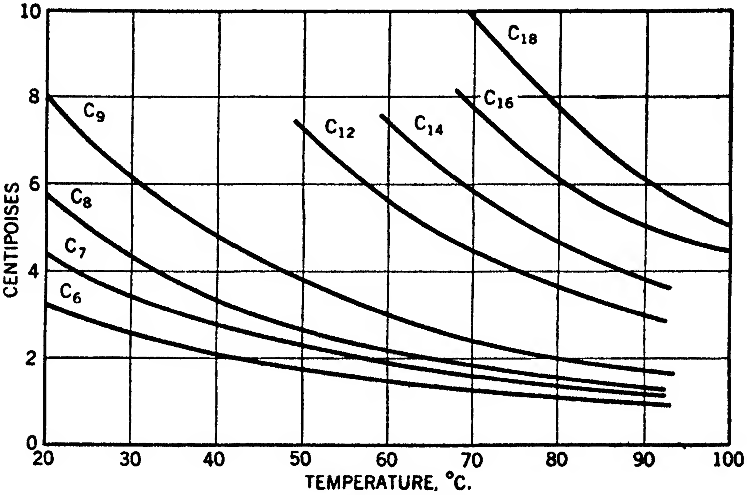

Fig. 63. Temperature–viscosity relationships for the saturated fatty acids from C_6 to C_{18}.

It has been observed that, in general, a decrease in viscosity of fatty acids and esters accompanies an increase in temperature, and that this decrease becomes continuously smaller, the higher the temperature. The influence of temperature is greatest in those substances having the greatest viscosity.

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[25] A. H. Gill and F. P. Dexter, Jr., *Ind. Eng. Chem.*, **26**, 881 (1934).

TABLE 86

VISCOSITY OF METHYL AND ETHYL ESTERS OF SATURATED FATTY ACIDS

Acid	Methyl ester		Ethyl ester	
	Temp., °C.	Viscosity, centipoises	Temp., °C.	Viscosity, centipoises
Formic	20	0.367	20	0.413
Acetic	20	0.383	20	0.452
Propionic	20	0.461	20	0.536
Butyric	20.38	0.572	20	0.666
Valeric	20	0.711	20	0.836
Heptanoic	...	...	25	1.11
Caprylic	25	1.26	25	1.38
Nonanoic	...	...	25	1.69
Lauric	25	3.08	25	3.08
Palmitic	...	...	25	5.76
Stearic	...	...	50	3.75

(c) *Viscosities of Unsaturated Acids and Esters*

Data relative to the viscosity behavior of the unsaturated aliphatic acids and esters are almost nonexistent. Oleic acid and its geometrical isomer, elaidic acid, are the only long chain unsaturated acids which have received any appreciable attention. Such data as are available are due almost entirely to Thole[26] and to Keffler and McLean.[27]

Thole's work on the unsaturated acids and esters was confined to the determination of the viscosities of oleic and elaidic acids, and the corresponding ethyl esters, in amyl acetate solution and at only one temperature, namely 24.70°C. Keffler and McLean determined the viscosity of relatively pure oleic acid over the temperature range 20° to 90°C., using a specially designed quartz viscometer of the capillary-flow type. These authors also prepared a series of *n*-alkyl oleates and determined the viscosities at 30°, 60°, and 90°C. The values for the density, viscosity, and fluidity for oleic acid and its esters obtained by Keffler and McLean are reproduced in Tables 87 and 88.

The logarithms of the viscosities of the alkyl oleates were plotted by Keffler and McLean against the number of carbon atoms in the chain but, unlike the normal saturated acid esters investigated by Thole,[26] no simple linear relationship was noted. The fluidities of the esters of oleic acid were observed to be about four times as great as that of the acid, which fact the authors attributed to the very high molecular association of oleic acid. The fluidity of the esters increased about threefold over the temperature

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[26] F. B. Thole, *J. Chem. Soc.*, **101**, 552–558 (1912).

[27] L. Keffler and J. H. McLean, *J. Soc. Chem. Ind.*, **54**, 178–185T (1935).

range 30° to 90°C., compared to a fivefold increase for the acid. The fluidity of the esters appeared to decrease with increasing molecular weight although the increment per CH_2 group varied from one pair to another.

TABLE 87

VISCOSITY OF OLEIC ACID[a]

Temp., °C.	Flow time, sec.	Density, d_4^t	Viscosity, poises	Fluidity, rhes
20	1313	0.8906	0.3880	2.96
25	1078	0.8870	0.2764	3.62
30	901	0.8836	0.2301	4.35
35	765	0.8802[b]	0.1946	5.14
45	558	0.8735[b]	0.1408	7.10
60	377	0.8634	0.0941	10.63
90	199	0.8429	0.0485	20.63

[a] L. Keffler and J. H. McLean, *J. Soc. Chem. Ind.*, **54**, 178–185T (1935).
[b] Interpolated.

TABLE 88

VISCOSITIES OF *n*-ALKYL OLEATES[a]

Ester	Iodine value	Temp., °C.	Flow time, sec.	Density, d_4^t	Viscosity, poises	Fluidity, rhes
Methyl	85.2	30	149.9	0.8666	0.0488	20.5
		60	107.1	0.8450[b]	0.0262	38.2
		90	68.8	0.8234[b]	0.0164	61.1
Ethyl	81.7	30	208.0	0.8622	0.0518	19.3
		60	113.7	0.8409	0.0276	36.2
		90	72.2	0.8192	0.0171	58.5
Propyl	77.9	30	235.8	0.8601	0.0586	17.1
		60	126.3	0.8389	0.0306	32.7
		90	79.0	0.8175	0.0187	53.6
Butyl	74.4	30	261.1	0.8599	0.0649	15.4
		60	137.8	0.8390	0.0334	29.9
		90	87.5	0.8178	0.0207	48.4

[a] L. Keffler and J. H. McLean, *J. Soc. Chem. Ind.*, **54**, 178–185T (1935).
[b] Interpolated.

Effect of Pressure on the Viscosity of Oleic Acid.—The effect of pressure on the viscosity of many liquids was determined by Bridgman,[28] who included oleic acid among the liquids investigated. The oleic acid used in this work was obtained from a chemical supply house and was used without further purification. The viscosity was measured at several pressures and at two temperatures, namely, 30° and 75°C. The results, expressed as logarithms of the relative viscosities as functions of pressure and temperature, and with the viscosity at 30°C. and atmospheric pres-

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[28] P. W. Bridgman, *Proc. Natl. Acad. Sci. U. S.*, **11**, 603–606 (1925); *Proc. Am. Acad. Arts Sci.*, **61**, 57–99 (1926).

Table 89

EFFECT OF PRESSURE ON VISCOSITY OF OLEIC ACID[a]

Pressure, kg./sq. cm.	$\log_{10} \eta/\eta^{30}$		η^{30}/η^{75}
	30°C.	75°C.	
1	0.000	9.419	3.811
500	0.306	9.671	4.315
1000	0.616	9.989	4.236
2000	...	0.255	...
4000	...	0.843	...

[a] P. W. Bridgman, *Proc. Natl. Acad. Sci. U. S.*, **11**, 603–606 (1925); *Proc. Am. Acad. Arts Sci.*, **61**, 57–99 (1926).

sure as unity, are given in Table 89. Bridgman used the logarithm of the viscosity instead of the viscosity itself because the variation with pressure was very rapid, and the curve of viscosity against pressure exhibited rapidly varying curvature, whereas the curve of the logarithm of viscosity against pressure was found to approach a straight line at high pressures and was not too much curved at low pressures. Like practically all liquids, except water, the viscosity of oleic acid increases with increasing pressure. At low pressures, the viscosity increases linearly with pressure, but beyond a pressure of the order of 1000 kg. the rate of increase rapidly increases. Under the influence of increasing pressure, oleic acid solidifies at 30°C. between 100 and 1600 kg. per sq. cm., and at 75°C. it melts below 5000 kg. per sq. cm.

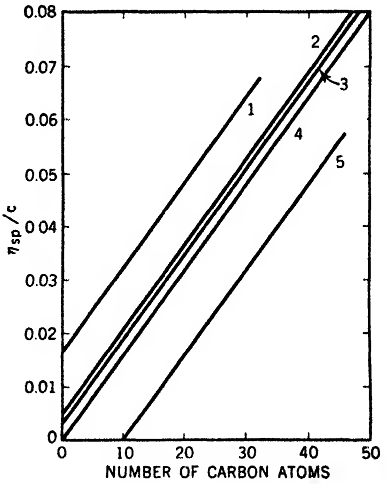

Fig. 64. Relation between specific viscosity (in 1.4% solutions of carbon tetrachloride) to carbon chain length[29] of (1) *n*-fatty acids in pyridine, (2) *n*-fatty acids, (3) esters of *n*-fatty acids, (4) *n*-paraffins, and (5) *n*-alcohols.

(*d*) *Specific Viscosity*

Staudinger[29] introduced the term *specific viscosity*, $\eta_{sp.}$, which he defined as the increase in viscosity produced in a solvent by dissolving a unit quantity of a substance in a unit volume of solvent. He related the specific viscosity to the carbon chain length by the expression $\eta_{sp.}/c = KL$, where c is the concentration of a primary molal solution (1.4% = $CH_2/1000$), K a constant, and L the length in angstrom units of the carbon chain of the compound.

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[29] H. Staudinger, *Die hochmolekularen organischen Verbindungen.* Springer, Berlin, 1932.

For example, in the case of normal organic compounds such as the aliphatic acids and esters, the specific viscosity of a molal solution may be expressed as $\eta_{sp.}$ (1.4%) $= ny + x$, where n is the number of carbon atoms in the chain, y the viscosity of a single carbon atom, and x that of oxygen. For many compounds y is approximately constant. The linearity of the specific viscosity as a function of carbon chain length of the fatty acids and other homologous aliphatic series is evident from Figure 64 which is reproduced from Staudinger's work.[29] From the plot of the specific viscosity against the carbon chain length of the various homologous series shown in Figure 64, the values of x for each series can be determined from intercepts on the $\eta_{sp.}/c$ axis.

4. Surface and Interfacial Tension

Between particles of a liquid, as in solids, there are attractive forces which keep the liquid together, and these forces must be overcome by external forces if the particles are to be separated. These forces are molecular in nature and are exerted over only very short distances. The evaporation of a liquid entails overcoming these molecularly attractive forces and the heat required for evaporation is a measure of the strength of the force.

To demonstrate directly the existence of the molecular attractive force of a liquid is very difficult, but the order of magnitude of these forces can be observed by a simple experiment. If a glass tube is completely filled with water at an elevated temperature and then sealed, it will be found on cooling that the water will continue to fill the tube even after it is cooled to a low temperature. The water will not contract until it has exerted a tensile force of about 73 lbs. per sq. in. on the walls of the tube.

These molecular forces within the body of a liquid produce certain remarkable effects at the surface of the liquid. For example, the surface of a liquid tends to contract to the smallest admissible area. The ultimate contraction results in the production of a sphere, because a sphere presents the least surface area for a given volume. The tendency to assume a spherical surface is observed in the formation of raindrops, liquid lead falling from a shot tower, the rounding of a rod of glass or sealing wax when heated, soap bubbles, etc., and this tendency to form a surface of minimum area is a manifestation of the phenomenon of *surface tension.*

Many analogies have been used to illustrate the phenomenon of surface tension. One of the simplest is the consideration of a particle, A, in the body of the liquid at some distance below the surface. This particle may be considered as being in the center of a sphere of force produced by the attractive force of all the surrounding particles If a second particle, B, is situated at or very close to the surface, it too is subject to a sphere of force which is, however, not uniform since the particle is more strongly attracted by the force due to surrounding liquid than it is to the vapor above it.

It will, therefore, be attracted inward more than outward. To take a particle from position *A* to position *B* requires that work be done against this inward attraction.

When the surface of a liquid is increased, for example in stretching a soap film, more particles are drawn to the surface; hence work is done by the stretching force and an opposing force is overcome. The required stretching force is parallel to the surface and the liquid exerts an opposing or contractile force parallel to the plane of the surface and this force is known as *surface tension.* Although the field of force giving rise to surface tension is actually downward, it is defined and expressed mathematically as a *force parallel to the surface.* Thus, surface tension is defined as the force in dynes per unit length (1 cm.) of surface of liquid in a direction parallel to the surface.

The tension produced at the surface of a liquid in contact only with vapors of the liquid phase, or with air, or an inert gas such as nitrogen, is referred to as *surface tension,* whereas the tension at the interfacial surface of a solid–liquid system or a liquid–liquid system is referred to as *interfacial tension.* Strictly speaking, surface tension should refer only to a liquid–vapor interface containing only one component.

The surface tension and the interfacial tension of liquids have within recent years become of importance in the control and development of industrial processes. By means of surface tension measurements small changes in the concentration of impurities may be detected during the refining of petroleum. The effect of oxidation on lubricating oils is readily detected by changes in the surface tension. Likewise, the presence of very small amounts of alkali soaps remaining in vegetable oils after refining may be detected by surface tension measurements. This property is also of importance in the application of vegetable oils in the tinning of sheet steel to produce tin plate and in other industrial operations involving emulsification, miscibility, solubility, and absorption phenomena.

(a) *Measurement of Surface Tension*

The three most common methods generally used in measuring the surface tension of liquids are (*1*) the capillary-height method, (*2*) the drop-weight method, and (*3*) the method of maximum pull on a ring. These methods are described in standard textbooks and manuals on physical chemistry. Of the three methods the drop-weight method is probably the most precise, since it gives results accurate to 0.1% at a water interface and about 1.0% at a mercury interface.

Although possibly somewhat less accurate, the method of maximum pull on a ring is most commonly used and is especially applicable to the measurement of the surface tension of fats and oils and their derived products. The application by du Noüy,[30] of the Rockefeller Institute for Medical Research, of the torsion balance to the ring method of determining surface and interfacial tension has simplified the method and increased the rapidity with which measurements can be made. With the best du Noüy instrument, surface tension measurements of fats and oils can be made with a precision in good agreement with those obtained by the capillary-rise method and with a reproducibility of the order of 0.05 dyne. Both upward and downward interfacial measurements, as well as surface tensions, can be made with the same instrument.

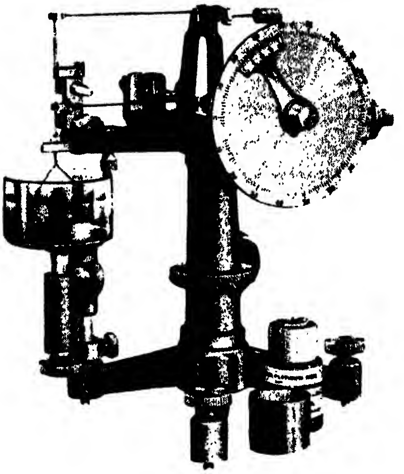
Fig. 65. Du Noüy tensiometer (courtesy *Central Scientific Company*).

The du Noüy tensiometer, illustrated in Figure 65, consists of a sensitive torsion balance which applies a slowly increasing force to an accurately constructed platinum-iridium ring in contact with the surface of the liquid under measurement. The amount of applied force is indicated upon a circular graduated scale which, when calibrated, gives readings in dynes of force. For a detailed discussion of the application of the du Noüy ring method of determining surface and interfacial tensions of liquids, as well as the comparative accuracy of the method, the reader is referred to Adam's[31] *The Physics and Chemistry of Surfaces*, as well as to the work of Alexander and Teorell,[32] Zuidema and Waters,[33] and others.

(*b*) *Surface Tension of Fatty Acids*

Despite the availability of equipment, the simplicity of the method, and the value and utility of surface and interfacial tension data, relatively few systematic measurements have been reported for these important properties of the fatty acids and esters. Typical of the data of this type which can be found in the literature are those compiled in Table 90.

The surface tension of the fatty acids varies with temperature, decreasing with increasing temperatures and reaching zero at the critical tem-

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[30] P. L. du Noüy, *Surface Equilibria of Biological and Organic Colloids.* Chemical Catalog Co., New York, 1926.

[31] N. K. Adam, *The Physics and Chemistry of Surfaces.* 3rd ed., Oxford Univ. Press, London, 1941.

[32] A. E. Alexander and T. Teorell, *Trans. Faraday Soc.*, **35**, 727–733 (1939).

[33] H. H. Zuidema and G. W. Waters, *Ind. Eng. Chem., Anal. Ed.*, **13**, 312–313 (1941).

perature. For the greater part of the temperature range, the relation between surface tension and temperature is nearly linear. The interfacial tension at the phase boundary is generally influenced more by the presence of impurities than is the case with the surface tension. Since the acids and esters which have been used in determining surface and interfacial tensions have not always been of the highest purity, the reported values are not always reliable.

TABLE 90

SURFACE AND INTERFACIAL TENSION OF TYPICAL FATTY ACIDS AND ESTERS

Compound	Temperature, °C.	Surface tension against air, dynes/cm.	Interfacial tension against water, dynes/cm.
Heptanoic acid	20	28.31	7.00
Caprylic acid	18.1	28.82	8.217
Undecanoic acid	25	30.64	10.14
Oleic acid	20	32.50	15.59
Ricinoleic acid	16	35.81	14.25
Ethyl caproate	20	25.81	19.80
Ethyl nonanoate	20	28.04	23.88
Ethyl oleate	20	...	21.34

(c) *Surface Tension of Fatty Acid Soaps*

Because of the importance of surface tension phenomena to detergency, various investigations have been made of the surface tension of aqueous soap solutions. Data available up to 1929 with respect to the surface tension of such solutions, which include the soaps of lauric, myristic, palmitic, and stearic acids, and dilute solutions (0.1%) of the acids from C_{10} to C_{20} have been assembled by McBain.[34]

The surface tension of sodium oleate has been more thoroughly investigated than that of any other soap.[30] Cavier[35] measured the surface tension of the sodium soaps of oleic, linoleic, linolenic, ricinoleic, dibromoricinoleic, lauric, α-bromolauric, hydroxystearic, hydnocarpic, and chaulmoogric acids. He concluded from these measurements that the greater the degree of unsaturation in the hydrocarbon chain, the lower was the surface tension. Ricinoleic acid, containing a hydroxyl group and one double bond, was found to give a greater lowering at high concentrations and a lesser lowering of surface tension at low concentrations than was observed with the soaps of the saturated acids.

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[34] J. W. McBain, "Properties of Soaps and Their Aqueous Solutions," in *International Critical Tables*. Vol. V, McGraw-Hill, New York, 1929, pp. 446–460.

[35] R. Cavier, *Compt. rend.*, **212,** 1146–1148 (1941).

5. Refractivity and Refractive Index

It has been known since ancient times that a beam of light is more or less deviated or refracted in passing from air into water, and the law of refraction was established by Willebrod Snell in 1621. He found by experiment that the ratio of the sines of the angles of incidence and of refraction is a constant at the boundary between two media, *i.e.*, $\sin i/\sin r = n$. The refractive index, n, of any substance is the ratio of the velocity of light in a vacuum to the velocity of light in the substance. It is a measure of the interaction of the electrostatic and electromagnetic fields set up by atoms in a molecule with the electromagnetic and electrostatic components of the traversing light waves, and it is dependent upon the intermolecular attractive forces which determine molecular volume and internal pressure.

Except for the thermal expansion effect, the refractive index is independent of temperature, but it varies with the wave length of light, therefore it is necessary to specify the wave length at which any given measurement of the refractive index is made. This is usually done by means of a subscript, *e. g.*, n_D indicates the refractive index was observed with the sodium D line; n_α the hydrogen α line, n_{5461} the green line of mercury, etc.

Related to the refractive index are specific refractivity, molecular refraction, and molecular dispersion. The dependence of the refractive index upon specific volume has been related by the equation $r = (n - 1)/d$, where r is the *specific refraction* and d the density. A more useful relation proposed by Lorenz[36] and Lorentz[36a] is:

$$r = \frac{n^2 - 1}{n^2 + 2} \cdot \frac{1}{d}$$

a relation nearly independent of temperature and pressure. The difference between the specific refractions for any two wave lengths is a measure of the dispersion for these two wave lengths. This difference is called the *coefficient of dispersion* and is expressed as $\Sigma_{\alpha-\beta}$.

The molecular refraction, M, of a substance is obtained by multiplying its specific refraction by the molecular weight. The difference between the molecular refractions measured at any two wave lengths is known as the *molecular dispersion* and is designated as $M_{\alpha-\beta}$.

(a) *Refractive Indices and Molar Refractivities of Saturated Fatty Acids*

The refractive index, specific refractivity, and molecular refractivity are especially useful properties of fatty acids, esters, and natural fats. Although numerous measurements have been made of the refractive indices

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[36] L. Lorenz, *Ann. Physik Chem.*, **11**, 70–103 (1880).
[36a] H. A. Lorentz, *Ann. Physik Chem.*, **9**, 641–665 (1880).

of various fatty acids, esters, glycerides, and natural fats, only a few systematic investigations, and these are of very recent origin, have been made of these substances. Some of the investigations are more than fifty years old[37,38] and were made with products of dubious purity.

The earlier reported determinations of the refractive indices of the fatty acids were made at arbitrary and scattered temperatures, although the work of Falk[39] on butyric acid is an exception to this statement. Falk determined the densities and refractive indices of a sample of butyric acid at 10° intervals from 10° to 80°C.

In 1942, Dorinson, McCorkle, and Ralston[40] reported the results of their systematic investigation of the refractive indices of the saturated fatty acids from caproic to stearic. Determinations were made over a temperature range of 20° to 80°C. for the lowest molecular weight acids and from just above the melting point to 80°C. for the remainder of the series. Their results were presented in tabular form, and are reproduced in part in Table 91 and in graphic form in Figure 66.

The values for the refractive indices in Table 91 were not corrected for the effect of temperature on the refractometer prism, whereas those in Figure 66 have been corrected by applying the factor 0.00006 $\cdot(t - 20)$, where t is the temperature at which the measurement was made. The refractivities for each acid fall on a straight line between 40° and 80°C. but, as indicated by the dotted line, deviate from linearity below 40°C.

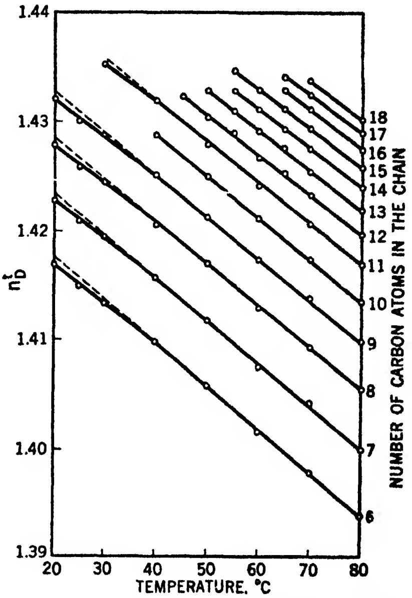

Fig. 66. Variation of refractive index with temperature[40] of the normal saturated fatty acids from C_6 to C_{18}.

These authors calculated the molar refractivities at 80°C. by the Lorenz-Lorentz equation:

$$R_m = \frac{n^2 - 1}{n^2 + 2} \cdot \frac{M}{d}$$

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[37] J. F. Eijkman, *Rec. trav. chim.*, 12, 157–197 (1893).

[38] L. T. C. Scheij, *Rec. trav. chim.*, 18, 169–210 (1899).

[39] K. G. Falk, *J. Am. Chem. Soc.*, 31, 86–107 (1909).

[40] A. Dorinson, M. R. McCorkle, and A. W. Ralston, *J. Am. Chem. Soc.*, **64**, 2739–2741 (1942).

and with the values of n from Table 91 and of d from Table 77. Dorinson *et al.* also used their own equation $R_m = 4.654\,n + 3.83$. The two values

TABLE 91

REFRACTIVE INDICES (n_D^t) OF NORMAL SATURATED FATTY ACIDS[a]

Acid	20.0°C.	25.0°C.	30.0°C.	40.0°C.	50.0°C.	60.0°C.	70.0°C.	80.0°C.
Caproic	1.4170	1.4150	1.4132	1.4095	1.4054	1.4012	1.3972	1.3931
Heptanoic	1.4230	1.4209	1.4192	1.4155	1.4114	1.4073	1.4037	1.3993
Caprylic	1.4280	1.4260	1.4243	1.4205	1.4167	1.4125	1.4089	1.4049
Nonanoic	1.4322	1.4301	1.4287	1.4250	1.4210	1.4171	1.4132	1.4092
Capric	....	....	....	1.4288	1.4248	1.4210	1.4169	1.4130
Undecanoic	....	....	....	1.4319	1.4279	1.4240	1.4202	1.4164
Lauric	....	....	...	....	1.4304	1.4267	1.4230	1.4191
Tridecanoic	....	....	....	....	1.4328	1.4290	1.4252	1.4215
Myristic	....	....	....	....	....	1.4310	1.4273	1.4236
Pentadecanoic	....	....	....	....	....	1.4329	1.4292	1.4254
Palmitic	....	....	...	....	....	....	1.4309	1.4272
Margaric	....	....	....	....	....	....	1.4324	1.4287
Stearic	....	....	....	....	....	....	1.4337	1.4299

[a] A. Dorinson, M. R. McCorkle, and A. W. Ralston, *J. Am. Chem. Soc.*, **64**, 2739–2741 (1942).

are in excellent agreement, as indicated by the comparison in Table 92. From the results of Dorinson *et al.*, Davis[41] constructed a nomograph for use in determining the refractive index of the normal saturated acids from caproic to stearic at any given temperature within the applicable temperature range.

TABLE 92

MOLAR REFRACTIVITIES OF NORMAL SATURATED FATTY ACIDS AT 80°C.[a]

Acid	R_m (exptl.)[b]	R_m (calcd.)[c]	Acid	R_m (exptl.)[b]	R_m (calcd.)[c]
Caproic	31.70	31.75	Tridecanoic	64.35	64.33
Heptanoic	36.34	36.40	Myristic	69.00	68.99
Caprylic	41.08	41.06	Pentadecanoic	73.65	73.64
Nonanoic	45.66	45.71	Palmitic	78.30	78.30
Capric	50.36	50.37	Margaric	83.01	82.95
Undecanoic	55.02	55.02	Stearic	87.59	87.61
Lauric	59.73	59.68			

[a] A. Dorinson, M. R. McCorkle, and A. W. Ralston, *J. Am. Chem. Soc.*, **64**, 2739–2741 (1942).
[b] Calculated from the Lorenz-Lorentz equation.
[c] Calculated from the equation of Dorinson *et al.*

(*b*) *Refractive Indices of Methyl Esters of Saturated Fatty Acids*

No data comparable to those for the fatty acids are available for the refractive indices of the monoesters of these acids. Incidental to an in-

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[41] D. S. Davis, *Ind. Eng. Chem.*, **35**, 1302 (1943).

vestigation of the degree of separation obtainable by fractional distillation, Wyman and Barkenbus[42] determined the refractive indices of the methyl esters of the even-numbered fatty acids from caprylic to stearic. The measurements which were made at only one temperature (45°C.) with an Abbe refractometer are given in Table 93.

The work of Wyman and Barkenbus was extended by Mattil and Longenecker,[43] who determined the variation in refractive index as a function of temperature for the series of methyl esters from caprate to stearate. They also determined the variation in refractive index as a function of composition of a series of binary mixtures of the methyl esters of both saturated and unsaturated acids. These relationships which are shown in Figures 67 and 68 are especially useful in following the fractionation of fatty acid mixtures by distillation or by low-temperature crystallization.

TABLE 93

REFRACTIVE INDICES OF METHYL ESTERS OF EVEN-NUMBERED FATTY ACIDS FROM CAPRYLIC TO STEARIC[a]

Methyl ester	n_D^{45}
Caprylate	1.4069
Caprate	1.4161
Laurate	1.4220
Myristate	1.4281
Palmitate	1.4317
Stearate	1.4346

[a] F. W. Wyman and C. Barkenbus, *Ind. Eng. Chem., Anal. Ed.*, **12**, 658–661(1940).

(c) *Refractive Indices of Unsaturated Acids and Esters*

Few data are available relative to the refractive indices of the unsaturated acids and esters. Wood *et al.*[44] reported the refractive indices of pure oleic, elaidic, linoleic, and linolenic acids at 50°C. to be 1.4487, 1.4468, 1.4588, and 1.4678, respectively. McCutcheon[45] determined the refractive indices of ethyl linoleate and ethyl linolenate over the temperature range 23° to 60°C. with the results shown in Tables 94 and 95. The refractive indices for ethyl linoleate were measured with a butyrorefractometer with light filtered through a dichromate solution to approximate sodium light, while those for ethyl linolenate were determined by means of an Abbe refractometer with sodium light.

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[42] F. W. Wyman and C. Barkenbus, *Ind. Eng. Chem., Anal. Ed.*, **12**, 658–661 (1940).

[43] K. F. Mattil and H. E. Longenecker, *Oil & Soap*, **21**, 16–19 (1944).

[44] T. R. Wood, F. L. Jackson, A. R. Baldwin, and H. E. Longenecker, *J. Am. Chem. Soc.*, **66**, 287–289 (1944).

[45] J. W. McCutcheon, *Can. J. Research*, **B16**, 158–175 (1938); **B18**, 231–239 (1940).

Values for the refractive indices obtained by Mattil and Longenecker for methyl oleate, and for mixtures of methyl oleate–methyl linoleate and methyl linoleate–methyl linolenate, are included in Figures 67 and 68 below.

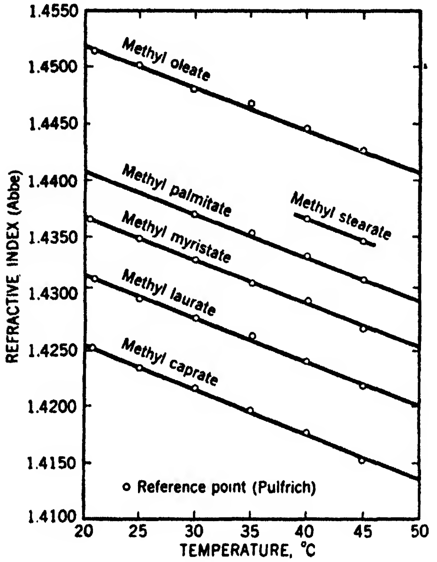

Fig. 67. Relation of refractive index to temperature for highly purified methyl esters.[43]

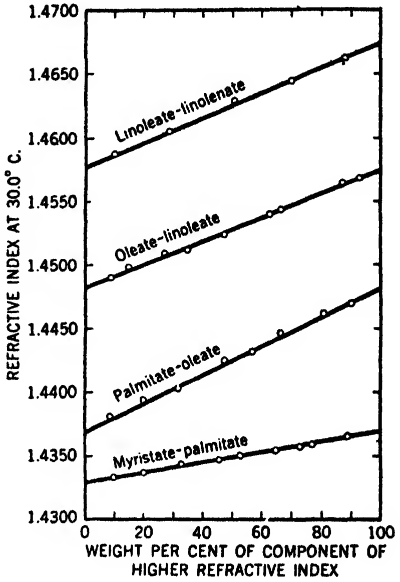

Fig. 68. Relation of refractive index to weight percentage composition of binary mixtures of highly purified methyl esters.[43]

TABLE 94

REFRACTIVE INDICES OF ETHYL LINOLEATE ACCORDING TO McCUTCHEON[a]

Temperature, °C.	Butyrorefractometer reading	Refractive index
25.8	47.70	1.4578
29.0	45.85	1.4565
34.0	43.10	1.4546
35.0	42.60	1.4542
39.0	40.25	1.4526
41.0	39.10	1.4518
44.0	37.40	1.4505
48.0	35.20	1.4489
60.0	28.75	1.4443

[a] J. W. McCutcheon, *Can. J. Research*, **B16**, 158–175 (1938); **B18**, 231–239 (1940).

TABLE 95

REFRACTIVE INDICES OF ETHYL LINOLENATE ACCORDING TO McCUTCHEON[a]

Temperature, °C.	Butyrorefractometer reading (calc.)	Refractive index
23.0	63.7	1.4683
30.2	58.9	1.4652
33.6	56.9	1.4639
38.0	54.2	1.4621
43.7	50.7	1.4598
47.6	48.3	1.4582
60.0	40.9	1.4530

[a] J. W. McCutcheon *Can. J. Research,* **B16,** 158–175 (1938); **B18,** 231–239 (1940).

(*d*) *Molecular Refractivity and Unsaturation*

It has been known for many years that when molecular refractivities are calculated from the atomic constants, adding in such constitutive factors as may be necessary, it is often found that an appreciable difference exists between the calculated value and the measured value calculated in terms of the Lorenz-Lorentz formula. This difference, called *molecular exaltation*, EM, has been traced to certain peculiarities in structure, and particularly to the presence of conjugated double bonds. Although the effect is evident in the refractive index and the density, it is magnified when expressed in molar terms. However, this multiplication may result in obscuring the effect in comparing compounds of different molecular weights. To avoid this difficulty it is customary to use *specific exaltation*, or $E\Sigma = 100(EM/m)$, where m is the molecular weight.

From the analysis of exaltation data, certain generalizations have been made relative to the effect of unsaturation on molecular refraction. One double bond in a compound produces no exaltation beyond that involved in the double bond increment used in calculating the theoretical molecular refraction. Two isolated double bonds in the compound likewise produce no abnormal exaltation. However, if the two double bonds are conjugated, a distinct exaltation is produced. The amount of the exaltation due to conjugation is, however, influenced by the length of the conjugated system, the presence of substituents, and branching of the conjugated chain. Exaltation increases as the length of conjugated chain increases, and is greatest for a linear conjugated system and decreases as the system becomes more branched.

The phenomenon of molecular exaltation should be especially significant in the study of polyunsaturated fatty acids, monoesters, and glycerides, and, particularly, in investigations involving shifts of isolated double bonds to conjugated positions. Actually, but little attention has been given to systematic studies of this type, and now that emphasis is being placed on absorption spectrophotometry, exaltation phenomena have lost considerable practical value in isomerization investigations.

6. Specific Conductivity

The electrical conductivity of any substance is its ability to carry an electric current or it is the reciprocal of its resistance. The resistance offered by conductors depends upon their nature and form; consequently, to compare the resistances of different substances they must possess the same form. Two such forms have been used, namely, a cube whose edge is one centimeter long, and a cylinder one meter in length and one square millimeter in cross section.

The conductance of a homogeneous substance of uniform cross section is proportional to its cross section, a, and inversely proportional to its length, l, *i. e.*, $L = \lambda a/l$. The proportionality factor, λ, which is the conductance when the cross section is one square centimeter and the length one centimeter, is called the *specific conductance* and is the reciprocal of the *specific resistance.*

In the case of the fatty acids the conductance may be determined for the acid *per se*, or in solution in some solvent. When measured in an ionizing solvent such as water, the conductance of a fatty acid arises from the motion of its ions. In order to compare such solutions it is necessary to do so on a gram equivalent weight basis. These conductances are therefore referred to as *equivalent conductances.* It was pointed out in a previous chapter that the conductances of the fatty acids in aqueous solution are accurate measures of the degree of their dissociation in that medium.

The conductivity can also be measured in other solvents, such as acetone, and its value calculated as the difference between that of the pure solvent and of the solution. Under these conditions the conductivity can be measured over only a limited temperature range, which for the fatty acids is generally too low to be of value in many industrial applications, consequently it is preferable to measure their conductivities directly. At room temperature the tendency of the higher fatty acids to dissociate, and hence act as conductors, is small, but with increasing temperature this tendency is markedly increased.

Lederer and Hartleb[46] determined the *specific conductivities* of caproic, myristic, and palmitic acids, and of technical stearic (m.p. 56°C.) and oleic acids. Measurements were made on the liquid acids at various temperatures between 100° and 200°C. with the results given in Table 96 and Figure 69. From the curves in Figure 69 the temperature coefficients of conductivity can be determined. The specific conductivity decreases with increasing chain length in correspondence with the well-known decrease

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[46] E. L. Lederer and O. Hartleb, *Seifensieder-Ztg.*, **56**, 345–347 (1929).

TABLE 96

SPECIFIC CONDUCTIVITIES OF SEVERAL FATTY ACIDS AT VARIOUS TEMPERATURES[a]

Caproic acid		Myristic acid		Palmitic acid		Stearic acid		Oleic acid	
°C.	$\lambda \times 10^{11}$	°C.	$\lambda \times 10^{11}$	°C.	$\lambda \times 10^{11}$	°C.	$\lambda \times 10^{11}$	°C.	$\lambda \times 10^{11}$
108	2.5	105	1.8	105	1.5	100	0.6	100	2
116	3.5	112	3.0	116	1.8	116	1.4	114	5
130	6.5	133	5.3	131	4.4	128	2.3	134	11
138	9.5	143	7.4	140	6.0	143	4.0	140	14
155	15.5	153	10.3	151	7.4	152	5.6	153	23
160	21.5	158	11.8	160	10.3	159	7.3	158	26
165	24.5	165	14.8	166	13.3	165	9.3	165	32
168	28.1	...	...	171	16.3	170	10.7	170	38
...	...	175	20.7	...	...	175	12.3	175	44
...	...	180	23.6	181	19.2	180	14.0	180	50
...	...	188	29.6	189	25.1	188	17.3	188	62
...	...	...	...	191	26.6	191	19.0	192	68
...	...	195	38.4	...	...	196	22.3	197	74
...	...	...	...	...	...	...	...	200	83

[a] E. L. Lederer and O. Hartleb, *Seifensieder-Ztg.*, **56**, 345–347 (1929)

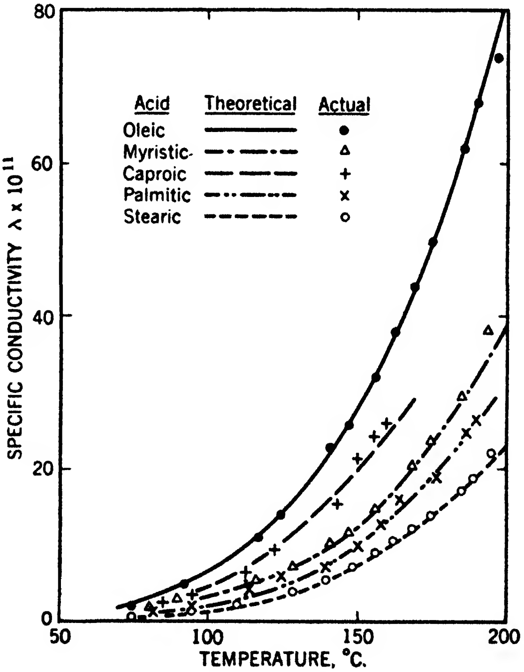

Fig. 69. Specific conductivity as a function of temperature for several fatty acids.[46]

in the strength of the acids and corresponding ease of hydrolysis of their salts as the series is ascended.

The marked increase in conductivity of oleic acid compared with stearic acid is in accord with the known fact that the salts of unsaturated acids are more strongly dissociated and, therefore, better conductors than those of the saturated acids of the same chain length.

It has been observed that the curves for the temperature *vs.* the logarithm of the coefficient of electrical conductance of fused salts are generally linear in form. Lederer and Hartleb found that this was only partly true for the fatty acids which they examined. When the logarithm of the conductivity was plotted against the temperature, the curves (Fig. 70) were found to be linear up to about 140°C. but above this temperature they tended to become concave to the temperature axis.

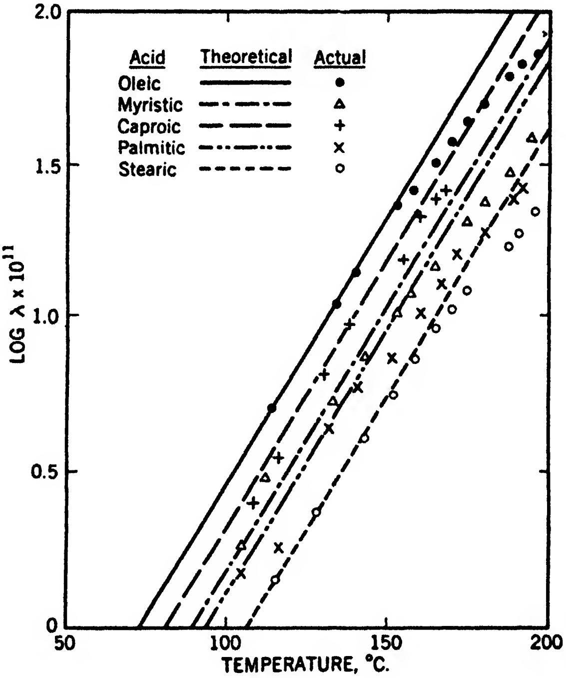

Fig. 70. Relation between the logarithm of the specific conductance and temperature of the higher fatty acids.[46]

Lederer and Hartleb found that their data could be fitted to the equation $\ln \lambda = -a + bt - ct^2$ in which λ is the specific conductance and a, b, and c are constants having the values shown in Table 97 opposite the corresponding acid. By substituting for t the temperatures corresponding to the melting and boiling points of the acids, the specific conductances for these temperatures were found to correspond to those given in Table 98.

TABLE 97

CALCULATED CONSTANTS FOR TEMPERATURE COEFFICIENT EQUATION OF SPECIFIC CONDUCTANCE[a]

Acid	*a*	*b*	*c*
Caproic	13.007	0.0274	0.000042
Myristic	13.143	0.0278	0.000042
Palmitic	13.407	0.0281	0.000042
Stearic, tech.	13.692	0.0289	0.000042
Oleic, tech.	12.843	0.0275	0.000042

[a] E. L. Lederer and O. Hartleb, *Seifensieder-Ztg.*, **56**, 345–347 (1929).

TABLE 98

CALCULATED SPECIFIC CONDUCTIVITY FOR SEVERAL FATTY ACIDS AT THEIR MELTING AND BOILING POINTS[a]

Acid	$\lambda \times 10^{11}$ at m.p.	$\lambda \times 10^{9}$ at b.p.
Caproic	0.07	2.1
Myristic	0.16	1.7
Palmitic	0.15	1.9
Stearic	0.14	1.7
Oleic	0.03	2.8

[a] E. L. Lederer and O. Hartleb, *Seifensieder-Ztg.*, **56**, 345–347 (1929).

7. Dielectric Constant

Dielectric constant is that property of a solid or liquid which, when the material is used as the dielectric medium in an electrical condenser, causes the capacitance of that condenser to be greater by some factor than when air is used as the dielectric in the same condenser. The specific inductive capacity or dielectric constant, ϵ, is a function of the force f of repulsion between two point charges, e, e', of electricity at a distance, r, apart in a uniform medium of great extent, *i. e.*, $f = ee'/\epsilon r^2$.

The theory underlying this effect may be explained by stating that the molecules of substances align themselves in an electric field and so add the unbalanced electron charges existing in the molecule to the electron charges existing on the condenser plates. The greater the extent of their alignment and the greater their unbalanced electron charges, the higher will be the dielectric constant, therefore an increase in either viscosity or temperature tends to oppose this alignment. Increasing the temperature causes greater random distribution of the molecules. The higher the frequency of the current used, the more difficult it is for the molecules to follow the current reversals against the viscosity of the medium.

It should be mentioned that the dielectric strength, S, of a material is defined as the minimum value, in the material, of the electric field intensity, *E*, at which a disruptive charge occurs. In many cases it is doubtful if *S* is a constant, as it appears to vary with certain experimental conditions.

The dielectric constant may be determined by several methods, namely, from measurements of electrical capacities of mechanical forces between charged conductors, or of the wave lengths of electrical waves. Hazlehurst[47] has described a simple apparatus and a method for determining the dielectric constants of fats and oils. The test cell consists of a brass bar 0.75 in. in diameter and 13 in. long, insulated from, and held concentric within, a brass tube 1 in. in inside diameter, together with the necessary end caps and means for making electrical contact. This device is constant in capacitance, and is easily dismantled and cleaned. The cell must be accurately checked for replacement capacitance, that is, the area that is filled by the liquid under test, and since the dielectric constant of pure benzene has been accurately determined it can be used as the standardizing medium. There is also required a precision variable condenser, a special Shering-type bridge, a.c. voltage sources covering the desired frequency ranges, and bridge balance detectors. These items of equipment are all standard and can be purchased from instrument manufacturers. According to Hazlehurst, a temperature of 30°C. and for most purposes a frequency of 200 kilocycles per second, are satisfactory for making dielectric measurements.

At one time considerable interest was evinced in the dielectric constants of the fatty acids and the corresponding esters. During the 1890's, a considerable number of papers appeared with reference to the dielectric constants of the lower members of the fatty acid series (formic to caprylic), and of the corresponding methyl, ethyl, propyl, butyl, isobutyl, and amyl esters. Many such measurements were reported prior to 1900 by Drude,[48] Löwe,[49] Jahn and Möller,[50] Tereschin,[51] Linebarger,[52] Landolt and Jahn[53] and others. Between 1910 and 1925, Dobroserdov,[54] Jackson,[55] Grimm and Patrick,[56] and others reported the results of new determinations on many of these same acids and esters.

Although there is a considerable accumulation of data with reference to the dielectric constants of the lower members of the fatty acid series, those for the higher members are much less extensive. Kahlenberg[57] determined the dielectric constants of oleic acid and a number of its metallic salts.

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[47] E. Hazlehurst, *Paint Ind. Mag.*, **58**, 262, 264, 266, 268, 270 (1943).

[48] P. Drude, *Ann. Physik*, **58** ,1–20 (1896); *Z. physik. Chem.*, **23**, 267–325 (1897).

[49] K. F. Löwe, *Ann. Physik Chem.*, **66**, 390–410, 582–596 (1898).

[50] H. Jahn and G. Möller, *Z. physik. Chem.*, **13**, 385–397 (1894).

[51] S. Tereschin, *Ann. Physik*, **36**, 792–804 (1889).

[52] C. E. Linebarger, *Z. physik. Chem.*, **20**, 131–134 (1896).

[53] H. Landolt and H. Jahn, *Z. physik. Chem.*, **10**, 289–320 (1892).

[54] D. K. Dobroserdov, *J. Russ. Phys.-Chem. Soc.*, **43**, 73–130, 225–318, 454–496 (1911).

[55] L. C. Jackson, *Phil. Mag.*, **43**, 481–489 (1922).

[56] F. V. Grimm and W. A. Patrick, *J. Am. Chem. Soc.*, **45**, 2794–2802 (1923).

[57] L. Kahlenberg, *Trans. Am. Electrochem. Soc.*, **7**, 167–169 (1905).

Three samples of reagent-grade oleic acid were measured at 20°C. and the dielectric constants were found to be 2.50, 2.57, and 2.60. The dielectric constants for the corresponding salts at 20°C. were: ferric 2.68, aluminum 2.40, copper 2.80, sodium 2.75 to 2.83, and lead 3.27 at 18°C. and 3.70 at the melting point.

Kahlenberg also examined a number of natural oils (olive 2.60, corn 2.50, cottonseed 2.30) having a high content of oleic acid and found that the free acid and oils had relatively similar values. In view of the presence of a carboxyl group and a double bond in oleic acid, he considered the dielectric constant of this acid to be abnormally low. He also stated that it was curious that the specific inductive capacity of oleic acid was so slightly changed by the introduction of heavy metals. It is possible that the dielectric constants observed by Kahlenberg were due to the poor quality of oleic acid which was available at the time (1905) that these measurements were made.

Walden[58] measured the dielectric constant of isobutyl ricinoleate at 21°C. which he found to be 4.7. Morgan and Yager[59] reported the dielectric constants of a large number of organic compounds including several esters of fatty acids which are assembled in Table 99. These authors concluded that the dielectric constants of the esters of fatty acids are not large, ranging from 6 to 7 for esters of lower molecular weight, such as methyl and ethyl acetate, down to 3 to 4 for the long chain esters, such as butyl stearate and oleate.

TABLE 99

DIELECTRIC CONSTANTS OF SEVERAL FATTY ACID ESTERS[a]

Ester	Dielectric constant, ε	Temperature, °C.
Methyl acetate	6.7	25
Ethyl acetate	6.15	20
Bornyl acetate	4.6	21
Butyl stearate	3.3	25
Butyl oleate	4.0	25
Glyceryl triacetate	9.4	24

[a] S. O. Morgan and W. A. Yager, *Ind. Eng. Chem.*, **32**, 1519–1528 (1940).

Because of the anomalous transitions exhibited by ethyl behenate, Buckingham[60] determined the dielectric constant, density, and molecular volume of ethyl behenate in the liquid and solid states. The results of the dielectric constant measurements were expressed in the form of graphs in

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[58] P. Walden, *Z. physik. Chem.*, **70**, 569–619 (1910).
[59] S. O. Morgan and W. A. Yager, *Ind. Eng. Chem.*, **32**, 1519–1528 (1940).
[60] R. Buckingham, *Trans. Faraday Soc.*, **30**, 377–386 (1934).

which the dielectric capacity was plotted against temperature. From the changes in the dielectric capacity and density between the melting point and room temperatures, Buckingham concluded that this ester exists in at least four polymorphic modifications which he designated α_1, α_2, β_1, and β_2. The α_1-form was metastable but could be observed between 45°C. and the melting point, and could be produced by cooling a melt. At 45°C. it was found to pass irreversibly into the α_2-form which was also metastable but could be examined between 43°C. and the melting point. At 43°C. the α_2-form passed to the β_1-form which in turn passed reversibly to the β_2-form at 30°C. The inversion of the α_2-form to the β_1-form was accompanied by marked changes in the density, polarization, x-ray spacing, and energy content. The changes from α_1 to α_2, and from β_1 to β_2 were not accompanied by abrupt alteration of these properties.

D. CHEMICAL REACTIONS OF THE FATTY ACIDS

CHAPTER IX

SALTS OF FATTY ACIDS

1. Introduction

In the opening chapter it was mentioned that one of the reasons for the neglect of the natural fats and fatty acids during the period of development of the classical organic reactions could be attributed to the fallacious views which were current concerning the lack of reactivity of these substances. In the following chapters it will be shown that the fatty acids are not only capable of participating in a wide variety of reactions but that many of the products possess utility and economic value. Some of these reactions offer a challenge to the organic chemist to solve various problems with respect to the mechanisms involved, to the physical chemist to determine the kinetics of these reactions, and to the physicist to determine the specific properties and physical phenomena exhibited by the reaction products.

Although our knowledge of the chemistry of petroleum products is considerably greater than that of the fatty acids, this is true not because the components of petroleum are more reactive than those of the fats, but primarily because they have received the attention of more workers. The natural fats represent raw materials equally as attractive and interesting as petroleum, but with the difference that the former await the same intensive attention which has been accorded the latter. The primary reason for the disparity in our knowledge of the chemistry of the two raw materials is not a result of a greater degree of reactivity of the hydrocarbons compared to fatty acids, but rather a difference in economy. Petroleum has been a relatively abundant and inexpensive raw material compared to the natural fats, but this may not always be the case.

It is true that the higher fatty acids possess relatively simple structures, consisting as they do of long hydrocarbon chains and a terminal carboxyl group. However, the hydrocarbon chains vary in degree of unsaturation, isomerism, and substitution both in the natural state and after they have been subjected to modification by reaction with various chemical reagents. The fatty acids undergo many of the reactions of the petroleum hydrocarbons, as well as other specific reactions associated with inherent molecular configurations not found in the natural hydrocarbons.

2. Ionic Reactions

The simplest reactions which the fatty acids undergo consist in the formation of salts on treatment with bases or base exchange salts. A number of these salts are of considerable economic importance and by far the most important from the standpoint of volume of production are the sodium and potassium salts. These salts are widely employed as detergents, and as wetting and emulsifying agents. Lead, aluminum, calcium, and other water-insoluble salts are important constituents of greases; lead, manganese cobalt, and other heavy metal salts of the unsaturated acids are used extensively as driers in the protective coating industry; sodium, calcium, tin, lead, zinc, and other metallic salts are used as catalysts for various chemical reactions; and zinc and other metallic salts are used in the preparation of pharmaceuticals and cosmetics.

The production of metallic salts of the fatty acids consists in the simple replacement of the hydrogen of the carboxyl group with a metal. This can be accomplished in several ways, *e.g.*, by the action of a base (hydroxide or oxide) on a fatty acid; by double decomposition of a soluble salt of a fatty acid and a salt of a mineral acid; or by saponification of glycerides or other esters of fatty acids with a base or metallic oxide.

The term soap, which is usually used to designate the sodium or potassium salts of the higher fatty acids, is also applied to the salts of other metals whether soluble or insoluble in water. Generally, soaps are made by heating fats and oils with aqueous alkali, usually caustic soda, but for special soaps, potash, slaked lime, and barium hydroxide may be used. The latter two reagents form, with many higher fatty acids, water-insoluble soaps used principally in the manufacture of lubricating greases. The process of saponification is discussed elsewhere in this volume since it does not directly involve the replacement of hydrogen atoms with a metal.

(a) *Preparation of Metallic Soaps for Use as Driers*

Many special soaps are produced from fatty acids by the action of bases or oxides on the free acid or by double decomposition reactions. Driers which are manufactured for use in preparing paints, varnishes, enamels, and other protective coatings, are of three general types which are designated as *kettle-cooked, fused,* and *precipitated.* In the kettle-cooked type of drier, metallic salts or oxides such as lead oxide or acetate, manganese oxide or borate, cobalt acetate, zinc oxide, calcium oxide or hydroxide are generally heated with oils, primarily linseed oil. The oxides or salts split the glycerides and react with the acid residues to form fatty acid salts.

The fused type of driers are prepared by reacting fatty acids with metallic oxides or salts to form the corresponding salt of the fatty acid in accordance with the following types of reactions:

$$(1)\quad 2\,\mathrm{RCOOH} + \mathrm{PbO} \longrightarrow \mathrm{Pb(OOCR)_2} + \mathrm{H_2O}$$

$$(2)\quad 2\,\mathrm{RCOOH} + \mathrm{Co(Ac)_2} \longrightarrow \mathrm{Co(OOCR)_2} + 2\,\mathrm{HAc}$$

Precipitated driers, which are the principal type used today, are formed by the interaction of the sodium soap of the fatty acid and a water-soluble metallic salt. A solution of sodium linoleate, made by the reaction of caustic soda and commercial linoleic acid, is treated with an aqueous solution of a metallic salt, such as lead acetate or nitrate, manganese sulfate, cobalt sulfate, or zinc sulfate. Other fatty acids, such as elaeostearic, may be used in place of linoleic acid. The reaction may be illustrated as follows:

$$\underset{\text{Sodium linoleate}}{2\,\mathrm{Na(C_{17}H_{31}COO)}} + \underset{\text{Lead acetate}}{\mathrm{Pb(CH_3COO)_2}} \longrightarrow \underset{\text{Lead linoleate}}{\mathrm{Pb(C_{17}H_{31}COO)_2}} + \underset{\text{Sodium acetate}}{2\,\mathrm{NaOOC{\cdot}CH_3}}$$

Since the heavy metal salts of many of the fatty acids are insoluble in water they precipitate and are readily recovered by filtration or decantation. For more detailed information on the methods of producing various types of driers the reader is referred to Mattiello's[1] *Protective and Decorative Coatings.*

(b) *Preparation of Metallic Soaps for Use in Greases*

Greases consist primarily of a liquid phase, generally mineral or vegetable oil, and a dispersed or gel phase which is generally a soap of a fatty acid. A wide variety of metallic soaps are used to produce an equally wide variety of greases. Cup greases, for example, usually consist of calcium oleate or stearate dispersed in mineral lubricating oils. Highly unsaturated acids or saturated acids with less than eight carbon atoms find little use in the manufacture of greases. A wide variety of fats, oils, and waxes are employed in compounding lubricating greases or for the production of soaps used in formulating these products. These include castor, rapeseed, corn, cottonseed, soybean, and palm oils, tallow, lard oil, bone and other greases, fish and sperm oils, beeswax, spermaceti, etc.

The calcium soaps of fatty acids which are used in the preparation of lubricating greases are generally produced by the action of calcium chloride on the sodium soaps of the fatty acids according to the equation:

$$\mathrm{CaCl_2} + \underset{\text{Sodium stearate}}{2\,\mathrm{C_{17}H_{35}COONa}} \longrightarrow \underset{\text{Calcium stearate}}{\mathrm{Ca(C_{17}H_{35}COO)_2}} + 2\,\mathrm{NaCl}$$

However, the calcium soap can be and often is produced by the direct action of hydrated lime on the glycerides according to the equation:

$$\underset{\text{Triglycerylstearate}}{2\,\mathrm{C_3H_5(C_{17}H_{35}COO)_3}} + 3\,\mathrm{Ca(OH)_2} \longrightarrow 2\,\mathrm{C_3H_5(OH)_3} + \underset{\text{Calcium stearate}}{3\,\mathrm{Ca(C_{17}H_{35}COO)_2}}$$

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[1] J. J. Mattiello, *Protective and Decorative Coatings.* Vol. I, Wiley, New York, 1941.

or by the direct action of hydrated lime on the fatty acids as follows:

$$\underset{\text{Stearic acid}}{2\,C_{17}H_{35}COOH} + Ca(OH)_2 \longrightarrow \underset{\text{Calcium stearate}}{Ca(C_{17}H_{35}COO)_2} + 2\,H_2O$$

Aluminum soaps, for example aluminum oleate, are generally produced by the double decomposition of water-soluble sodium soaps of the fatty acids and a solution of aluminum sulfate or alum according to the equation:

$$\underset{\text{Sodium oleate}}{6\,NaCOOC_{17}H_{33}} + \underset{\substack{\text{Aluminum}\\ \text{sulfate}}}{Al_2(SO_4)_3} \longrightarrow \underset{\text{Aluminum oleate}}{2\,Al(C_{17}H_{33}COO)_3} + 3\,Na_2SO_4$$

McBain and McClatchie[2] investigated this reaction and found that the composition of the reaction product corresponded more nearly to the mono-oleate than to either the di- or trioleate. Even when aluminum sulfate was added in considerable excess, the aluminum content of the precipitated soap was found to correspond to the mono-oleate.

Lead soaps are also used extensively in the manufacture of greases. Lead oleate is prepared by the reaction of sodium oleate and a lead salt in aqueous solution. The sodium soaps of a variety of fats and oils such as whale, castor, and linseed are often used in the place of commercial oleic acid. The lead soaps of stearic, iso-oleic, and erucic acids are also used in formulating special greases. Lithium soaps, and especially lithium stearate which has become important in airplane lubrication, are generally produced by treating fatty acids with lithium hydroxide. The resulting soaps are incorporated with lubricating oil by mixing and working in a batch or continuous process to produce a product with the desired lubricating properties.[3] Zinc soaps, especially the stearate and oleate, are used in lubricants and are produced by the reaction of zinc sulfate or acetate with the corresponding sodium soaps.

Barium and magnesium soaps are used in some types of lubricating greases. The former are prepared by the direct saponification of fats, generally rapeseed oil or tallow, with barium hydroxide or by the reaction of barium hydroxide and the fatty acids. Chromium, iron, cobalt, and nickel soaps have been proposed or used for producing special effects in lubricating greases. Their manufacture is accomplished by the methods mentioned above. Many other metallic soaps have been produced and a few are used to a limited extent in special greases. These include cadmium, mercury, strontium, cerium, copper, silver, and tin. For detailed information on the manufacture of greases the reader is referred to Klemgard's[4] *Lubricating Greases: Their Manufacture and Use.*

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[2] J. W. McBain and W. L. McClatchie, *J. Am. Chem. Soc.*, 54, 3266–3268 (1932).

[3] H. G. Houlton, B. D. Miller, P. A. Lenton, J. A. Taylor, and B. E. Adams, *Oil & Soap*, 21, 258–263 (1944).

[4] E. N. Klemgard, *Lubricating Greases: Their Manufacture and Use.* Reinhold, New York, 1937.

(c) *Preparation and Use of Metallic Soaps in Products Other Than Driers and Greases*

Sodium and calcium soaps are used as catalysts in the manufacture of mono- and diglycerides. These soaps may be formed *in situ* by addition of sodium or calcium hydroxide to the fat or they may be prepared from fatty acids and added to the fat. Tin, lead, zinc, and other metallic salts of the fatty acids act as catalysts for esterification or rearrangement of glycerides. In the rearrangement reaction, glycerol, which is added to the fat, may be considered as the primary catalyst and the metallic salt as the secondary catalyst.

Many of the metallic salts serve as catalysts in oxidative reactions for fatty acids or glycerides. Metallic soaps, for example, lead and chromium, are used as hydrogenation catalysts in preparing fatty alcohols from fatty acids. Sodium soaps are important as emulsifiers in the polymerization of butadiene, or in the copolymerization of butadiene and such polymerizable compounds as acrylonitrile, styrene, acrylic esters and the like, to produce synthetic rubber.[5,6] For this purpose, the acid radicals must possess relatively low unsaturation, *i. e.*, they must contain no acids more unsaturated than linoleic because the more unsaturated acids poison or destroy the polymerization catalyst and materially reduce the yield of polymer. However, according to a recent patent,[7] the use of the free acid or partially neutralized acid is preferred to neutral soaps because the reaction can be materially hastened, the temperature of polymerization materially lowered, the yield increased, and the quality of the polymer improved as compared with the use of sodium soaps of the same acids. According to this patent, myristic and palmitic acids or the mixed fatty acids of coconut oil are preferable to other acids and other types of oils.

Zinc salts, *e. g.*, zinc oleate and zinc stearate, are used as antiseptic and astringent agents in pharmaceutical preparations. Calcium oleate is used in modeling waxes to control their hardness. When relatively pure metallic salts are required they are prepared either by the direct action of the metallic base or oxide on the fatty acid or by the double decomposition reaction mentioned above.

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[5] C. F. Fryling, *Ind. Eng. Chem., Anal. Ed.*, **16**, 1–4 (1944).

[6] C. F. Fryling and E. W. Harrington, *Ind. Eng. Chem.*, **36**, 114–117 (1944).

[7] C. F. Fryling (to B. F. Goodrich Co.), U. S. Pat. 2,366,325 (Jan. 2, 1945).

CHAPTER X

ESTERIFICATION AND INTERESTERIFICATION

1. Introduction

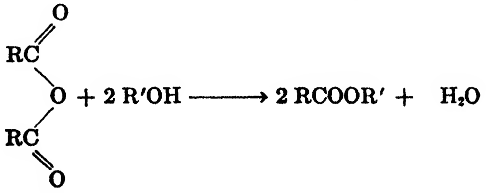
Constitutionally the fatty acid esters have been considered to be analogous to metallic salts and hence have been defined as alkyl salts of fatty acids. This definition arose from the assumption that esters are formed as a result of the replacement of the hydrogen atom of the carboxyl group by an alkyl group derived from an alcohol. According to more recent concepts of esterification, the fatty acid esters are presumed to be formed through substitution of the hydroxyl group of the carboxyl by the alkoxy group of an alcohol. An ester is therefore preferably defined as a compound which, on hydrolysis, yields an alcohol and an acid.

Esters may be formed by the reaction of an acid chloride and an alcohol or an alcoholate:

(*1*) $$RCOCl + R'OH \longrightarrow RCOOR' + HCl$$

by the reaction of an acid anhydride and an alcohol:

(*2*)



$$(RCO)_2O + 2\,R'OH \longrightarrow 2\,RCOOR' + H_2O$$

by the reaction of a salt or an organic acid and an alkyl halide or sulfate:

(*3*) $$RCOONa + R'Cl \longrightarrow RCOOR' + NaCl$$

by direct esterification of an acid and an alcohol:

(*4*) $$RCOOH + R'OH \longrightarrow RCOOR' + H_2O$$

by interesterification of an ester with an alcohol, acid, or another ester:

(*5*) $$RCOOR' + R''OH \longrightarrow RCOOR'' + R'OH$$

Of the above-mentioned methods only those of esterification and interesterification are considered in detail.

Esterification reactions and the products of esterification, whether prepared artificially or found in nature, are of foremost importance in the chemistry of the fatty acids. All vegetable and animal fats and waxes are esters of mono- or polyhydric alcohols. The occurrence of esters in nature is, however, not limited to fats and waxes. Many so-called essences consist of one or more esters of the lower aliphatic acids and low molecular weight monohydric alcohols. Also many esters of complex alcohols and fatty acids, *e. g.*, vitamin A palmitate, sterol esters, sapogenic esters, etc., are known to occur in nature. These and other types of esters are found throughout the plant and animal kingdom and esterification may, therefore, be considered as one of the fundamental vital processes.

2. Classification of Esters

Since the number and kind of acids and alcohols which may react to form esters are very large, an extremely large number of esters are theoretically possible. For example, if the first twenty members of the homologous series of *n*-fatty acids were each reacted in turn with the first twenty alcohols of the corresponding homologous series, there would result a total of four hundred esters. When the number of iso-alcohols and iso-acids are considered, not to mention various classes of substituted alcohols and acids, it is obvious that an almost infinite number of esters are possible.

Although the number of esters which are theoretically possible is very great, their consideration may be simplified by division into a few types or classes. One method of classifying these compounds may be made on the basis of the alcohols which may be esterified with a given acid. The alcohols may be divided into: (*1*) monohydric alcohols, containing an alkyl chain and a hydroxyl group, ROH; and (*2*) the polyhydric alcohols, containing an alkyl chain and two or more hydroxyl groups, *e. g.*, glycol, $HOCH_2CH_2OH$, glycerol, $CH_2OHCHOHCH_2OH$, erythritol, $CH_2OHCHOHCHOHCH_2OH$. The monohydric alcohols may in turn be subdivided into primary alcohols, RCH_2OH; secondary alcohols, $R'R''CHOH$; and tertiary alcohols, $R'R''R'''COH$. In the primary alcohols, the hydroxyl group is attached to the terminal carbon atom, but in the secondary or tertiary alcohols it may be attached anywhere along the carbon chain except at the terminal carbon atom. Any of these alcohols may be either saturated or unsaturated with respect to their carbon-carbon bonds, or they may contain other substituents in place of one or more hydrogens of the carbon chain. Also the carbon chains may be linear, branched, or cyclized.

3. Esters of Aliphatic Monohydric Alcohols

(*a*) *Properties of Monoesters*

The homologous series of methyl and ethyl esters of the saturated fatty acids are fairly complete and relatively well known, and a considerable number of the esters of the next higher alcohol homologs (propyl, butyl, amyl, etc.) have been prepared and investigated. However, data are still lacking with respect to many of the physical properties even of the simpler esters.

The calculated molecular weights, saponification values, and in the case of the unsaturated acids, the iodine values, are given in Tables 100, 101, and 102 for the methyl and ethyl esters of the more common or better known fatty acids. Data with respect to the vapor pressure, boiling point, and related properties are given in Chapter VI. The melting points of a number of low molecular weight monoesters are given in Table 103 while those of the high molecular weight esters are given in Chapter IV together with other crystal properties of these compounds.

TABLE 100

MOLECULAR WEIGHTS AND SAPONIFICATION VALUES[a] OF THE METHYL AND ETHYL ESTERS OF THE SATURATED FATTY ACIDS

Acid radical	Formula	Methyl ester, $C_nH_{2n+1}COOCH_3$		Ethyl ester, $C_nH_{2n+1}COOC_2H_5$	
		Molecular weight	Saponification value	Molecular weight	Saponification value
Formate	$HCOOR$	60.05	934.26	74.08	757.36
Acetate	CH_3COOR	74.08	757.36	88.10	636.79
Propionate	C_2H_5COOR	88.10	636.79	102.13	549.34
Butyrate	C_3H_7COOR	102.13	549.34	116.16	483.00
Valerate	C_4H_9COOR	116.16	483.00	130.18	430.96
Caproate	$C_5H_{11}COOR$	130.18	430.96	144.21	389.05
Heptanoate	$C_6H_{13}COOR$	144.21	389.05	158.23	354.56
Caprylate	$C_7H_{15}COOR$	158.23	354.56	172.26	325.69
Nonanoate	$C_8H_{17}COOR$	172.26	325.69	186.29	301.17
Caprate	$C_9H_{19}COOR$	186.29	301.17	200.31	280.08
Undecanoate	$C_{10}H_{21}COOR$	200.31	280.08	214.34	261.75
Laurate	$C_{11}H_{23}COOR$	214.34	261.75	228.36	245.68
Tridecanoate	$C_{12}H_{25}COOR$	228.36	245.68	242.39	231.46
Myristate	$C_{13}H_{27}COOR$	242.39	231.46	256.42	218.80
Pentadecanoate	$C_{14}H_{29}COOR$	256.42	218.80	270.44	207.45
Palmitate	$C_{15}H_{31}COOR$	270.44	207.45	284.47	197.22
Margarate	$C_{16}H_{33}COOR$	284.47	197.22	298.49	187.96
Stearate	$C_{17}H_{35}COOR$	298.49	187.96	312.52	179.52
Nonadecanoate	$C_{18}H_{37}COOR$	312.52	179.52	326.55	171.81
Arachidate	$C_{19}H_{39}COOR$	326.55	171.81	340.57	164.73
Behenate	$C_{21}H_{43}COOR$	354.60	158.22	368.62	152.20
Lignocerate	$C_{23}H_{47}COOR$	382.65	146.62	396.68	141.44
Cerotate	$C_{25}H_{51}COOR$	410.70	136.60	424.73	132.09
Montanate	$C_{27}H_{55}COOR$	438.75	127.87	452.78	123.91
Melissate	$C_{29}H_{59}COOR$	466.81	120.19	480.83	116.68
Dotriacontanoate	$C_{31}H_{63}COOR$	494.86	113.37	508.88	110.25
Tetratriacontanoate	$C_{33}H_{67}COOR$	522.91	107.29	536.94	104.49
Hexatriacontanoate	$C_{35}H_{71}COOR$	550.96	101.83	564.99	99.30

[a] Saponification value equals the number of milligrams of potassium hydroxide required to saponify one gram of ester or 56.104 × 1000/M.W. ester.

The melting and boiling points of the methyl and ethyl esters are lower than those of the corresponding acids. With increasing chain length of the alcohol, the values for the melting and boiling points increase and ultimately become higher than those of the corresponding acids. The esters are generally insoluble in water but are soluble in various organic liquids and the lower members are themselves good solvents for many organic compounds, including most lipids, and especially for cellulose-type lacquers. The esters of the lower and medium molecular weight acids and alcohols are pleasantly aromatic and are used in the manufacture of synthetic essences. The natural fruit essences consist of mixtures of these esters. Most of the monoesters of the higher saturated fatty acids are colorless, odorless, crystalline solids. Those of the very long chain acids and alcohols are hard, brittle, lustrous, crystalline solids which are generally referred to as waxes. Most of the highest molecular weight esters of this class are generally not known in pure form but only as complex mixtures comprising the naturally occurring waxes. A number of straight chain esters containing an unsaturated acid or an unsaturated alcohol, or both, are known to occur naturally both in plants and animals.

The monoesters are neutral substances but the lower members slowly hydrolyze in water to form free acids and alcohols. This reaction is accelerated by high temperature, the presence of alkalies, and various catalysts. As the molecular weight increases, the tendency to hydrolyze decreases, so that elevated temperatures and the presence of an alkali or catalyst are necessary for rapid reaction. Since many of the monoesters are relatively stable toward heat in the absence of moisture, they are generally distillable without decomposition. They are, therefore, often employed in processes of separation and identification of mixed fatty acids.

(*b*) *Structure of Monoesters*

The constitution of the aliphatic monoesters has long been established by double decomposition reactions and indirect alkylation methods. These methods employ the reaction of alkyl halides or dialkyl sulfates with aliphatic acids or their salts, or the reaction of monohydric alcohols with acid chlorides. Both of these types of reactions generally proceed smoothly with the formation of esters as illustrated in the following equations:

$$C_nH_{2n+1}COOAg + IC_2H_5 \longrightarrow C_nH_{2n+1}COOC_2H_5 + AgI$$

$$C_nH_{2n+1}COCl + HOC_2H_5 \longrightarrow C_nH_{2n+1}COOC_2H_5 + HCl$$

A unique indirect method of ester formation especially applicable to difficultly esterifiable acids, or acids impossible of direct esterification, has been described by Prelog and Piantanida.[1] It is especially applicable to

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[1] V. Prelog and M. Piantanida, *Z. physiol. Chem.*, **244**, 56–58 (1936).

TABLE 101

MOLECULAR WEIGHTS, SAPONIFICATION VALUES[a] AND IODINE VALUES OF THE METHYL AND ETHYL ESTERS OF MONOETHENOID FATTY ACIDS

Ester	Methyl				Ethyl			
	Formula	Molecular weight	Saponification value	Iodine value	Formula	Molecular weight	Saponification value	Iodine value
Caproleate	$C_{11}H_{20}O_2$	184.27	304.47	137.75	$C_{12}H_{22}O_2$	198.30	282.93	128.01
Lauroleate	$C_{13}H_{24}O_2$	212.32	264.24	119.55	$C_{14}H_{26}O_2$	226.35	247.78	112.14
Myristoleate	$C_{15}H_{28}O_2$	240.37	233.40	105.60	$C_{16}H_{30}O_2$	254.40	220.53	99.78
Palmitoleate	$C_{17}H_{32}O_2$	268.43	209.01	94.57	$C_{18}H_{34}O_2$	282.45	198.63	89.87
Petroselinate Oleate Vaccenate	$C_{19}H_{36}O_2$	296.48	189.23	85.62	$C_{20}H_{38}O_2$	310.50	180.69	81.75
Gadoleate	$C_{21}H_{40}O_2$	324.53	172.88	78.22	$C_{22}H_{42}O_2$	338.56	165.72	74.98
Cetoleate Erucate	$C_{23}H_{44}O_2$	352.58	159.12	71.99	$C_{24}H_{46}O_2$	366.61	153.04	69.24
Selacholeate	$C_{25}H_{48}O_2$	380.63	147.40	66.69	$C_{26}H_{50}O_2$	394.66	142.16	64.32
Hexacosenoate	$C_{27}H_{52}O_2$	408.69	137.28	62.11	$C_{28}H_{54}O_2$	422.71	132.72	60.05
Octacosenoate	$C_{29}H_{56}O_2$	436.74	128.46	58.12	$C_{30}H_{58}O_2$	450.76	124.46	56.31
Tricosenoate	$C_{31}H_{60}O_2$	464.79	120.71	54.61	$C_{32}H_{62}O_2$	478.82	117.17	53.01

[a] See footnote to Table 100.

TABLE 102

MOLECULAR WEIGHTS, SAPONIFICATION VALUES[a] AND THEORETICAL IODINE VALUES[b] OF THE METHYL AND ETHYL ESTERS OF POLYETHENOID AND SUBSTITUTED UNSATURATED ACIDS

Ester	Number of double bonds	Methyl				Ethyl			
		Formula	Molecular weight	Saponification value	Theoretical iodine value	Formula	Molecular weight	Saponification value	Theoretical iodine value
Hiragonate	3	$C_{17}H_{28}O_2$	264.39	212.20	288.02	$C_{18}H_{30}O_2$	278.42	201.51	273.51
Linoleate	2	$C_{19}H_{34}O_2$	294.46	190.53	172.41	$C_{20}H_{36}O_2$	308.49	181.87	164.57
Linolenate Elaeostearate	3	$C_{19}H_{32}O_2$	292.45	191.84	260.40	$C_{20}H_{34}O_2$	306.47	183.06	248.48
Parinarate	4	$C_{19}H_{30}O_2$	290.43	193.18	349.60	$C_{20}H_{32}O_2$	304.46	184.28	333.50
Arachidonate	4	$C_{21}H_{34}O_2$	318.48	176.16	318.81	$C_{22}H_{36}O_2$	332.51	168.73	305.36
Clupanodonate	5	$C_{23}H_{36}O_2$	344.52	162.85	368.40	$C_{24}H_{38}O_2$	358.54	156.48	353.99
Nisinate	6	$C_{25}H_{38}O_2$	370.55	151.40	411.02	$C_{26}H_{40}O_2$	384.58	145.88	396.03
Ricinoleate	1	$C_{19}H_{36}O_3$	312.48	179.54	81.23	$C_{20}H_{38}O_3$	326.50	171.83	77.74
Licanate	3	$C_{19}H_{32}O_3$	308.45	181.89	246.89	$C_{20}H_{34}O_3$	322.47	173.98	236.15
Hydnocarpate	1	$C_{17}H_{30}O_2$	266.41	210.59	95.28	$C_{18}H_{32}O_2$	280.44	200.06	90.52
Chaulmoograte	1	$C_{19}H_{34}O_2$	294.46	190.53	86.20	$C_{20}H_{36}O_2$	308.49	181.87	82.28
Gorlate	2	$C_{19}H_{32}O_2$	292.45	191.84	173.60	$C_{20}H_{34}O_2$	306.47	183.06	165.65

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[a] See footnote to Table 100.

[b] Conjugated acid esters do not add iodine normally. Experimental values are always lower than theoretical.

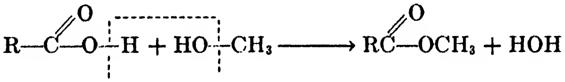
TABLE 103

MELTING POINTS IN DEGREES CENTIGRADE OF SOME ESTERS OF LOW MOLECULAR WEIGHT

Ester	Formate	Acetate	Propionate	Butyrate	Valerate
Methyl	−99.8	−98.0	−87.5	...	−91.0
Ethyl	−80.5	−82.4	−72.6	−93.3	−91.2
Propyl	−92.9	−92.5	−75.9	−95.2	...
Butyl	−90.0	−76.8	...	...	....
Amyl	−75.0	−75.0	...	...	...

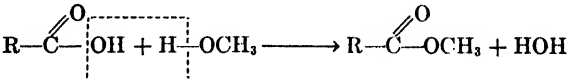
the polyterpenoid acids and sapogenins, such as oleanolic acid, chinovic acid, elaemolic acid, etc. The method depends on the thermal decomposition of the tetramethylammonium salt of the acid, which occurs readily at fairly high temperatures but within the thermal stability range of the polyterpenoid esters. The polyterpenoid acid is dissolved in methanol and treated with a methyl alcoholic solution of tetramethylammonium hydroxide. The corresponding salt is recovered and heated to decompose it to the methyl ester. The method is not especially valuable for the preparation of esters of *n*-aliphatic acids.

Although the double decomposition methods mentioned above are of general applicability, esters are ordinarily prepared by interaction of an acid and an alcohol. For many years it was assumed that ester formation of this type consisted in the replacement of the acidic hydrogen of the carboxyl group by the alkyl group of the alcohol:



$$R{-}\overset{\overset{O}{\|}}{C}{-}O{-}H + HO{-}CH_3 \longrightarrow R\overset{\overset{O}{\|}}{C}{-}OCH_3 + HOH$$

However, evidence has been obtained that the obverse course may be followed, *i.e.*, the acid furnishes the hydroxyl group and the alcohol furnishes the hydrogen:



$$R{-}\overset{\overset{O}{\|}}{C}{-}OH + H{-}OCH_3 \longrightarrow R{-}\overset{\overset{O}{\|}}{C}{-}OCH_3 + HOH$$

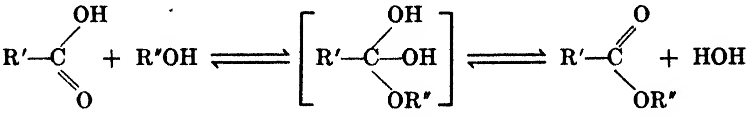
Evidence that the latter and not the former reaction occurs may be found in the reactions of the thio acids and thio alcohols. For example, when thiobenzoic acid is reacted with ethyl alcohol, ethyl benzoate and hydrogen sulfide are formed according to the following reaction:

$$C_6H_5COSH + HOC_2H_5 \longrightarrow C_6H_5COOC_2H_5 + H_2S$$

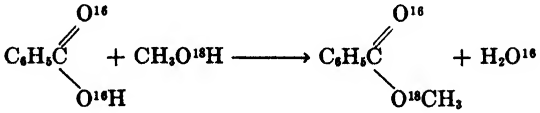
On the other hand, when benzoic acid is reacted with ethyl mercaptan an ester of thiobenzoic acid and water are obtained according to the following equation:

$$C_6H_5COOH + HSC_2H_5 \longrightarrow C_6H_5COSC_2H_5 + H_2O$$

The esterification of neopentyl alcohol or *tert*-butylcarbinol, $(CH_3)_3C{-}CH_2OH$, with carboxylic acids lends further support to the view that the alcohol provides the hydrogen rather than the hydroxyl radical in this reaction. All of the reactions which lead to a loss of the hydroxyl group in neopentyl alcohol result in the formation of *tert*-amyl derivatives. However, when this alcohol is esterified with acetic acid it forms neopentyl acetate exactly like any other alcohol. On hydrolysis of neopentyl acetate, neopentyl alcohol and acetic acid are regenerated.[1a] The reactions of neopentyl alcohol with acids lend support to the hypothesis of Henry[2] that both esterification of acids and the hydrolysis of esters take place through addition reactions at the carbonyl group according to the following scheme:



Other evidence bearing on the source of the oxygen entering the esterification reaction has been obtained by the use of isotopic oxygen. Roberts and Urey[3] investigated the esterification of benzoic acid, containing oxygen of normal isotopic composition, with methyl alcohol, containing a larger proportion of O^{18}, and found the reaction to occur as follows:



Additional evidence bearing on this mechanism may be observed in reactivities of the primary, secondary, and tertiary alcohols with fatty acids as compared with the reactivities of the same alcohols with highly ionized acids like hydrochloric. As will be discussed in more detail later, the rates of reaction of *n*-aliphatic acids with monohydric alcohols decrease in the order primary > secondary > tertiary, whereas the reverse is true with hydrochloric acid. Hydrochloric acid does not react at a measurable rate with *n*-butyl alcohol at room temperature, whereas *tert*-butyl alcohol reacts instantly to form *tert*-butyl chloride under the same conditions. On the other hand, acetic acid reacts to the extent of 48.6% with *n*-butyl alcohol in one hour at 155°C. compared to 1.4% with *tert*-butyl alcohol (see Table 104) under the same conditions. This difference in reactivity is

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[1a] F. C. Whitmore, *Organic Chemistry*. Van Nostrand, New York, 1937, p. 128.

[2] P. Henry, *Z. physik. Chem.*, **10**, 96–129 (1892).

[3] I. Roberts and H. C. Urey, *J. Am. Chem. Soc.*, **60**, 2391–2393 (1938); **61**, 2584–2587 (1939).

explainable in the case of the fatty acids if it is assumed that the hydroxyl group entering into the formation of water is supplied by the fatty acid and the hydrogen is supplied by the alcohol. In the case of the halogen acids, the hydroxyl group must be derived from the alcohol since no hydroxyl group is present in these acids.

(c) *Esterification Kinetics*

The esterification reaction which is readily reversible represents a classical example of the mass action law. If an alcohol and acid are allowed to react to form an ester and water under conditions which do not allow any of the products to escape, the same equilibrium will be attained with respect to the concentration of the reactants and products as would be obtained by hydrolysis of the ester with water under the same conditions, *i. e.*, $\mathrm{RCOOH} + \mathrm{HOR'} \rightleftharpoons \mathrm{RCOOR'} + \mathrm{HOH}$.

According to the mass action law the velocity of a reaction is proportional to the amounts of the reactants which are present in a unit volume, usually expressed as gram moles per liter. The *velocity constant* for the forward reaction (esterification) may be written:

$$v = k\,[\mathrm{RCOOH}]\,[\mathrm{HOR'}]$$

that for the reverse reaction (hydrolysis):

$$v' = k'[\mathrm{RCOOR'}]\,[\mathrm{HOH}]$$

and at equilibrium:

$$k[\mathrm{RCOOH}]\,[\mathrm{HOR'}] = k'[\mathrm{RCOOR'}]\,[\mathrm{HOH}] \quad \text{or} \quad \frac{[\mathrm{RCOOR'}]\,[\mathrm{HOH}]}{[\mathrm{RCOOH}]\,[\mathrm{HOR'}]} = \frac{k}{k'} = K$$

As the ratio of the velocity constants k and k' is a constant, it may be represented by K which is the *equilibrium constant*. The magnitude of K indicates which substance will predominate when equilibrium is reached. If K is large, the product $[\mathrm{RCOOR'}][\mathrm{HOH}]$ will be large compared with $[\mathrm{RCOOH}][\mathrm{HOR'}]$ and, if the reaction starts with the ester, it will disappear only to a small extent. If K is small the reverse will be true, while if K has a medium value, considerable concentrations of all four reactants will coexist.

The mass action law, and hence the equilibrium constant, applies only when all the reacting substances coexist in homogeneous solution. If one reactant or reaction product escapes, or is removed from the reaction medium, the equilibrium is readjusted accordingly. In the case of the uncatalyzed, homogeneous esterification of one mole of ethyl alcohol with one mole of acetic acid, equilibrium is established at 66.6% of the ester. If the concentration is increased to two moles of alcohol per mole of acetic acid, equilibrium is established at about 82% of the ester. Beyond this concentration of alcohol the equilibrium is not greatly affected and esterification cannot be made complete regardless of the excess of alcohol.

In esterifying high molecular weight alcohols and acids which dissolve little water, the water which forms by esterification separates in a layer and may be removed. As will be discussed later, when glycerol and a high molecular weight acid such as stearic acid is esterified under reduced pressure the water may be removed by bubbling a stream of inert gas through the esterification mixture. With volatile alcohols or acids other expedients must be resorted to if the reaction is to be carried beyond that indicated by the equilibrium constant obtaining with all reactants present in the reaction mixture.

The equilibrium constant is generally affected by temperature, but in the case of esterification of aliphatic acids and alcohols this change is relatively small. The change in the equilibrium constant with temperature is given by the equation:

$$\frac{d \ln K}{dT} = \frac{\Delta H}{RT^2}$$

where $\ln K$ is the natural logarithm of the equilibrium constant, T is the absolute temperature, R is the gas constant, and ΔH is the heat evolved by the reaction. In esterification reactions the heat evolved is relatively small and the change in the equilibrium constant is, therefore, correspondingly small.

The equilibrium constant in the homogeneous reaction is unaffected by the presence of catalysts but the velocity constant may be markedly affected. Thus, the addition of 3% to 5% of anhydrous hydrochloric or sulfuric acid to a mixture of acetic acid and ethyl alcohol will enormously accelerate the rate of esterification but the reacton will come to equilibrium with the formation of the same percentage of ester which would be obtained at equally effective concentrations of reactants in the absence of a catalyst. The same statement holds true for the reverse reaction; hydrolysis of ethyl acetate in the presence of hydrochloric acid will come to the same equilibrium as the forward reaction either with or without the added catalyst. In the case of vapor phase esterification in the presence of a catalyst, both the equilibrium and velocity constants may be affected by the temperature of the reaction. However, there is an optimum temperature at which the maximum esterification occurs.

The equilibrium and velocity constants for the esterification of numerous fatty acids and monohydric alcohols were determined in the course of many classical investigations of this subject, and especially by Menschutkin,[4] Kistiakowsky,[5] Meyer,[6,7] Sudborough,[7–13] Goldschmidt,[14,15] Hinshelwood,[16–18] and others.

Menschutkin[4] established the fact that branched chain acids were more difficultly esterified with a given alcohol than normal acids, and that the degree of branching and increasing molecular weight of the side chains tended to retard esterification. The data given in Tables 104 and 105 from the work of Menschutkin indicate the relative rates of esterification of various alcohols and acids in the absence of added catalyst. These data illustrate the effect of branching in the alcohol chain. Esterification with a given acid occurs to the extent of 65% to 70% in the case of primary alcohols, 50% to 60% in the case of secondary alcohols, and less than 5% in the case of tertiary alcohols.

TABLE 104

PERCENTAGE OF ESTERIFICATION OF VARIOUS ALCOHOLS BY ACETIC ACID IN ONE HOUR AT 155°C.

Primary alcohol	Per cent	Secondary alcohol	Per cent	Tertiary alcohol[a]	Per cent
Methyl	55.6	Dimethylcarbinol	26.5	Trimethylcarbinol	1.4
Ethyl	46.9	Methylethylcarbinol	22.6	Dimethylethylcarbinol	0.8
Propyl	46.9	Methylhexylcarbinol	21.2		
n-Butyl	46.8	Methylisopropylcarbinol	18.9	Methyldiethylcarbinol	1.0
n-Octyl	46.6	Diethylcarbinol	16.9	Dimethylpropylcarbinol	2.1
				Dimethylisopropylcarbinol	0.9

[a] Dehydration also takes place.

The comparison of acids with respect to their relative rates of reaction with a given alcohol cannot be made as readily as it can with a given acid and a series of alcohols, because the rate of esterification is a function of the concentration of the catalyst and the catalyst is the acid or one of its dis-

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[4] N. Menschutkin, *Ann.*, **195**, 334–364 (1879); **197**, 193–225 (1879); *Ann. chim. phys.*, **20**, 289–361 (1880); **23**, 14–85 (1881); **30**, 81–144 (1883).

[5] W. A. Kistiakowsky, *Z. physik. Chem.*, **27**, 250–266 (1898).

[6] V. Meyer, *Ber.*, **27**, 510–512 (1894).

[7] V. Meyer and J. J. Sudborough, *Ber.*, **27**, 1580–1592; 3146–3153 (1894).

[8] J. J. Sudborough and L. L. Lloyd, *J. Chem. Soc.*, **75**, 467–483 (1899).

[9] W. A. Bone, J. J. Sudborough, and C. H. G. Sprankling, *J. Chem. Soc.*, **85**, 534–555 (1904).

[10] J. J. Sudborough and E. R. Thomas, *J. Chem. Soc.*, **91**, 1033–1036 (1907).

[11] J. J. Sudborough and J. M. Gittins, *J. Chem. Soc.*, **93**, 210–217 (1908); **95**, 315–321 (1909).

[12] J. J. Sudborough and M. K. Turner, *J. Chem. Soc.*, **101**, 237–240 (1912).

[13] E. R. Thomas and J. J. Sudborough, *J. Chem. Soc.*, **101**, 317–328 (1912).

[14] H. Goldschmidt and O. Udby, *Z. physik. Chem.*, **60**, 728–755 (1907).

[15] H. Goldschmidt and A. Thuesen, *Z. physik. Chem.*, **81**, 30–67 (1912).

[16] C. N. Hinshelwood and A. R. Legard, *J. Chem. Soc.*, **1935**, 587–596.

[17] A. T. Williamson and C. N. Hinshelwood, *Trans. Faraday Soc.*, **30**, 1145–1149 (1934).

[18] R. A. Fairclough and C. N. Hinshelwood, *J. Chem. Soc.*, **1939**, 593–600.

TABLE 105

PERCENTAGE OF ESTERIFICATION OF VARIOUS ACIDS BY ISOBUTYL ALCOHOL IN ONE HOUR AT 155°C.

Acid	Per cent	Acid	Per cent	Acid	Per cent
Formic	61.7	Butyric	33.3	α-Methylbutyric	21.5
Acetic	44.4	Caprylic	30.9	Trimethylacetic	8.3
Propionic	41:2	Isobutyric	29.0	Dimethylethylacetic	3.5

sociation products, the solvated proton. Therefore, when the rates of esterification of two acids are measured, the resultant rate is a function of the rate of reaction of the acid and also of the activity of the acid as a catalyst. In the range of concentration where the rate of esterification is proportional to the hydrogen ion concentration, it is possible to calculate the rate of reaction to a standard hydrogen-ion concentration.

Goldschmidt[19] observed that although the reaction between an alcohol and an acid, in the presence of hydrogen chloride, is bimolecular, when a large excess of alcohol is present it may be regarded as monomolecular. It will be recalled that for a bimolecular reaction the equation:

$$k = \frac{x^2}{(a-x)(b-x)}$$

is generally applied and that the original data of Berthelot and de St. Gilles[20] for the reaction of acetic acid and ethyl alcohol agree within limits of experimental error for this bimolecular equation. Goldschmidt also showed that the velocity of esterification depends on the catalytic agent employed. It is relatively constant with hydrochloric or hydrobromic acids but is appreciably reduced with picric acid. In dilute alcoholic solutions, the velocity is proportional to the concentration of the hydrogen chloride.

Kistiakowsky[5] found that under identical conditions the velocity constants of esterification and hydrolysis are identical and that in the presence of hydrochloric acid the constants are proportional to the concentration of hydrochloric acid, *i. e.*, the velocity constant of hydrolysis of an ester, $RCOOC_2H_5$, by a solution of hydrogen chloride in a mixture of water and alcohol is identical with the esterification constant of the acid, RCOOH, when an aqueous alcoholic solution of hydrogen chloride of exactly the same strength is employed.

Sudborough and co-workers calculated the velocity constants for a large number of esterification reactions of methyl and ethyl alcohols and a wide variety of acids, including many of the common aliphatic acids. They

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[19] H. Goldschmidt, *Ber.*, **28**, 3218–3227 (1895).

[20] M. Berthelot and P. de Saint-Gilles, *Ann. chim. phys.*, **65**, 385–442; **66**, 5–110 (1862).

applied the equation for monomolecular reactions, namely, $k = \frac{1}{t} \ln \frac{a}{a-x}$, in which t is the time in hours and a is the initial concentration of the acid. In order to determine the velocity constant for any esterification reaction he assumed that it was only necessary to determine by titration the amount of unreacted organic acid after any interval of time t, and substitute these values in the equation given above.

Since the velocity of the reaction is proportional to the concentration of hydrogen chloride in the mixture and is affected by the temperature, Sudborough and Lloyd[8] proposed the use of the expression $E^{10°}_{MeOH}$, $E^{15°}_{EtOH}$, etc., to represent the esterification constant calculated on the basis of a concentration of hydrochloric acid in the reaction mixture equal to one normal hydrochloric acid.

The velocity constants of esterification determined by Sudborough and co-workers are those generally referred to at the present time. However, these constants have been recalculated to a more comparable basis which leads to somewhat different though entirely comparable values. The recalculated values for $k^{15°}_{MeOH}$ referred to HCl = 1 which are given in Table 106 are those found in the *International Critical Tables.*[21] Reference to Table 106 will reveal the fact that in the case of the saturated acids the value of the velocity constant decreases rapidly with the increase in the number of CH_2 groups in the acid up to butyric acid after which it is nearly the same for all of the homologous acids. The velocity constant for the

TABLE 106

VELOCITY CONSTANTS FOR THE ESTERIFICATION OF VARIOUS FATTY ACIDS AND METHYL ALCOHOL CATALYZED BY HYDROCHLORIC ACID[a]

Acid	k	Acid	k
Formic	2568	Lauric	121.9
Acetic	239	Myristic	120.9
Propionic	211.7	Palmitic	114.4
Butyric	115.2	Stearic	123.7
Valeric	123.2	Undecenoic	53.0
Caproic	118.7	Oleic	54.4
Heptanoic	120.9	Elaidic	54.4
Caprylic	125.8	Erucic	51.2
Nonanoic	123.5	Brassidic	51.8
Capric	119.3	$\Delta^{2,3}$-Oleic	1.3

[a] A. Skrabal, "Chemical Kinetics," in *International Critical Tables.* Vol. VII, McGraw-Hill, New York, 1930, p. 138.

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[21] A. Skrabal, "Chemical Kinetics," in *International Critical Tables,* Vol. VII, McGraw-Hill, New York, 1930, p. 138.

corresponding unsaturated acids having a double bond near the center of the hydrocarbon chain is less than half that for the corresponding saturated acid. *Cis-* and *trans-*isomers have almost identical velocity constants. When the double bond is adjacent to the carboxyl group the velocity constant decreases to a very low order, *e. g.*, 1.3 for $\Delta^{2,3}$-oleic acid compared to 54.4 for $\Delta^{9,10}$-oleic acid and 123.7 for stearic acid.

Smith and Reichardt[22] reinvestigated the acid-catalyzed esterification of the normal fatty acids from acetic to lauric, in dry methanol, and determined the rate constant and energy of activation of the reaction. Throughout the series of normal acids the activation energy was a constant and had a value of 10,000 cal. per mole.

Although the mineral acids, particularly hydrochloric and sulfuric, are primarily used as esterification catalysts with low molecular weight monohydric alcohols, other catalysts, especially the aromatic sulfonic acids, are also used. Zaganiaris and Varvoglis[23] investigated the utility of Twitchell's reagent in the preparation of esters of low molecular weight alcohols and a variety of fatty acids from acetic to palmitic. An excess of alcohol equivalent to 3 to 10 times the weight of acid was used with 1% to 2% of catalyst. For example, palmitic acid esterified for 8 hours with 10 times its weight of absolute ethanol containing 1% of Twitchell reagent gave approximately 81% of ester.

Swern and Jordon[24] described the preparation of a series of alkyl esters of 9,10-dihydroxystearic acids (m.p. 95° and 130°C.) in which esterification was accomplished by heating the acids for eight hours with the corresponding alcohols in benzene solution containing naphthalene-β-sulfonic acid as catalyst. The water formed during the reaction was removed azeotropically and the benzene was returned to the reaction mixture.

The action of the sulfonation catalysts in esterification has been ascribed to the formation of intermediate compounds between the —SO_3H radical and alkyl group of the alcohol, and in the case of hydrolysis, especially of fats, to the increased solubility of the ester in water.

(*d*) *Preparation of Monoesters*

The foregoing discussion of the esterification of monohydric alcohols and monocarboxylic acids indicates that the reaction varies with the nature of the reactants and the medium employed. In general, esterification is carried out by heating a concentrated mixture of alcohol and acid in the presence of a catalyst. The catalyst most commonly employed is anhydrous sulfuric or hydrochloric acid. The concentration of mineral acid employed

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[22] H. A. Smith and C. H. Reichardt, *J. Am. Chem. Soc.*, 63, 605–608 (1941).
[23] J. N. Zaganiaris and G. A. Varvoglis, *Ber.*, 69, 2277–2282 (1936).
[24] D. Swern and E. F. Jordon, Jr., *J. Am. Chem. Soc.*, 67, 902–903 (1945).

is usually 3% to 5%. However, some workers[25] use methyl alcohol saturated with dry hydrochloric acid or saturate the esterification mixture with dry hydrogen chloride prior to refluxing. Dehydrating agents such as calcium chloride are also employed in conjunction with hydrochloric acid.

Since the lower molecular weight alcohols and acids are liquids which are mutually soluble over a considerable temperature range, no solvent is necessary in these esterifications. With mixtures of high molecular weight alcohols and acids a solvent such as benzene or toluene may be employed.

Although the method of esterification used in the preparation of the methyl and ethyl esters of the higher molecular weight fatty acids may be stated simply in the general terms indicated above, the details given in the literature are surprisingly variable. Most authors are prone to state that so many grams or moles of fatty acid and alcohol, containing a specified percentage of catalyst, were refluxed for a specified number of hours, or until the reaction was completed, after which the ester was recovered from the reaction mixture. Some authors recover the unesterified acid and subject it to a second esterification.

Standard references on fat chemistry devote little space to the subject of esterification in so far as it pertains to laboratory procedures, and especially to the optimum conditions for carrying out the reaction. Hilditch,[26] in his latest edition of *The Chemical Constitution of Natural Fats*, states that mixed fatty acids "are converted into methyl esters by boiling with about twice their weight of methyl alcohol in the presence of about 2 per cent. of concentrated sulfuric acid, and subsequently removing unesterified acid by washing the ether solution of the esters with dilute potassium carbonate solution. The conversion into methyl esters is usually 97 to 98 per cent., but if by accident it falls below this figure, the unesterified acid should be recovered and re-esterified."

In his monograph, *The Industrial Chemistry of the Fats and Waxes*, Hilditch[27] states: "Each of the fractions of the fatty acids resulting from the lead salt separation is converted to methyl or ethyl esters by dissolving in about four times its weight of the alcohol (to which 2 per cent. of concentrated sulfuric acid is added), and boiling under reflux for about two hours. Esterification proceeds very readily and almost to completion, and, after removal of as much alcohol as possible by distillation on a water-bath, the residue is dissolved in ether and washed, first with water to remove mineral acid, and then cautiously with dilute sodium carbonate in order to remove unchanged fatty acid with as little formation of soap–ether emulsion as possible."

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[25] A. O. Cruz and A. P. West, *Philippine J. Sci.*, 48, 77–88 (1932).

[26] T. P. Hilditch, *The Chemical Constitution of Natural Fats.* Wiley, New York, 1940, p. 373.

[27] T. P. Hilditch, *The Industrial Chemistry of the Fats and Waxes.* 2nd ed., Baillière, Tindall & Cox, London, 1941, p. 88.

Dean[28] in his monograph, *Utilization of Fats*, states: "The 'solid' and 'liquid' acids are then esterified by boiling with two to three times their weight of methyl alcohol containing 4 per cent. of sulfuric acid." Jamieson,[29] Bull,[30] and Bloor[31] fail to discuss esterification from the preparatory standpoint. Several special methods have been described[32] for the preparation of specific esters, as for example *n*-butyl-*n*-butyrate, ethyl adipate, and ethyl-*n*-tridecanoate. In the preparation of *n*-butyl-*n*-butyrate simultaneous oxidation of butyl alcohol and esterification by means of sodium dichromate and sulfuric acid is employed. The yield of ester in this process is only 41% to 47% of theory.

For preparing ethyl adipate, a mixture of toluene and ethyl alcohol is employed to form an azeotropic mixture of alcohol–toluene–water which distills between 75° and 78°C. The distillate can be freed of water with a dehydrating agent and returned to the reaction mixture. This method makes it possible to obtain a high yield of ester without using an unduly large proportion of alcohol; actually an excess of only two moles of alcohol per mole of adipic acid is required with a concentration of sulfuric acid equal to one per cent of the weight of organic acid used.

A similar method of esterification has been described by Locquin and Elghozy[33] using toluene and hydrochloric acid, while van Rysselberge[34] employed benzene and sulfuric acid for the same purpose. Direct esterification of adipic acid and ethyl alcohol has also been described by Arppe,[35] Curtius,[36] and Bouveault and Locquin.[37]

Ethyl-*n*-tridecanoate is prepared by refluxing 95% alcohol containing 3% to 5% by weight of anhydrous hydrogen chloride with crude *n*-tridecanoic acid. Anhydrous calcium chloride is added to the mixture after which it is refluxed for 24 hours. The ester layer is separated and refluxed for an additional 24 hours with alcohol, hydrogen chloride, and calcium chloride. Despite the use of an excess of 13 moles of alcohol the yield is 84% or less of the theoretical. This esterification procedure while obviously useful for some preparations is not very efficient or economical. Ethyl pentadecanoate has been prepared by the same procedure.

Although the esterification of a given quantity of fatty acids is usually considered fairly complete as described by many authors, actually this is often not the case. However, the actual degree of esterification can be readily determined by withdrawing a sample of the esterification mixture

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[28] H. K. Dean, *Utilization of Fats*. Chemical Pub. Co., Brooklyn, 1938, p. 75.
[29] G. S. Jamieson, *Vegetable Fats and Oils*. 2nd ed., Reinhold, New York, 1943.
[30] H. B. Bull, *The Biochemistry of the Lipids*. Wiley, New York, 1937.
[31] W. R. Bloor, *Biochemistry of the Fatty Acids*. Reinhold, New York, 1943.
[32] *Organic Syntheses*, Collective Volumes I and II. Wiley, New York, 1932, 1942.
[33] R. Locquin and F. Elghozy, *Bull. soc. chim.*, **41**, 445–448 (1927).
[34] M. van Rysselberge, *Bull. soc. chim. Belg.*, **35**, 311–328 (1926).
[35] A. E. Arppe, *J. prakt. Chem.*, **95**, 193–211 (1865).
[36] T. Curtius, *J. prakt. Chem.*, **91**, 1–38 (1915).
[37] L. Bouveault and R. Locquin, *Bull. soc. chem.*, **3**, 437–441 (1908).

and titrating it with alkali. If an acid catalyst is used due allowance must be made for its presence.

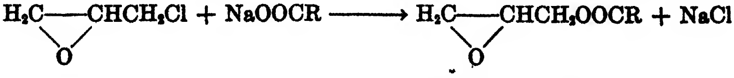
When the esterification mixture contains any appreciable amount of unreacted fatty acids, troublesome emulsions are often encountered if sodium or potassium hydroxide or carbonate is used in an effort to remove them. Buxton and Kapp[38] have described a method for circumventing this difficulty, especially when large amounts of high molecular weight esters are prepared. Their procedure is as follows. The unreacted alcohol is distilled from the esterification mixture, and the residue of free acids, crude ester, and catalyst is dissolved in two to five parts by weight of ethylene dichloride to one part of ester. After determination of the amount of free acid by titration with 0.5 *N* alcoholic potassium hydroxide, an equivalent weight of concentrated aqueous potassium hydroxide (38%) is added slowly with stirring. The potassium soaps of the unreacted fatty acids will rise to the surface and the potassium salt of the mineral acid catalyst will precipitate. Both products may be separated by filtration. After washing the separated precipitate with ethylene dichloride the combined washings and filtered ester is distilled. The advantage of the method is that it eliminates the use of ether with its attendant hazards and avoids the formation of emulsions.

4. Esters of Other Monohydric Alcohols

In addition to the monoesters formed by the reaction of the normal and branched chain aliphatic alcohols, many esters of other monohydric alcohols and fatty acids are known. Many of these monohydric alcohols are cyclic; some are heterocyclic compounds, such as the ether alcohols, furfurol, tetrahydrofurol, etc.

(a) *Esters of Heterocyclic Alcohols*

The ether alcohols, obtained by dehydration of polyhydric alcohols, have been used in the preparation of monoesters. For example, glycidol,  $\underset{\diagdown O \diagup}{H_2C\text{—}CHCH_2OH}$, which may be considered as the dehydration product of glycerol, may be esterified with fatty acids. Kester, Gaiser, and Lazar[39] prepared a series of glycidyl esters by reacting epichlorohydrin with lauric, myristic, palmitic, stearic, and oleic acids according to the equation:



$$\underset{\diagdown O \diagup}{H_2C\text{——}CHCH_2Cl} + NaOOCR \longrightarrow \underset{\diagdown O \diagup}{H_2C\text{——}CHCH_2OOCR} + NaCl$$

In contrast to glycidol, the glycol ethers generally retain their polyhydric structures since the dehydration may be considered as occurring

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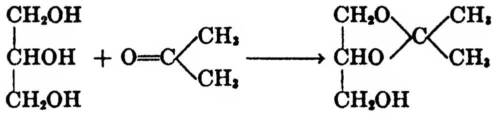
[38] L. O. Buxton and R. Kapp, *J. Am. Chem. Soc.*, 62, 986 (1940).

[39] E. B. Kester, C. J. Gaiser, and M. E. Lazar, *J. Org. Chem.*, 8, 550–556 (1943).

between two or more molecules of glycol rather than intramolecularly. Another series of ether alcohols is obtained through substitution of an alkyl group for one of the hydrogen atoms in one of the two hydroxyl groups of the glycols. The ethylene glycol monoalkyl or monoaryl ethers, $ROCH_2CH_2OH$, which are also known as *Cellosolves*, have been used in the preparation of fatty acid esters. Diethylene glycol forms a similar series of ether alcohols of the general formula $ROCH_2CH_2OCH_2CH_2OH$ which are referred to as *Carbitols*. The Cellosolve and Carbitol acetates are liquids which have application as solvents for gums, resins, nitrocellulose, etc.

The isopropylidene monohydric alcohol esters are of considerable importance in the synthesis of glycerides. The isopropylidene group is introduced into glycerol by allowing freshly distilled, anhydrous glycerol to stand in contact with acetone saturated with dry hydrogen chloride and fused anhydrous sodium sulfate. The excess hydrogen chloride is then removed, the acetone distilled off, and the isopropylideneglycerol is distilled. The reaction may be represented as follows:



The isopropylidene derivative is therefore a monohydric alcohol which can be esterified with fatty acids in the presence of dry hydrogen chloride. If desired, the isopropylidene group may then be removed by reaction of the ester in ether solution with concentrated hydrochloric acid. With esters below lauric acid the hydrolysis must be carried out below −15° to 0°C. in 5 to 10 minutes.

Benzaldehyde reacts with glycerol in a similar manner to produce 1,2-benzylideneglycerol which, like isopropylideneglycerol, contains a free hydroxyl group and may, therefore, be esterified with fatty acids.

Esters of furfuryl and tetrahydrofurfuryl alcohols have been prepared and described. For example, Norris and Terry[40] prepared the furfuryl esters of palmitic, oleic, and linseed oil fatty acids using an ester interchange method. Van Schaack[41] patented the preparation of the fatty acid esters of tetrahydrofurfuryl alcohol. The esterification is carried out in benzene solution using a slight excess of the alcohol and 0.1% of sulfuric acid, based on the weight of fatty acid, as catalyst.

(*b*) *Esters of Hydroaromatic Alcohols*

Various esters of hydroaromatic alcohols have been described. For example, a number of bornyl esters of *n*-aliphatic acids have been prepared by

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[40] F. A. Norris and D. E. Terry, *Oil & Soap*, 21, 193–196 (1944).

[41] R. H. Van Schaack, Jr. (to Van Schaack Bros. Chemical Works, Inc.), U. S. Pat. 1,802,623 (April 28, 1931).

Minguin and de Bollemont.[42] The menthyl esters of the *n*-aliphatic acids from formic to stearic have been prepared by Hilditch[43] and some of their properties, especially their molecular rotatory power, have been determined. These esters were not prepared by direct esterification but by reaction of the acid chlorides and menthol. The related brucine and cinchonine salts of the higher fatty acids (myristate to stearate) were likewise prepared by Hilditch.

Van Schaack[44] patented the preparation of the fatty acid esters of the hydrogenated aromatic alcohols, such as cyclohexanol.

5. Esters of Polyhydric Alcohols

The fatty acid esters of many polyhydric alcohols have been prepared and, in some cases, their properties and reactions studied in detail. Comparatively few investigations have, however, been made of the reaction mechanisms owing to the inherently greater complexity of these reactions compared to those involved in the formation of monoesters.

The most important polyhydric esters are the natural fats, or the glyceryl esters of the higher fatty acids, but the esters of a number of other polyhydric alcohols have attained industrial importance and all are of scientific interest. The polyhydric alcohols which have been esterified with various fatty acids include the diols, triols, tetrols, pentitols, and hexitols. The closely related polyhydric ethers which have been reacted with fatty acids include the polyalkylene glycols, polyglycerols, polymerized pentaerythritols (hexitols), hydroxyalkyl ethers or polyhydric alcohols, as well as the simpler carbohydrates (mono-, di-, and trisaccharides).

Two classes of polyhydric alcohol esters may be distinguished, namely, (*1*) those in which all the alcoholic hydroxyl groups have been esterified; and (*2*) those which are incompletely esterified. The esters formed by partial as well as by complete esterification of polyhydric alcohols are of considerable industrial importance.

It is now more than 100 years since the first synthesis of a triglyceride was reported by Pelouze and Gélis (1844) who esterified glycerol with butyric acid. The first nonglycerol, polyhydric alcohol esters of the fatty acids were described in 1855 by Berthelot[45] who prepared various esters of erythritol, dulcitol, mannitol, and glucose. The first glycol esters were prepared in 1859 by Wurtz.[46]

Goldsmith[47] has published a comprehensive review of the literature on

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[42] J. Minguin and E. G. de Bollemont, *Compt. rend.*, **134**, 608–610 (1902).

[43] T. P. Hilditch, *J. Chem. Soc.*, **95**, 331–341, 1570–1583 (1909); **101**, 192–202, 202–207 (1912).

[44] R. H. Van Schaack, Jr. (to Van Schaack Bros. Chemical Works, Inc.), U. S. Pat. 1,697,295 (Jan. 1, 1929).

[45] M. Berthelot, *Compt. rend.*, **41**, 452–456 (1855).

[46] A. Wurtz, *Ann. chim. phys.*, **55**, 400–478 (1859).

[47] H. A. Goldsmith, *Chem. Revs.*, **33**, 257–349 (1943).

the preparation, physical and chemical data, and industrial applications of the higher fatty acid esters of the polyhydric alcohols and polyhydroxy ethers.

Menschutkin[48] included in his classical investigation of esterification both monohydric and polyhydric alcohols. The polyhydric alcohols include a series of glycols (ethylene, propylene, and trimethylene), glycerol, erythritol, mannitol, and dulcitol. The reaction velocities were determined for a number of different acids with each polyhydric alcohol and with varying ratios of alcohol to acid. For example, ethylene glycol was esterified with one to six moles of acetic acid. The esterification velocity was found to be affected by isomerism (chain branching) in the polyhydric alcohols just as was found to be the case with the monohydric alcohols.

The tri-, tetra-, and hexahydric alcohols were likewise esterified with one to six moles of acetic acid. With increasing numbers of hydroxyl groups, and with molar ratios of acid equal to the number of hydroxyl groups in the alcohol, the reaction velocity progressively decreased as indicated by the equilibrium concentrations of the esters shown in Table 107. When, however, the same alcohols were esterified with only one mole of acid the equilibrium was not greatly different; methanol, 69.59; glycol, 69.86; glycerol, 70.08; erythritol, 65.73; mannitol, 62.53%. The experiments of Menschutkin refer to uncatalyzed, homogeneous conditions of esterification. However, like monohydric alcohols, the esterification of polyhydric alcohols is affected by catalysts, temperature, agitation, and removal of water produced during the reaction.

TABLE 107

EQUILIBRIUM VALUES OF ESTERIFICATION OF VARIOUS ALCOHOLS WITH ACETIC ACID

Alcohol	Mole ratio acid/alcohol	Equilibrium concentration of ester, %
Ethanol	1	66.57
Ethylene glycol	2	53.94
Glycerol	3	46.00
Erythritol	4	40.07
Mannitol	5	26.42

Unlike monohydric alcohols, an excess of polyhydric alcohol cannot be employed when complete esterification is desired. Because of the tendency of specific hydroxyl groups to esterify preferentially, *i. e.*, to form mono- rather than polysubstituted alcohol esters, the fatty acids tend to distribute themselves among all the molecules of alcohol present rather than to completely esterify any given molecule of the polyhydric alcohol.

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[48] N. Menschutkin, *Ann. chim. phys.*, 23, 14–85 (1881).

Water may be removed in a variety of ways depending on the nature of the polyhydric alcohol employed in esterification. If the alcohol is water-soluble, another solvent may be added and the water removed by azeotropic distillation. If the alcohol is water-insoluble, the water may be distilled azeotropically by adding excess alcohol. Other methods make use of efficient vacuums, inert gases, combinations of vacuums and inert gases, the addition of a dehydration agent, and other expedients. Catalysts are generally employed to reduce the time of reaction and to reduce the temperature of esterification in the case of acids of low thermal stability.

(a) *Esters of Glycols and Ether Glycols*

The glycols consist of hydrocarbon chains with two hydroxyl groups attached to two of the carbon atoms and are, therefore, the simplest polyhydric alcohols which may be esterified with the higher fatty acids to form polyesters. The lowest member of the series is ethylene glycol, $HOCH_2$-CH_2OH. With more than two carbon atoms in the chain, positional isomers become possible since the two hydroxyl groups may be attached to any two of the carbon atoms in the chain, thus there are two propylene glycols, four butylene glycols, etc., exclusive of additional isomers resulting from branching of the hydrocarbon chain. Only a few of the large number of theoretically possible glycols have been used in the preparation of esters of higher fatty acids. The most important ones are listed in Table 108 together with some of their properties.

TABLE 108

GLYCOLS USED IN THE PREPARATION OF ESTERS

Glycol	Formula	Boiling point, °C.	Melting point, °C.
Ethylene	CH_2OHCH_2OH	197.2	−11.5
1,2-Propylene	$CH_3CHOHCH_2OH$	187.4	
1,3-Propylene	$CH_2OHCH_2CH_2OH$	210 (214 dec.)	
1,2-Butylene	$CH_3CH_2CHOHCH_2OH$	192	
2,3-Butylene	$CH_3CHOHCHOHCH_3$	184 (180)	27
1,3-Butylene	$CH_3CHOHCH_2CH_2OH$	204	
1,4-Tetramethylene	$CH_2OH(CH_2)_2CH_2OH$	230 ($108^{4\text{ mm.}}$)	
1,5-Pentamethylene	$CH_2OH(CH_2)_3CH_2OH$	239	
1,6-Hexamethylene	$CH_2OH(CH_2)_4CH_2OH$	250	42

The lower members of the glycol series are high boiling liquids which are heavier than water. Since they contain two hydroxyl groups they can form mono- and diesters. The monoesters containing a primary alcohol group and an ester group have solvent properties, especially when the ester group is of low molecular weight. The higher molecular weight monoesters of the glycols are useful interface-modifying agents. The high molecular weight diesters of glycol are similar to the glycerol esters, while those of the highest molecular weight are waxlike substances. Depending on the nature of the attached fatty acid, they may serve as lubricant modifiers, plasticizers, emulsifying agents, etc.

Another closely related group of glycols are the polyethylene glycols which have the general formula $HOCH_2CH_2(OCH_2CH_2)_nOH$, where *n* may have any value from one to nine. The simplest member of the series is diethylene glycol, $HOCH_2CH_2OCH_2CH_2OH$. Structurally, these compounds are dihydric ethers, hence the name glycol ethers. The best known polyethylene glycols are, in addition to diethylene glycol, triethylene glycol, $HOCH_2(CH_2OCH_2)_2CH_2OH$; tetraethylene glycol, $HOCH_2(CH_2O-CH_2)_3CH_2OH$; hexaethylene glycol, $HOCH_2(CH_2OCH_2)_5CH_2OH$; and nonaethylene glycol, $HOCH_2(CH_2OCH_2)_8CH_2OH$. These glycols are higher boiling liquids (244° to 325°C.) than the corresponding simple glycols, and they become increasingly viscous with increasing molecular weight.

The polyethylene glycols, like the simple glycols, may be esterified with fatty acids to produce corresponding mono- and diesters. Both classes of glycols may be directly esterified with fatty acids in the same manner as the monohydric alcohols. For complete direct esterification an excess of fatty acid is required, whereas for the preparation of monoesters an excess of glycol is used. The reaction, although random with respect to the hydroxyl group first attacked, obviously takes place in two steps involving first one and then the second hydroxyl group. The reaction velocity is increased by high temperature, the addition of catalysts, agitation and removal of moisture.

Dry hydrogen chloride has been suggested or used as a catalyst at elevated temperatures. Sulfuric and phosphoric acids, and various acid salts have been recommended as catalysts for the esterification of the glycols. Acetyl chloride and the Twitchell reagents (sulfonic acids of benzene, toluene, naphthalene, or camphor) have also been proposed or used. Finely powdered metals such as zinc, tin, iron, manganese, etc., have been proposed as catalysts for the esterification of the glycols.

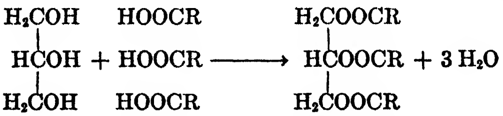
The use of agitation and/or carrier solvents increase the speed and effectiveness of the esterification, particularly where the fatty acid and glycol are not completely miscible. Aeration with various gases speeds the reaction both by agitation and removal of water and in certain cases may protect the reactants or products from oxidation. Glycol esters may also be prepared by reaction of fatty acid anhydrides or chlorides and glycols.

(*b*) *Esters of Glycerol*

As has been mentioned previously, the oldest known esterification reaction involving polyhydric alcohols and fatty acids is that employed in the formation of triglycerides. In 1844, approximately twenty years after Chevreul established the constitution of natural fats, Pelouze and Gélis[49] synthesized tributyrin by direct esterification of glycerol and butyric acid in the presence of sulfuric acid as a catalyst. Ten years later Berthelot[50] began his systematic synthesis of the glycerides in the course of which he prepared the mono-, di-, and triglycerides of practically all of the then available fatty acids. The higher fatty acids included palmitic, stearic, and oleic. The glycerides were obtained principally by variations in the method of direct esterification, although in some cases acetonebromohydrin and diacetonechlorohydrin were used in the synthesis of specifically oriented glycerides. The direct esterification of glycerol and fatty acids has been the subject of many investigations since the appearance of Berthelot's classical work.

The process of esterification of glycerol with the higher fatty acids is often referred to as re-esterification because the original source of the acids is the natural fats or waxes from which acids are obtained by hydrolysis. When a homotriglyceride is required, direct esterification is oftentimes the easiest and most desirable method of preparation. However, the reaction cannot be made sufficiently specific to produce any desired mono- or diglyceride with respect either to configuration or to homogeneity, and it is not possible to produce, by direct esterification, specifically oriented triglycerides with two or three different fatty acids in the molecule. In these cases recourse must be had to less direct methods of synthesis.

The formation of triglycerides by esterification of glycerol with fatty acids may be represented in its simplest form by the following equation:



$$\begin{array}{l} H_2COH \\ \;| \\ HCOH \\ \;| \\ H_2COH \end{array} + \begin{array}{l} HOOCR \\ \\ HOOCR \\ \\ HOOCR \end{array} \longrightarrow \begin{array}{l} H_2COOCR \\ \;| \\ HCOOCR \\ \;| \\ H_2COOCR \end{array} + 3\,H_2O$$

Actually the reaction proceeds in stages beginning with the formation of monoglycerides which are further esterified to form diglycerides, and these in turn are esterified to form triglycerides. The esterification reaction is, however, further complicated by the fact that acyl radicals tend to migrate from one position to another within the glycerol molecule. It is a well established fact that β-monoacylglycerides tend to rearrange to α-monoacylglycerides[51] and that this reaction is accelerated by the presence of small quantities of acids and alkalies.[52,53] The tendency of the β-acyl-

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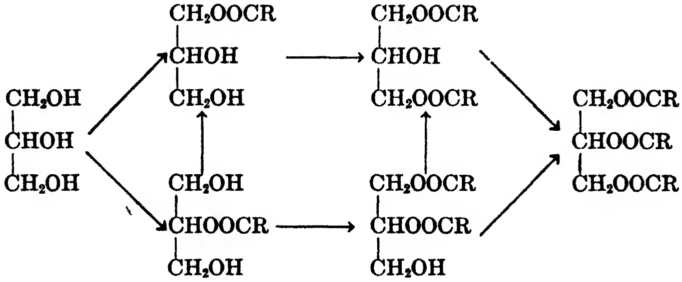
[49] J. Pelouze and A. Gélis, *Ann. chim. phys.*, **10**, 434–456 (1844).
[50] M. Berthelot, *Compt. rend.*, **36**, 27–29 (1853); **37**, 398–403, 403–406 (1853); **38**, 668–673 (1854); *Ann. chim.*, **41**, 216–319 (1854). See *Chimie organique fondée sur la synthese*, Mallet-Bachelier, Paris, 1860, Vol. II, pp. 17–164.
[51] E. Fischer, *Ber.*, **53**, 1621–1633 (1920).
[52] B. F. Stimmel and C. G. King, *J. Am. Chem. Soc.*, **56**, 1724–1725 (1934).
[53] B. F. Daubert and C. G. King, *J. Am. Chem. Soc.*, **60**, 3003–3005 (1938).

glycerides to rearrange to α-acylglycerides is in line with the observed differences in the heats of combustion and specific heats of these two isomeric glycerides.[54]

The course of the esterification reaction can, therefore, be more accurately represented by the following scheme:



The selection of the particular hydroxyl group of the glycerol molecule for attack by any given molecule of acid to form the original monoglyceride is apparently relatively random in nature and is probably only slightly affected by environmental conditions. Although the reaction cannot be made entirely specific with respect to the particular hydroxyl group or groups which undergo esterification, the reaction can be made relatively complete in the case of the higher fatty acids with respect to triglyceride formation. This is not the case, however, with respect to mono- or diglyceride formation since these reactions are nonspecific and incomplete regardless of the ratio of glycerol used. Also, it is not the case where esterification of very low molecular weight fatty acids is involved. For example, esterification of glycerol and acetic acid, regardless of the excess of acetic acid, results in the formation of a mixture of mono-, di-, and triacetin which is extremely difficult to separate. Triacetin has, therefore, generally been prepared by the reaction of glycerol and acetic anhydride. However, it is claimed that triacetin can be produced by direct esterification which employs a process of continuous distillation patented by Grolea and Weyler.[55] This process involves the continuous removal by distillation from the esterification mixture of a weak solution of acetic acid and continuous addition of fresh glycerol and acetic acid.

When only one kind of acid is involved in the esterification only one triglyceride can be formed. However, if two or more acids are involved in the esterification, the reaction product will consist of a mixture of esters in various proportions. A number of factors are operative in determining the ultimate composition of the mixture, including the concentration of each acid present and the relative rates of esterification and acyl migration

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[54] T. H. Clarke and G. Stegeman, *J. Am. Chem. Soc.*, 62, 1815–1817 (1940).
[55] J. Grolea and J. L. Weyler, British Pat. 131,678 (Sept. 4, 1919).

under the conditions employed. It might be expected that equilibrium would be established when maximum heterogeneity, with respect to the distribution of the fatty acids among the glycerol molecules, occurred under the conditions of the reaction. The tendency for this to occur is undoubtedly considerable, but differences in the activity of the hydroxyl groups in the glycerol molecule and differences in the rates of reaction of the different fatty acids would prevent this result from being completely realized experimentally. In some cases it may be very closely approached, *e. g.*, in the esterification of equimolar quantities of palmitic and oleic acids which have nearly the same reaction velocities.

Esterification Conditions.—A wide variety of conditions have been described for the esterification of glycerol with the higher fatty acids, but few kinetic investigations have been made of the reactions under the various conditions employed. Each modification appears to have been introduced or employed by a given author because of some particular advantage which it appeared to offer. Because of lack of adequate comparative data, it is often difficult to determine which of the many esterification methods is most advantageous. The following are typical of the conditions which have been described by workers since Berthelot's contributions in this field.

Berthelot[50] heated glycerol and a large excess of fatty acid to temperatures between 200° and 270°C. in a sealed tube. Since the water produced in the reaction remained in the reaction mixture, equilibrium was established between the reactants under the conditions employed. Scheij[56] employed a stream of air or inert gas to remove the water from the reaction, and Bellucci and co-workers[57–59] accomplished the same result by means of reduced pressure. Either method tends to displace the equilibrium toward complete esterification but provision must be made for returning the glycerol to the reaction or supplying fresh glycerol which may be lost.

Steger and van Loon[60] esterified dry glycerol which had been distilled *in vacuo* with the theoretical quantity of petroselinic acid and 2% of powdered zinc as catalyst. The reaction mixture was maintained at 180°C. under a partial vacuum while a stream of carbon dioxide was drawn through it to provide agitation and to assist in the removal of the water formed during esterification. After 5 hours it was found that the acid value did not further decrease. Owing to the loss of about 10% of the glycerol, the fatty acid remained in excess, thus assuring the absence of mono- and diglycerides.

[56] L. T. C. Scheij, *Rec. trav. chim.*, **18**, 169–210 (1879).
[57] I. Bellucci, *Gazz. chim. ital.*, **42**, II, 283–305 (1912).
[58] I. Bellucci and R. Manzetti, *Atti accad. Lincei*, **20**, I, 125–128, 503–504 (1911).
[59] I. Bellucci, *Atti accad. Lincei*, **20**, I, 235–238 (1911).
[60] A. Steger and J. van Loon, *Rec. trav. chim.*, **46**, 703–708 (1927).

Locquin and Elghozy[61] suggested the use of benzene, toluene, and similar solvents as esterification media and to remove the water of reaction. For this purpose the reaction flask is provided with an air condenser which condenses and returns the glycerol and allows the solvent–water mixture to escape. After condensation and removal of the water, the solvent can be returned to the reaction mixture. Xylene is now generally preferred for removal of the water of reaction.

Most of the Twitchell saponification catalysts have been used as esterification catalysts following their original application for this purpose by Twitchell[62] himself. For example, Bhattacharya and Hilditch[63] prepared various heteroglycerides by heating a mixture of fatty acids (about 110 g.) with 80% to 90% of the theoretical quantity of glycerol and 0.5% of naphthalene-β-sulfonic acid at a temperature of 135–145°C. for 5 to 6 hours under a vacuum of 1 mm. Esterification under these conditions is relatively complete and no mono- or diglycerides are formed. Mixtures of oleic, linoleic, lauric, palmitic, and stearic acids in different proportions were submitted to esterification and the composition of the resulting glycerides were determined by acetone–permanganate oxidation. It was observed that the rate of esterification of the solid acids was a function of the molecular weight, lauric acid being more readily esterified than palmitic or stearic acids, while palmitic and oleic acids were esterified at approximately the same rates.

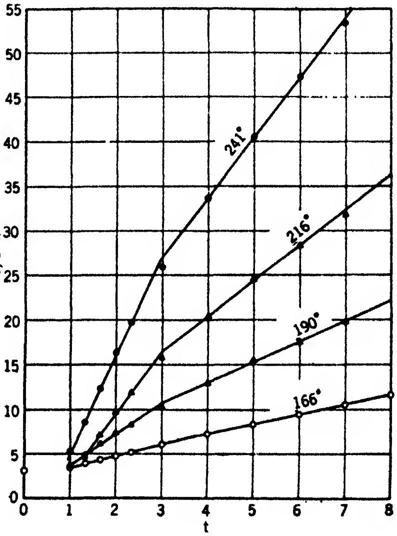

Fig. 71. Curves showing the bimolecular nature of the uncatalyzed reaction of peanut oil fatty acids and glycerol at various temperatures (°C.).[64] Reciprocal of acid concentration (moles/100 g.) *vs.* reaction time (hours).

Feuge, Kraemer, and Bailey[64] investigated various factors involved in the re-esterification, under reduced pressure, of the mixed fatty acids obtained by saponification of peanut oil. The uncatalyzed reaction was found to be bimolecular in character but proceeds in two stages, of which the latter has the lower velocity constant as is evident from the curves in

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[61] R. Locquin and F. Elghozy, *Bull. soc. chim.*, **41**, 445–448 (1927).

[62] E. Twitchell, *J. Am. Chem. Soc.*, **29**, 566–571 (1907).

[63] R. Bhattacharya and T. P. Hilditch, *Proc. Roy. Soc. London*, **A129**, 468–476 (1930).

[64] R. O. Feuge, E. A. Kraemer, and A. E. Bailey, *Oil & Soap*, **22**, 202–207 (1945).

Figure 71. Velocity constants were determined for the initial and final stages of the reaction, at intervals between 166° and 241 °C. The calculated heats of activation for the initial and final stages of the reaction were found to be respectively 12,300 and 10,800 cal. per mole. The free fatty acid concentration corresponding to the termination of the first stage decreased progressively as the temperature of the reaction increased.

Of a wide variety of metal oxides and chlorides tested, zinc and tin chlorides were outstanding in catalytic activity. The reaction, when catalyzed with these materials, is complex and no longer simply bimolecular. The authors believe that tin and zinc chlorides react initially with free fatty acids and free glycerol to form metal soaps and chlorohydrins, and that esterification proceeds through interaction of these two initial reaction products. Other metal chlorides, including the chlorides of aluminum, antimony, mercury, nickel, magnesium, manganese, lead, iron, and cadmium did not appear to be capable of reacting in this manner, and were relatively poor catalysts. The oxides of tin and zinc were also deficient in catalytic activity, as was hydrochloric acid.

The reaction proceeds at a reasonable speed, *i. e.*, the free fatty acid content of the product is reduced to about 3% in 6 hours, if 0.0008 mole of tin chloride per 100 g. of fatty acids is used as a catalyst at 175°C. or if a similar amount of zinc chloride is used as a catalyst at 200°C. Equally rapid esterification is obtained without a catalyst only above 250°C. Esterification is assisted by maintaining a vacuum above the reaction mixture to remove water vapor from the reacting material as rapidly as it is formed. A vacuum of about 20 mm. pressure of mercury is satisfactory.

If zinc or tin chloride catalysts are employed, the metals may be completely removed from the esterified oils by ordinary alkali refining. These catalysts do not cause the oil to polymerize during the course of esterification, do not cause conjugation in the oils, and are not detrimental to the color of the product.

Incomplete Esterification of Glycerol.—Similar but less extensive investigations have been made of the esterification of glycerol for the production of mono- and diglycerides. Hilditch and Rigg[65] found that, even with an excess of 10 moles of glycerol per mole of fatty acid, esterification in the presence of naphthalene-β-sulfonic acid led primarily to the production of diglycerides, while the monoglycerides scarcely ever exceeded 40% of the reaction product. This predominance of diglycerides is explained by Hilditch and Rigg on the basis of the comparative immiscibility of glycerol and the higher fatty acids or their glycerol esters, consequently the monoglycerides which are first formed pass mainly into the fatty acid phase where they undergo reaction to form di- and even triglycerides. It is pre-

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[65] T. P. Hilditch and J. G. Rigg, *J. Chem. Soc.*, **1935**, 1774–1778.

sumed that these conditions refer to unagitated or only moderately agitated reactions.

Hilditch and Rigg also found that by employing a reaction medium in which both free fatty acids and glycerol were freely soluble the reaction could be made relatively specific with regard to the formation of monoglycerides (about 90%). Camphor-β-sulfonic acid which is a more active catalyst than naphthalene-β-sulfonic acid was employed with phenol as solvent in the esterification of glycerol with lauric, palmitic, stearic, and oleic acids. It was found that the degree of esterification was a function of the ratio of glycerol to fatty acid, the amount of catalyst, the temperature, and duration of the reaction.

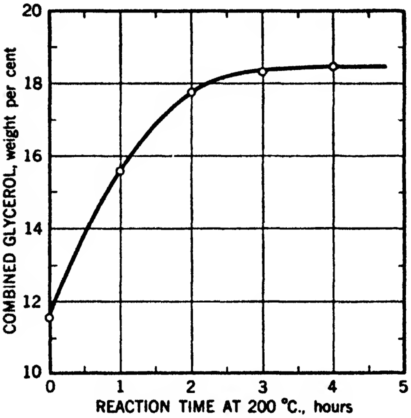

Fig. 72. Course of reaction of fat with 16.63% of its own weight of added glycerol.[67]

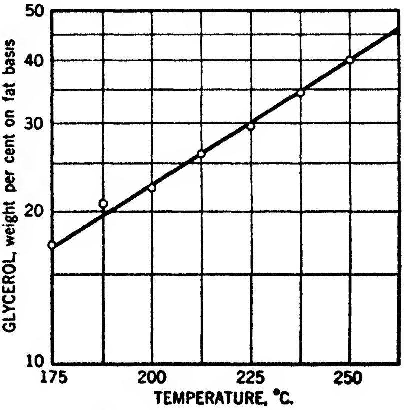

Fig. 72a. Maximum amount of glycerol miscible and reactable with fat at different temperatures.[67]

It was observed that, in general, the greater the ratio of glycerol to fatty acid, the higher the yield of monoglyceride. An increase in the concentration of catalyst, temperature, or duration of the reaction increased the total amount of glycerides produced but reduced the proportion of monoglyceride. Similar behavior was observed when ethylene glycol replaced glycerol in the esterification reaction.

Kawai[66] investigated the direct esterification of glycerol and oleic acid with respect to the ratio of mono- to diglyceride formation. With ratios of 1.0 to 1.4 moles of glycerol per mole of oleic acid and reaction times of 0.5 to 1 hour at 230° to 240°C., the best yield of monolein was about 40%.

A recent investigation by Feuge and Bailey[67] has shed new light on the nature of the glycerol–fatty acid reaction. Instead of starting with free fatty acid and excess glycerol they reacted a relatively completely hydro-

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[66] S. Kawai, *J. Soc. Chem. Ind.* (*Japan*), Suppl. bind., 43, 220–221B (1940).
[67] R. O. Feuge and A. E. Bailey, *Oil & Soap*, 23, 259–264 (1946).

genated fat with an excess of glycerol. This fat, hydrogenated cottonseed oil, which consisted essentially of heterotriglycerides containing palmitic and stearic acids, was reacted at 200°C. with 16.63% of its own weight of glycerol, *i.e.*, approximately sufficient glycerol to convert all the triglycerides to monoglycerides. In the presence of 0.1% of sodium hydroxide as catalyst, it was found that equilibrium was established after approximately 3.5 hours, and the reaction product which formed contained approximately 18.5% glycerol. The course of the reaction in terms of total glycerol combined as mono-, di-, and triglycerides in the reaction product is illustrated in Figure 72.

As has been previously mentioned, Hilditch and Rigg[65] have pointed out the limitation imposed on the esterification of glycerol and fatty acids by the comparative immiscibility of glycerol with the fat formed in the reaction. Feuge and Bailey experimentally determined the maximum amount of glycerol which is miscible and reactable with the fat at equilibrium at different temperatures. Their results are shown graphically in Figure 72a in which the logarithm of the percentages of glycerol *added* to the original fat, and exclusive of the glycerol originally combined with the fat in the form of triglycerides, are plotted against the reaction temperature It is apparent from these results that within the temperature range 175–250°C. there exists a linear relationship between the reaction temperature and the logarithm of the maximum content of glycerol which is miscible and reactable under equilibrium conditions of the reaction between fatty acids and glycerol. It follows, therefore, that if it is required to effect reaction of further proportions of glycerol, a solvent must be employed to increase the solubility of the glycerol in the fat phase as suggested by Hilditch and Rigg.

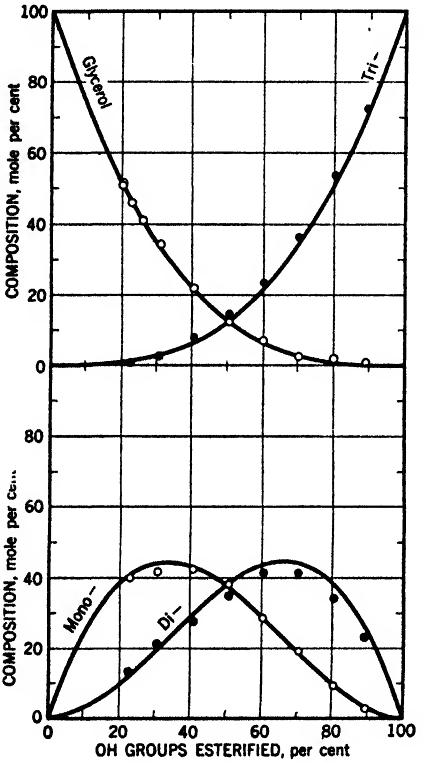

Fig. 72b. Glyceride–glycerol distribution curves for homogeneous solutions of glycerol and glycerides at equilibrium.[67] The curves represent theoretical values while the circles represent experimental values.

Feuge and Bailey extended their investigations to include an appreciable series of reactions with different proportions of fat and glycerol and different reaction temperatures. The conditions were chosen which would produce a condition of equilibrium within the allowed time of reaction, and which would yield a homogeneous reaction product, free from undissolved glycerol. The results are shown graphically in Figure 72b, in which the actual compositions of the equilibrium reaction mixtures are compared with compositions calculated on the basis of random distribution of fatty acid radicals to the esterifiable hydroxyl groups of glycerol present. The graphical comparison indicates that, at temperatures below 200°C., at equilibrium, and within the range of glycerol concentration in which the reaction product becomes homogeneous, the proportions of free glycerol, mono-, di-, and triglycerides conform closely to a pattern of random distribution with respect to glycerol hydroxyl groups esterified.

Technical Preparation of Glycerol Esters.—In recent years re-esterification of fatty acids with glycerol, as well as with other polyhydric alcohols, has assumed appreciable industrial importance and a number of processes have been described for conducting this operation. In general temperatures of 160° to 170°C. are employed but in some cases they may be as high as 220° to 250°C. Franzen[68] has described a stepwise process of esterification of glycerol with fatty acids in which the temperature is maintained for one hour at 160°C., then raised to 165°C. for another hour, then to 195°C. for a third hour, and finally to 210°C. for a fourth hour.

Mineral acids are generally not used as catalysts in industrial esterification but rather aromatic sulfonic acids (Twitchell reagents), zinc, tin and other metals. A variety of other esterification catalysts have been claimed in various patents[69,70] including lead, antimony, bismuth, titanium, manganese; alkali, alkaline earth, and aluminum silicates; soaps, and tin in the form of alloys, colloidal suspensions, and soaps.

Processes have been described which employ reduced pressures varying from 30 to 40 mm.[71] down to 1 to 2 mm.[72] Vapor phase esterification of glycerol and glycols with higher fatty acids is covered by a number of patents.[73,74] Glycerol or glycol and the fatty acids are reacted in vapor form or as a fine mist at 220°C. and 50 mm. pressure. Esterification to the

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[68] H. Franzen, *Z. angew. Chem.*, **46**, 410 (1933).

[69] E. H. Zollinger (to E. Zollinger-Jenny), Swiss Pat. 94,452 (May 1, 1922); Swiss Pat. 95,455 (July 1, 1922); British Pat. 183,897 (Aug. 4, 1922); German Pat. 403,644 (Sept. 30, 1924). See E. Zollinger and A. Grün, U. S. Pat. 1,484,826 (Feb. 26, 1924); F. Gruber, French Pat. 677,711 (March 13, 1930).

[70] M. Luther and W. von Knilling (to I. G. Farbenindustrie), German Pat. 514,503 (June 10, 1927).

[71] I. Bellucci, *Gazz. chim. ital.*, **42**, II, 283–305 (1912).

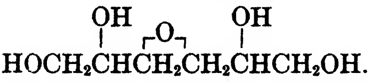
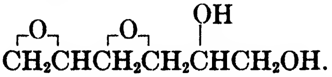
[72] Metallbank und Metallurgische Gesellschaft, British Pat. 291,767 (August 1, 1928).

[73] I. G. Farbenindustrie, British Pat. 341,158 (Jan. 15, 1931). See R. Held and H. Franzen (to I. G. Farbenindustrie), German Pat. 565,477 (Dec. 1, 1932).

[74] E. R. Bolton and E. J. Lush, British Pat. 163,352 (Sept. 30, 1919).

extent of 90% or more occurs rapidly and the reaction product condenses owing to its low vapor pressure. Unreacted alcohol and acid are recovered and recycled to the reaction chamber.

Various processes of continuous esterification have been patented. In one such process,[75] peanut oil fatty acids are emulsified with 87% of the calculated amount of glycerol and 0.1% of magnesium oxide. The emulsion is heated to 80° to 100°C. and fed continuously into a reaction chamber maintained at 170°C. and 20 mm. pressure, where a mixture of mono- and diglycerides is formed. The mixture then flows to a second chamber maintained at 210°C. where there is added 0.1% of alumina or colloidal tin suspended in oil. The reaction mixture leaves the second chamber with less than 10% free fatty acid and passes to a third chamber maintained at 240°C. where the remaining diglyceride and free fatty acid undergo reaction. Under proper operating conditions the final product contains some glycerol and less than 0.2% free fatty acid which are removed by steam distillation.

Polyglycerol Esters.—When glycerol is subjected to dehydration, variable mixtures of di-, tri-, and other polyglycerols are formed depending on the dehydration conditions. The dehydration may occur either inter- or intramolecularly to produce two types of products. When one molecule of water is eliminated intramolecularly from a molecule of glycerol, a glycide,  $\overbrace{CH_2CH}^{O}CH_2OH$, is produced. When the dehydration occurs intermolecularly, a di- or polycondensation product is formed, *e. g.*,  $HOCH_2\overset{OH}{\overset{|}{C}}H\overbrace{CH_2CH_2}^{O}\overset{OH}{\overset{|}{C}}HCH_2OH$. However, both intra- and intermolecular dehydration may occur with the formation of glycidic condensation products, *e. g.*,  $\overbrace{CH_2CH}^{O}\overbrace{CH_2CH_2}^{O}\overset{OH}{\overset{|}{C}}HCH_2OH$. In the same manner tri- and higher polyglycerols result from the dehydration of three or more molecules of glycerol. Methods have been described for the preparation of various polyglycerols which are presumed to consist principally of one or another of these dehydration products,[76] but the commercial product usually consists of a mixture of the various condensation products.

Since the polyglycerides always contain one or more free hydroxyl groups, they can be esterified under conditions similar to those employed with glycerol. Either partially or completely esterified polyglycerols may be produced depending on the reaction conditions. The esters prepared by react-

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[75] E. Wecker and R. Held (to I. G. Farbenindustrie), German Pat. 563,626 (Nov. 17, 1932). See German Pats. 563,203 (Nov. 17, 1932); 553,821 (June 30, 1932); 551,868 (June 7, 1932).

[76] J. W. Lawrie, *Glycerol and the Glycols*. Chemical Catalog Co., New York, 1928.

ing, for example, coconut oil fatty acids with polyglycerol are used as detergents.[77]

(c) *Esters of Erythritol and Pentaerythritol*

Erythritol, $CH_2OHCHOHCHOHCH_2OH$, and pentaerythritol, $C(CH_2OH)_4$, are the principal tetrahydric alcohols which have been esterified with the higher fatty acids. The esters of these polyhydric alcohols are prepared by methods similar to those used with the glycols except that a solvent is often required.

Pentaerythritol has been esterified with a variety of saturated and unsaturated fatty acids. The esters formed by the reaction of pentaerythritol and unsaturated fatty acids are valued for their film-forming properties. Acetic acid and pentaerythritol react on heating to form a tetra-acetate.[78] Soybean and linseed oil fatty acids react to form pentaerythritol esters of the mixed fatty acids[79] of these oils. Bruson,[80] Gauerke,[81] and Arvin[82] have been granted patents covering the reaction of pentaerythritol with the fatty acids of various oils (tung, linseed, soy, etc.).

Drinberg[83] has described the esterification of pentaerythritol with the fatty acids of tung, linseed, fish, and other oils and has presented detailed data on the properties of the films produced from these esters. Blagonravova and Drinberg[84] investigated the esterification of pentaerythritol and pure monoethenoid acids such as oleic and erucic, and determined a number of the properties of the resulting esters. Unlike triolein, pentaerythritol tetraoleate forms films which dry dust-free in 48 hours and completely in 60 hours.

Blagonravova and Lazarev[85] investigated the kinetics of the esterification of linoleic and oleic acids with pentaerythritol and found the reaction to be most effectively accomplished at temperatures of 200° to 240°C. With equimolar ratios of the polyhydric alcohol and these acids the process was strictly bimolecular. The reaction velocity with a mixture of C_{18} acids of varying degrees of unsaturation was found to be the same as for the individual members of the mixture. The magnitude of the energy of

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[77] Lever Brothers, Ltd., R. Furness, and A. Fairbourne, British Pat. 439,435 (Dec. 6, 1935). See Lever Brothers, Ltd., and R. Furness, British Pat. 442,950 (Feb. 19, 1936).

[78] H. T. Clarke (to Eastman Kodak), U. S. Pat. 1,583,658 (May 4, 1926).

[79] H. Krzikalla and W. Wolff (to I. G. Farbenindustrie), German Pat. 529,483 (July 17, 1930); French Pat. 703,792 (May 6, 1931).

[80] H. A. Bruson (to Röhm & Haas), U. S. Pat. 1,835,203 (Dec. 8, 1931).

[81] C. G. Gauerke (to E. I. du Pont de Nemours), U. S. Pat. 1,979,260 (Nov. 6, 1934); British Pat. 405,827 (March 8, 1934).

[82] J. A. Arvin (to E. I. du Pont de Nemours), U. S. Pat. 2,029,851 (Feb. 4, 1936).

[83] A. Y. Drinberg, *Org. Chem. Ind. U.S.S.R.*, **4**, 114–117 (1937).

[84] A. A. Blagonravova and A. Y. Drinberg, *J. Applied Chem. U.S.S.R.*, **11**, 1642–1647 (1938).

[85] A. A. Blagonravova and A. M. Lazarev, *J. Applied Chem. U.S.S.R.*, **13**, 879–883 (1940).

activation of esterification of the polyhydric alcohols was not greater than for the simple primary alcohols and the corresponding acids.

Burrell[86] compared esterification rates of erythritol and pentaerythritol with linseed fatty acids. The reactions were carried out with equivalent quantities of the alcohols and acids at 250°C. under an atmosphere of carbon dioxide. The rate of reaction was considerably more rapid with pentaerythritol than with erythritol indicating clearly the effect of secondary hydroxyl groups in the latter alcohol. Similar reactions with linseed oil fatty acids were carried out at 230° and 200°C. in the presence of an azeotropic solvent and various catalysts, and with an excess of the polyhydric alcohol in the absence of solvent and catalyst. Burrell concluded the account of his work on esterification of pentaerythritol and fatty acids with a detailed description of the commercial production of pentaerythritol esters with respect to temperature, agitation, preferred catalyst, removal of water, etc.

Konen, Clocker, and Cox[87] investigated the effect of various factors on the direct esterification of a number of polyhydric alcohols including glycerol, erythritol, pentaerythritol, dipentaerythritol, and sorbitol. The effect of temperature, catalysts, and methods of removing water on the characteristics of the esterification products were compared. Of the many catalysts investigated, none were found to be of appreciable value either for laboratory or industrial esterification. Generally, the catalyst increased the initial rate of esterification, but for relatively complete esterification the total reaction time was the same either with or without a catalyst. Alkaline earth catalysts had the least, and acid catalysts the most marked effect on the color of the final product.

Sulfur dioxide was used as an inert atmosphere to protect the reaction mixture and to remove water. It also acted as a catalyst in the early stages of the reaction but had little effect on the total reaction time. The use of steam under vacuum was also effective in removing the water of reaction. The optimum temperature for esterification of the polyhydric alcohols was found to be 450°F. (232°C.). An excess of 5% of the theoretical amount of alcohol was generally found to give the best esterification product.

The effect of the various factors mentioned above on the rate of esterification of linseed, soybean, and castor oil fatty acids with polyhydric alcohols was investigated and the results presented in a series of reaction velocity curves. In general, it was found that the initial esterification rate was relatively high but fell rapidly in the later stages of the reaction. Complete esterification generally could not be obtained irrespective of the conditions employed. Polymerization reactions during heating were found to be negligible under the best conditions of esterification.

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[86] H. Burrell, *Oil & Soap*, 21, 206–211 (1944).

[87] J. C. Konen, E. T. Clocker, and R. P. Cox, *Oil & Soap*, 22, 57–60 (1945).

Carson and Maclay[88] prepared a series of fatty acid esters of the next higher homolog of erythritol, namely xylitol, $CH_2OH(CHOH)_3CH_2OH$, and investigated their use as plasticizers.

(*d*) *Esters of Hexitols*

Sorbitol, mannitol, and dulcitol are the principal hexitols which have been esterified with fatty acids. Sorbitol and the isomeric hexahydric alcohol, mannitol, are widely distributed in nature and are now produced commercially by the hydrogenation of glucose.[89]

Both sorbitol and mannitol, as well as their anhydro derivatives, have been esterified with various monobasic aliphatic acids to form synthetic fats and oils. Owing to the high temperature required for the esterification, more or less dehydration of the alcohol occurs so that the final product, at least when produced on an industrial scale, is a mixture of hexitol and anhydrohexitol esters.

The polyhydroxy alcohols containing more than three hydroxyl groups form inner ethers by elimination of a molecule of water. Whereas glycidol, the inner ether of glycerol, contains but one ether linkage and one free hydroxyl group, tetra-, penta-, and hexahydric alcohol ethers may contain one or more ether linkages and one or more free hydroxyl groups. By splitting a molecule of water from sorbitol or mannitol, there are formed tetrahydroxymonoanhydro products, $C_6H_8O(OH)_4$, which are known as *sorbitans* or *mannitans*, and by splitting two molecules of water from the same alcohols they form dihydroxydianhydro products, $C_6H_8O_2(OH)_2$, which are known as *sorbides* or *mannides*.

Both drying and nondrying oils have been produced from sorbitol and mannitol by direct esterification with fatty acids, by alcoholysis, and by ester interchange.[90] Bradner, Hunter, Brewster, and Bonner[91] reported the results of a systematic investigation of the influence of temperature, ratio of reactants and catalysts on the esterification of sorbitol and linseed fatty acids. All of the products of the reactions were collected and analyzed to obtain accurate material balances and data for calculating the degree of esterification under each set of conditions. The esterifications were carried out at 180° or 200°C. until the reaction rate diminished to approximately 10% of its maximum value and then the temperature was raised to 250°C. and held until the reaction was completed. The rate of esterification was followed by determining at intervals the amount of unreacted acid in the mixture.

When the logarithm of the percentage of unreacted acid was plotted

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[88] J. F. Carson, Jr., and W. D. Maclay, *J. Am. Chem. Soc.*, **66**, 1609–1610 (1944).

[89] H. J. Creighton, *Trans. Electrochem. Soc.*, **75**, 289–307 (1939).

[90] R. M. Goepp, Jr., and K. R. Brown, *Ind. Eng. Chem.*, **30**, 1222–1227 (1938).

[91] J. D. Bradner, R. H. Hunter, M. D. Brewster, and R. E. Bonner, *Ind. Eng. Chem.*, **37**, 809–812 (1945).

against time, most of the points were found to fall on a straight line which has a curvature at the beginning, indicative of an induction period during which the reaction proceeds very slowly. The authors account for this induction period by the immiscibility of sorbitol and linseed fatty acids. Toward the end of the reaction, the rate again deviates from linear, presumably because of the steric effect of several adjacent fatty acid groups which hinder the esterification of the last hydroxyl group. First-order rate constants were calculated for the linear portion of the reaction curves.

The rate of reaction was determined at several temperatures and it was found that it doubled, approximately, when the temperature was raised from 180° to 200°C. The rate of reaction, measured by first-order rate constants, was found to increase with an increase in the ratio of linseed fatty acids to sorbitol. Several catalysts were found to accelerate the reaction of sorbitol and linseed fatty acids. The most effective catalysts are the acetates, carbonates, oxides, and hydroxides of calcium and barium. The addition of approximately 0.5% of a mixture of three parts calcium acetate and one of barium acetate was observed approximately to double the rate of esterification at all ratios of linseed fatty acids to sorbitol.

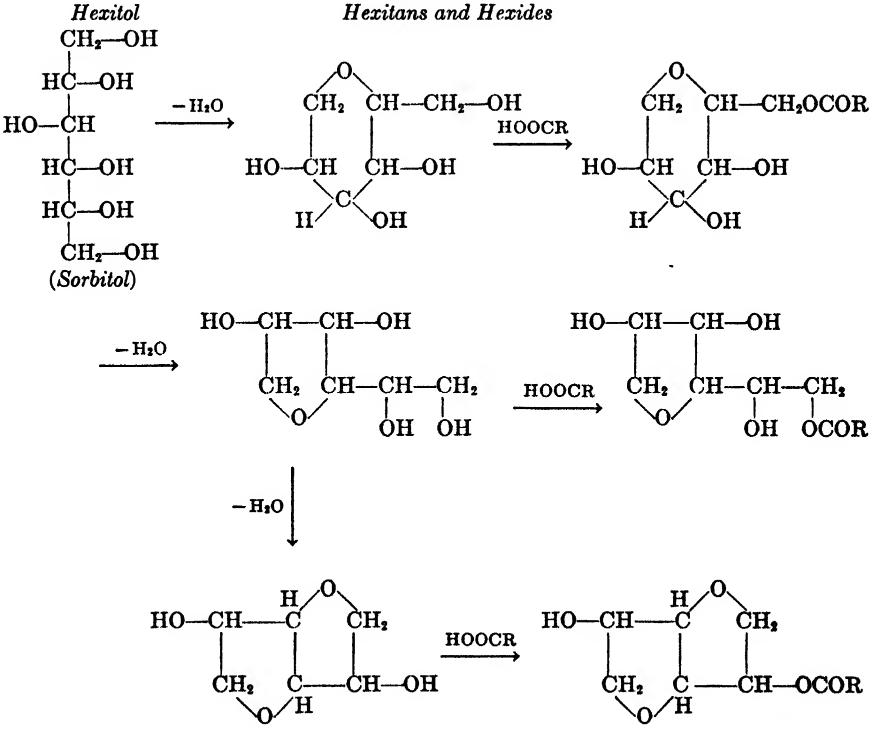
The degree of esterification of sorbitol is directly related to the mole ratio of linseed fatty acids to sorbitol and in general it is possible to vary the degree of esterification over a wide range by varying the ratio of the reactants. Thus, when 4 moles of fatty acids were heated with 1 mole of sorbitol without catalyst at 200°C., the product contained 2.5 moles of linseed fatty acids combined per mole of sorbitol, and when 6 moles of fatty acids were employed the product contained 4.3 moles of linseed fatty acids combined with each mole of sorbitol. In a series of catalyzed reactions at 180°C. in which 10 moles of fatty acids per mole of sorbitol were used, 5.2 moles of linseed fatty acids were combined.

The degree of esterification varied with the temperature of reaction. Usually, the lower the reaction temperature, the greater was the degree of esterification with a given mole ratio of reactants. However, if the reaction was carried out at a lower temperature the time for maximum esterification was greatly increased. The effect of catalysts was found to increase the rate of reaction at a given temperature.

As previously mentioned, more or less dehydration of sorbitol or mannitol may, and usually does occur during esterification but it is also possible to dehydrate these alcohols to form polyhydric alcohol ethers prior to esterification. It is, of course, not possible to produce a specific anhydro alcohol and mixtures of hexitans and hexides are generally formed. When these polyhydric alcohol ethers (alkylene oxides) are subjected to esterification with long chain fatty acids, a variety of products are formed which have considerable utility owing to the diversity of the substituents in the ester molecule.

The principal commercial products are monoesters of the higher acids. These commercially produced esters represent mixtures of products because dehydration of the hexitols produces a mixture of anhydro alcohols (hexitans and hexides), the acids which are derived from natural fats are not homogeneous, and esterification of the various available hydroxyl groups is not specific. The heterogeneity of the esterification product derived by reaction of a fatty acid with anhydrosorbitol may be illustrated by the accompanying formulas (reproduced from the literature of a manufacturer of these products[92]).

Artificial fats produced by esterification of sorbitol and mannitol with fatty acids have been investigated from the preparatory and nutritional point of view.[93–96]



Types of anhydro alcohol and esters formed by dehydrating sorbitol. R represents the residue of a long chain fatty acid.

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[92] Atlas Powder Company, *Spans and Tweens*, December, 1943.

[93] A. Lapworth and L. K. Pearson, *Biochem. J.*, **13**, 296–300 (1919).

[94] W. D. Halliburton, J. C. Drummond, and R. K. Cannan, *Biochem. J.*, **13**, 301–305 (1919).

[95] W. R. Bloor, *J. Biol. Chem.*, **11**, 141–159, 421–427 (1912).

[96] W. E. Evans, Jr., H. Wollenweber, M. Ruppersberger, and J. C. Krantz, Jr., *Proc. Soc. Exptl. Biol. Med.*, **51**, 222–223 (1942).

TABLE 109

MELTING POINTS (°C.) OF THE PALMITATE ESTERS OF VARIOUS POLYHYDRIC ALCOHOLS AND CARBOHYDRATES[a]

Compound	Mono	Di	Tri	Tetra	Penta	Hexa	Octa	Hendeca
Methylene glycol		49.5						
Ethylene glycol	52.5	72						
1,2-Propylene glycol	55–56	69.5–70						
1,3-Propylene glycol	42–43.5	56.5						
1,3-Butylene glycol		39–40						
1,4-Butylene glycol		63						
Glycerol: 1-; 1,3-	77	72.5	65					
Glycerol: 2-; 1,2-	69	64						
Erythritol		99.5–101	81–8					
l-Arabinose				69.5				
α-Methyl-*d*-glucoside			77	69				
α-Glucose					72–75			
β-Glucose					68–72			
Mannitol						64.5		
Dulcitol						74		
Sucrose							54–55	
Raffinose								52–3

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[a] H. A. Goldsmith, *Chem. Revs.*, 33, 257–349 (1943).

(e) *Esters of Mono- and Polysaccharides*

The mono- and polysaccharides which have been esterified with fatty acids include arabinose, glucose, sucrose, and raffinose. The esters of these sugars are prepared by methods similar to those used with glycols and other polyhydric alcohols except that a solvent is generally required.[97] However, products such as α-glucose pentacaproate have been prepared by heating glucose and caproic anhydride at 100°C. with zinc chloride.[98] Esterification of these sugars can be accomplished with acid anhydrides in the presence of a solvent and catalyst at temperatures below 100°C.[99]

(f) *Properties of the Polyhydric Alcohol Esters*

Extensive data with respect to the properties of pure polyhydric alcohol esters are lacking, but such data as are available have been compiled in readily available form by Goldsmith.[100] These data include melting points, densities, refractive indices, solubilities, boiling ranges, optical rotations, and in some cases saponification, iodine, and acetyl values. Although a wide variety of polyhydric alcohols and fatty acids have been investigated, few series of these derivatives are complete enough to permit many generalizations concerning their physical and chemical properties. However, a few such may be made. For example, the melting and boiling points of the polyhydric alcohol esters increase in proportion to the increase of the molecular weights of their acid radicals, while, in general, their solubilities decrease. As would be expected, the unsaturated acids form lower melting and more soluble esters than the saturated acids. The diesters of the glycols melt at distinctly higher temperatures than the corresponding monoesters which is in contrast to the glycerol esters. The monoesters of glycerol melt at higher temperatures than the corresponding diesters as may be seen from the data in Table 109.

Goldsmith's compilation includes data for the mono- and diesters of ethylene, propylene, and butylene glycols and the saturated fatty acids from lauric to stearic; the diesters of oleic, linoleic, and elaeostearic acids; the mono- and diesters of the mixed acids from coconut, rapeseed, linseed, tung and castor oils, and various fatty acid esters of diethylene, triethylene, tetraethylene, hexaethylene, nonaethylene, and dodecaethylene glycols.

The erythritol esters include di- and tripalmitate, mixed tri- and tetrapalmitate and stearate, and tetraoleate. The pentaerythritol esters include the palmitate, oleate, erucate, and the linseed oil fatty acid esters. The fatty acid esters of the higher polyhydric alcohols, mono- and polysaccha-

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[97] H. Gault and P. Ehrmann, *Chemie et industrie*, Special Number 574 (May, 1924).

[98] H. Staudinger and H. Schwalenstöcker, *Ber.*, **68**, 727–749 (1935).

[99] E. I. du Pont de Nemours and Co., British Pat. 436,885 (Nov. 14, 1935). See G. de W. Graves (to E. I. du Pont de Nemours), U. S. Pat. 1,990,483 (Feb. 12, 1935).

[100] H. A. Goldsmith, *Chem. Revs.*, **33**, 257–349 (1943).

rides include *l*-arabinose tetrapalmitate; the tri- and tetrapalmitates and stearates of α-methyl-*d*-glucoside; the mannitan and mannitol esters of lauric, myristic, palmitic, stearic, oleic, erucic, and ricinoleic acids; and various esters of sorbitol and dulcitol. The glucose esters of the higher fatty acids include di- and pentalaurate, pentapalmitate, mono-, di-, tri-, and pentastearate, and pentaoleate; the sucrose esters include the octapalmitate and stearate, the linoleate and elaeostearate; and the raffinose esters include the hendecapalmitate and stearate. For information concerning the properties of these esters and references to the original work the reader should consult Goldsmith's article.

(*g*) *Esters of Polycarboxylic Acids*

Polycarboxylic acids may be esterified with monohydric or polyhydric alcohols. The esterification velocity of the dibasic acids from oxalic to sebacic, containing from none to eight methylene groups in the carbon chain, with methyl alcohol has been rather thoroughly investigated and the two velocity constants determined.[101]

Esterification reactions between polyhydric alcohols and polybasic acids are of considerable industrial importance in the manufacture of synthetic resins. Although synthetic resins may be produced solely by direct esterification, they are more often produced by a combination of esterification and interesterification, hence discussion of these products are considered under the latter heading.

6. Interesterification

The term *interesterification* is used broadly herein to refer to a number of reactions in which an ester of a fatty acid may react with fatty acids, alcohols, or other fatty acid esters to produce an ester differing in composition from the original ester. The reaction involving the replacement of the alkoxy group of an ester with the alkoxy group of an alcohol is more specifically termed *alcoholysis*. *Ester interchange* should perhaps be restricted to those reactions involving an exchange of the alkoxy group of one ester for that of a different ester. By analogy with alcoholysis the displacement of the acid radical of an ester by another acid should be called *acidolysis*. Many authors make no distinction between these various reactions and refer to them generally as ester interchange or *Umesterung*.

The three types of interesterification reactions may be illustrated by:

(*1*) Alcoholysis, $RCOOR' + R''OH \rightleftharpoons RCOOR'' + R'OH$

(*2*) Ester interchange, $R'COOR'' + R'''COOR'''' \rightleftharpoons R'COOR'''' + R'''COOR''$

(*3*) Acidolysis, $R'COOR'' + R'''COOH \rightleftharpoons R'''COOR'' + R'COOH$

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[101] M. H. Palomaa, *Ann. Acad. Sci. Fennicae,* **A10**, (16), 1-26 (1917).

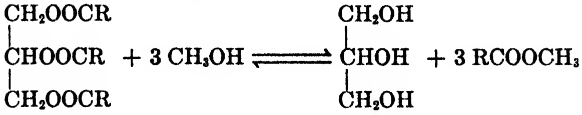
(a) *Alcoholysis*

Alcoholysis is, in many respects, similar to esterification of an acid with an alcohol. The reaction may occur between (*1*) monoesters and monohydric alcohols, (*2*) monoesters and polyhydric alcohols, (*3*) polyesters and monohydric alcohols, and (*4*) polyesters and polyhydric alcohols. When carried out with a specific alcohol it may be referred to as *methanolysis, ethanolysis, propanolysis, glycerolysis,* etc., depending on the nature of the alcohol.

Ordinarily, the ester of one alcohol can be transformed into the ester of another alcohol by refluxing the ester with an excess of the second alcohol in the presence of a catalyst, such as an alcoholate or an acid. Oftentimes only a trace of catalyst is necessary. In general, it is easier to replace a higher molecular weight alcohol by a lower one.[102]

The discovery of the phenomenon of alcoholysis has been ascribed to Purdie[103] by some authors, but actually it was known and applied as early as 1846 in which year Rochleder[104] described the ethanolysis of castor oil for the production of glycerol. Rochleder dissolved castor oil in absolute ethanol and passed into the warm solution a stream of dry hydrogen chloride. After the reaction was completed, water was added, and the acidified aqueous layer was siphoned off, evaporated to a syrup, and extracted with ether. The ether insoluble residue was shown to consist of glycerol, and the process was stated to consist of a reaction whereby the alcohol converted the glycerides of the fat to ethyl esters with the simultaneous liberation of glycerol.

Since 1846, alcoholysis has been the subject of many investigations. It is an especially useful process where ordinary saponification and reesterification leads to undesirable side reaction products. For example, the furfuryl esters of fatty acids cannot be prepared by direct esterification of furfuryl alcohol and fatty acids in the presence of an acid catalyst, because under these conditions the alcohol undergoes rapid polymerization. The method is most often applied to the preparation of monoesters from natural fats and has proved particularly valuable for the conversion of phosphatides to simple esters. When applied to the production of glycerol and monoesters, the reaction is entirely analogous to the splitting of a fat with water as indicated by the following equation for methanolysis.



$$\begin{array}{l} CH_2OOCR \\ | \\ CHOOCR \\ | \\ CH_2OOCR \end{array} + 3\,CH_3OH \rightleftharpoons \begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array} + 3\,RCOOCH_3$$

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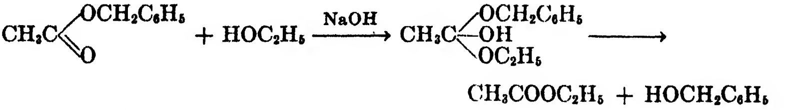
[102] E. M. Bellet, *Compt. rend.*, 193, 1020–1023 (1931).
[103] T. Purdie and W. Marshall, *J. Chem. Soc.*, 53, 391–398 (1888).
[104] F. Rochleder, *Ann.*, 59, 260–261 (1846).

Alcoholysis of Monoesters with Monohydric Alcohols.—Although of less practical importance than some of the other types of alcoholysis, the simplicity of the reaction between a monoester and a monohydric alcohol has led to the investigation of this reaction as a prototype of the kinetics involved in most interesterification phenomena. The mechanism of this type of alcoholysis has been investigated by Kremann,[105] Haller,[106] Jones and Lapworth,[107] Bellet,[108] Townshend,[109] and others. According to these authors, the reaction is catalyzed by both acids and bases and the reaction velocity is dependent on the structure of the acyl group as in the case of hydrolysis.

Bellet[108] investigated the alcoholysis of esters of high molecular weight alcohols with low molecular weight alcohols in the presence of small amounts of sodium hydroxide. He found the speed of the reaction was a function of the temperature and the difference in molecular weights of the two alcohols. Esters of the higher tertiary alcohols were observed to react more rapidly in alcoholysis reactions than those of the higher primary and secondary alcohols.

Although agreeing with previous workers that alcoholysis reactions were catalyzed by alkalies, Bellet concluded that they did not conform to the accepted definition of catalytic action. According to Bellet, when interesterification occurred between ethanol and benzylacetate, $CH_3COOCH_2C_6H_5$, in the presence of 1, 2, and 3% of the amount of alkali required for complete saponification, the reaction occurred in two stages, the first of which involved addition of ethanol, followed by the second stage in which benzyl alcohol was split from the addition product. The first stage was found to be very rapid and essentially complete in two hours, while the second stage is much slower. According to Bellet, the first stage of the reaction is proportional to the amount of alkali present, and ceases when it is consumed. The second stage is independent of the presence of alkali and in fact occurs in neutral solution. The reaction is presumed to involve addition of a molecule of alcohol at the carbonyl group followed by subsequent slow elimination of the displaced alcohol:



$$CH_3C\begin{matrix}\diagup OCH_2C_6H_5\\ \diagdown\!\!\diagdown O\end{matrix} + HOC_2H_5 \xrightarrow{NaOH} CH_3C\begin{matrix}\diagup OCH_2C_6H_5\\ -OH\\ \diagdown OC_2H_5\end{matrix} \longrightarrow$$
$$CH_3COOC_2H_5 + HOCH_2C_6H_5$$

Since the alkali also acts as a saponification agent, it is gradually consumed and upon its disappearance the first phase of the reaction ceases. Bellet assumed that saponification occurred by exactly the same mechanism,

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[105] R. Kremann, *Monatsh.*, **26**, 783–822 (1905).
[106] A. Haller, *Compt. rend.*, **143**, 657–661 (1906).
[107] M. Jones and A. Lapworth, *Proc. Chem. Soc. London*, **30**, 141–143 (1914).
[108] E. M. Bellet, *Compt. rend.*, **193**, 1020–1023 (1931); **194**, 1655–1658 (1932).
[109] A. S. Townshend, *Trans. Roy. Soc. Can.*, III, **23**, 225–226 (1929).

namely, the addition of alkali at the double bond of the carbonyl group followed by subsequent splitting out of the alcohol. These conclusions are probably valid provided some water is present in the reaction mixture. However, the smoothness, rapidity, and completeness with which the alcoholysis of natural fats occurs under relatively anhydrous conditions in the presence of very low concentrations of alkali would seem to indicate that a simpler mechanism is involved under the latter conditions.

The equilibrium constants for various alkyl groups have been calculated for the alcoholysis reaction, $ROH + AcOCH_3 \rightleftharpoons AcOR + CH_3OH$, and the relative values have been found to be similar to those for the corresponding esterification reaction, $ROH + AcOH \rightleftharpoons AcOR + HOH$. Reference to the values for the alcoholysis equilibrium constants for the alkyl and aryl groups given in Table 110 indicates that these are all greater than the value for hydrogen (0.19).[110,111]

TABLE 110

ALCOHOLYSIS EQUILIBRIUM CONSTANTS FOR VARIOUS ALKYL AND ARYL GROUPS

Alkyl or aryl group	Equilibrium constant[a]	Alkyl or aryl group	Equilibrium constant[a]
2-Ethylhexyl	1.02	*sec*-Heptyl	0.5
Methyl	1.00	2-Octyl	0.46
n-Amyl	0.95	Isobutyl	0.44
n-Heptyl	0.77	2-Phenylethyl	0.42
n-Dodecyl	0.71	Allyl	0.38
3-Phenylpropyl	0.69	Benzyl	0.35
Ethyl	0.66	Isopropyl	0.30
sec-Amyl	0.64	Cyclohexyl	0.32
n-Butyl	0.64	*sec*-Butyl	0.28
n-Propyl	0.62		

[a] Value for hydrogen (0.19) is less than for any alkyl group.[110,111]

The velocity constants have been determined for a few alcoholysis reactions by Dasannacharya[112] and Dasannacharya and Sudborough[113] where one of the alcohols was optically active. The constants are given in Table 111. The velocity is proportional to the concentration of hydrochloric acid used as catalyst and the constant *k* is referred to [HCl] as 1.

The reaction of monoesters with monohydric alcohols was investigated by Wright *et al.*[114] using methyl esters of the higher fatty acids and some

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[110] P. R. Fehlandt and H. Adkins, *J. Am. Chem. Soc.*, **57**, 193–195 (1935).

[111] G. B. Hatch and H. Adkins, *J. Am. Chem. Soc.*, **59**, 1694–1696 (1937).

[112] B. Dasannacharya, *J. Am. Chem. Soc.*, **46**, 1627–1640 (1924).

[113] B. Dasannacharya and J. J. Sudborough, *J. Indian Inst. Sci.*, **4**, 181–203 (1921).

[114] H. J. Wright, J. B. Segur, H. V. Clark, S. K. Coburn, E. E. Langdon, and R. N DuPuis, *Oil & Soap*, **21**, 145–148 (1944).

of the more complex alcohols, *e. g.*, furfurol, tetrahydrofurfurol, benzyl Cellosolve and methyl Cellosolve. Compared with the conversion of polyesters to monoesters, to be discussed later, these reactions required the use of higher temperatures and different catalysts.

TABLE 111

VELOCITY CONSTANTS FOR THE ALCOHOLYSIS OF ESTERS WITH VARIOUS ALCOHOLS

Ester	Alcohol	$k \times 10^6$
Menthyl butyrate	Methanol	6,200
Ethyl butyrate	Methanol	90,200
Ethyl butyrate	Menthol	58
Methyl butyrate	Menthol	94.4
Methyl butyrate	Ethanol	19,800

Alcoholysis of Monoesters with Polyhydric Alcohols.—Alcoholysis with polyhydric alcohols may be applied to monoesters or to polyesters. The reaction between monoesters and polyhydric alcohols is of much less practical importance than the reaction between polyesters and polyhydric alcohols, and only a few investigations have been made of the former type of reaction.

This reaction was investigated by Grün, Wittka, and Scholze[115] using ethyl and isoamyl esters of fatty acids and glycerol. Unless the lower boiling monohydric alcohol is continuously removed the reaction will be incomplete regardless of other reaction conditions. By continuously removing the more volatile alcohol 94% to 100% conversion of ethyl and isoamyl esters to the corresponding glycerides was attained in 15 hours at 270°C.

One of the most extensive investigations of the alcoholysis of monoesters with polyhydric alcohols was reported by Wright and co-workers.[114] These authors found that if the methyl esters of the higher fatty acids were heated from 200° to 300°C. with a polyhydric alcohol in the presence of catalysts such as lead salts or alkaline earths, methanol will distill from the reaction mixture and the esters of polyhydric alcohols will be formed. The method has been applied to the reaction of the methyl esters of fatty acids, methyl glusocide, and ethyl glucoside and a variety of polyhydric alcohols, including glycols, pentaerythritol, mannitol, and polyglycerol. The methyl esters of linseed oil fatty acids were reacted with pentaerythritol under various conditions of time, temperature, and concentrations of the polyalcohol. The acid and hydroxyl numbers of the reaction products indicated that complete reaction is difficult of attainment.

The natural waxes, which are composed of mixtures of monoesters of long chain fatty acids and monohydric alcohols, may be modified by inter-

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[115] A. Grün, F. Wittka, and J. Scholze, *Ber.*, 54, 290–299 (1921).

esterification with glycerol or other polyhydric alcohols. Several products have been described which are produced by the reaction of montan wax with glycerol.[116–118] Ethylene glycol, as well as monohydric alcohols, have also been reacted with montan wax to produce modified waxes.[119] Similarly, certain marine oils which consist largely of monoesters of higher fatty acids and monohydric alcohols may be modified by interesterification with polyhydric alcohols.

Alcoholysis of Polyesters with Monohydric Alcohols Catalyzed by Acids.—Haller[106] applied the method of alcoholysis to butter, cocoa butter, coconut oil, margarine, tallow, linseed oil, poppyseed oil, and castor oil. With methanol, Haller found that hydrochloric and phenolsulfonic acids were equally effective catalysts. Usually twice the weight of absolute methanol to fat and 1% to 2% of hydrochloric acid were used in the alcoholysis reaction. Complete homogeneity was usually not attained and the upper liquid layer was removed and additional alcohol added to complete the reaction. Yields seldom exceeded 95% to 96% of methyl ester. Butter, coconut oil, castor oil, and the drying oils were more difficult to interesterify than the other oils investigated. The use of a neutral solvent such as ethyl ether, benzene, and carbon tetrachloride materially accelerated the alcoholysis.

In a subsequent investigation of the alcoholysis of coconut oil, Haller and Youssoufian[120] employed both methanol and ethanol and carried out the reaction at 35°C. with continuous agitation. Haller[121] also subjected castor oil to alcoholysis using methanol, ethanol, propanol and isobutanol and 1% to 2% hydrochloric acid as catalyst. Distillation of the monoesters makes it possible to prepare relatively pure esters of ricinoleic acid with any of the above-mentioned alcohols. Haller reported the boiling points, densities, specific and molecular rotations, and refractive indices of methyl, ethyl, *n*-propyl, and isobutyl ricinoleates prepared by alcoholysis of castor oil and fractional distillation of the resulting esters.

Madinaveitia[122] subjected castor oil, almond oil, butterfat, and triacetin to methanolysis using 3% hydrochloric acid as catalyst. He also subjected spermaceti, isoamyl and cyclohexanyl acetates to ethanolysis under the same conditions. Taylor and Clarke[123] prepared the methyl esters of coco-

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[116] E. Schliemanns Export-Ceresin-Fabrik, G.m.b.H., German Pat. 244,786 (March 14, 1912).

[117] W. Pungs and M. Jahrstorfer (to I. G. Farbenindustrie), U. S. Pat. 1,737,975 (Dec. 3, 1929); German Pat. 563,394 (Nov. 8, 1932).

[118] F. W. Guthke and W. Pungs (to I. G. Farbenindustrie), U. S. Pat. 1,834,056 (Dec. 1, 1931); German Pat. 558,437 (Sept. 7, 1932); British Pat. 296,145 (Sept. 20, 1928).

[119] I. G. Farbenindustrie A.-G., British Pat. 376,276 (June 27, 1932). See French Pat. 726,773 (June 3, 1932).

[120] A. Haller and Youssoufian, *Compt. rend.*, **143**, 803–806 (1906).

[121] A. Haller, *Compt. rend.*, **144**, 462–466 (1907).

[122] A. Madinaveitia, *Anales soc. españ. fís. quím.*, **12**, 426–428 (1914).

[123] E. R. Taylor and H. T. Clarke, *J. Am. Chem. Soc.*, **49**, 2829–2831 (1927).

nut oil in large quantity (130 kg.) by methanolysis. The reaction was carried out by refluxing on the steam bath, for 48 hours, mixtures consisting of 8 kg. of coconut oil, 9.6 kg. of methanol, and 500 g. or 2.7% of sulfuric acid on the basis of the total weight of the mixture.

Toyama and Tsuchiya[124] found that ethanolysis of olive oil with hydrochloric acid as catalyst led to the formation of relatively large amounts of mono- and diglycerides. The acetyl value of the reaction mixture first increased to a maximum and then began to decrease. Under the same conditions methanolysis proceeded more rapidly than ethanolysis which was indicated by the fact that the acetyl value reached a maximum in a shorter time. Olcott and Mattill[125] prepared the monoesters of lard, palm oil, and hydrogenated cottonseed oil by methanolysis and ethanolysis in the presence of 2% to 3% of hydrogen chloride. Smull and Saylor[126] prepared the methyl esters of linseed oil fatty acids by refluxing alkali-refined, neutral linseed oil with an excess of absolute methanol containing hydrogen chloride, and distilling the methyl esters at 200°C. under 6 mm. pressure.

Coleman and Moore[127] patented the production of monoesters by alcoholysis of ethylene diesters and described particularly the production of ethylene glycol monoacetate from ethylene glycol diacetate. The use of substantially anhydrous ethanol, propanol, and butanol, as well as secondary and other iso alcohols, with hydrochloric, sulfuric, and phosphoric acids as catalysts, and reaction temperatures up to the boiling point of the mixtures was covered by their patent. Reaction times of two to ten hours were employed depending on the reaction conditions.

The conversion of the fatty acids, combined in the form of phosphatides, to monoesters is a tedious and troublesome process when conducted by a combination of saponification and re-esterification. Shinowara and Brown[128] observed that this conversion could be more readily accomplished by direct alcoholysis. Failure of previous workers to accomplish the direct alcoholysis of phosphatides appeared to be due to the use of insufficient mineral acid to catalyze the reaction. When hydrochloric acid is used in ordinary amounts (1% to 2%) its concentration is apparently reduced by reaction with the choline of the phosphatides to an amount insufficient for catalytic effect. By increasing the concentrations of hydrochloric acid in the reaction mixture to 5%, or by the use of 7.5% to 12% of sulfuric acid, direct alcoholysis of phosphatides gave good yields of methyl, ethyl, propyl, butyl, and *n*-amyl esters.

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[124] Y. Toyama and T. Tsuchiya, *J. Soc. Chem. Ind. Japan.*, Suppl. bind., **36**, 232–233B (1933).

[125] H. S. Olcott and H. A. Mattill, *J. Am. Chem. Soc.*, **58**, 2204–2208 (1936).

[126] J. G. Smull and J. S. Saylor, *J. Am. Chem. Soc.*, **64**, 3054 (1942).

[127] G. H. Coleman and G. V. Moore (to Dow Chemical Co.), U. S. Pat. 2,010,689 (Aug. 6, 1935).

[128] G. Y. Shinowara and J. B. Brown, *Oil & Soap*, **15**, 151–152 (1938).

Alcoholysis of Polyesters with Monohydric Alcohols Catalyzed by Alkalies.—As indicated by the foregoing examples, the acid-catalyzed reaction between polyesters and monohydric alcohols has considerable utility. However, the alkali-catalyzed reaction possesses many advantages over the corresponding acid-catalyzed reaction, especially with respect to the speed, completeness, and relatively low temperature at which it can be effected.

Rowe[129] investigated the ethanolysis of coconut oil, lard, olive oil, triolein, linseed oil and butterfat dissolved in various organic solvents to which were added alcohol and caustic potash in concentrations varying from one to one-twentieth of the exact equivalent required to saponify the fat. The reaction conditions were generally not such as permitted complete reaction, consequently large amounts of mono- and diglycerides were formed.

Toyama and co-workers[130] found that in a homogeneous solution both ethanolysis and methanolysis were completed rapidly (two hours) at room temperature when olive oil was shaken with equivalent amounts of 0.50 *N* to 0.75 *N* alcoholic sodium hydroxide. Experiments conducted over a temperature range of 0° to 60°C. indicated that the reaction rate increased with increase in temperature. The amount of soap formed was very small in relatively anhydrous media but increased with an increase in the amount of water in the reaction mixture.

Kurz[131] investigated the velocity of the methanolysis and ethanolysis of a number of vegetable oils (olive, sesame, linseed, and tung). The alcoholysis reaction was carried out at 20°C. in the presence of ethyl ether with potassium hydroxide as catalyst. The extent of interesterification was followed by determining the percentage of the total glycerol which was liberated, and by determining the saponification and acetyl values of the reactants.

It was found, in agreement with Rowe[129] and with Toyama and coworkers,[130] that alcoholysis catalyzed by potassium hydroxide consisted of two reactions, namely, saponification followed by re-esterification. The velocity of the saponification reaction was found to be increased, within limits, with the increase of water in the alcohol, and with an increase in the concentration and total alkali content of the reaction mixture. The reaction was found to be comparatively rapid and under optimum conditions resulted in the liberation of approximately 95% of the glycerol from sesame, linseed, and tung oils within 60 minutes. The reaction velocity became very slow after one hour as may be seen from the data in Table 112

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[129] G. K. Rowe, *J. Soc. Chem. Ind.*, 52, 49–52T (1933).

[130] Y. Toyama, T. Tsuchiya, and T. Ishikawa, *J. Soc. Chem. Ind. Japan*, Suppl. bind., 36, 230–231B, 231–232B (1933).

[131] H. Kurz, *Fette u. Seifen*, 44, 144–145 (1937).

for the methanolysis of olive oil which was determined as follows. To each 50 ml. of a 20% solution of olive oil in ethyl ether, there were added 35 ml. of neutralized methanol and 1.05 ml. of 0.5 *N* potassium hydroxide in methanol. The mixture was allowed to stand at 20°C. and at the end of a specified time, the reaction was stopped by the addition of sufficient 0.5 *N* sulfuric acid to neutralize the alkali. Owing to the mild reaction conditions, namely, low temperature (20°C.) and low concentration of alkali, the method of Kurz possesses considerable superiority over the usual method of saponification and re-esterification for the preparation of methyl and ethyl esters, especially when applied to fats containing acids whose structures are easily altered.

TABLE 112

ALKALI-CATALYZED METHANOLYSIS OF OLIVE OIL AT 20°C.

Reaction time, hrs.	Glycerol liberated, %	
	By weight	Of total
24	10.47	98.31
48	10.52	98.78
72	10.59	99.44

Norris and Terry[132] prepared the furfuryl esters of linseed oil fatty acids by reacting furfuryl alcohol and linseed oil containing 0.5% metallic sodium as catalyst at a temperature of 60°C. for three hours. Furfuryl oleate and palmitate were prepared from the corresponding methyl esters by a similar process of alcoholysis. Other furfuryl esters have been prepared by various workers using modifications of the alcoholysis process.

The process of alcoholysis for the preparation of soaps and recovery of glycerol was patented by Bradshaw and Meuly.[133,134] Somewhat different reaction conditions are used in the commercial process as compared to the laboratory process where completeness of the reaction and minimization of alteration in the structure of the acids are paramount. The reaction is carried out in ordinary iron vessels. Neutral fat and anhydrous commercial grade methanol (99.7%) containing 0.1% to 0.5% caustic soda or potash are mixed in the molar ratio of approximately 1 to 1.6, and heated to 80°C. After stirring for a few minutes the mixture is allowed to stand, whereupon the glycerol begins to separate immediately and settle to the bottom of the reaction vessel. The reaction is about 98% complete within an hour but only about 90% of the glycerol separates from the mixture, the remainder is present in the upper layer of methyl esters, unreacted alcohol, alkali, and soap. The methyl esters can be freed of impurities by washing with water.

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[132] F. A. Norris and D. E. Terry, *Oil & Soap*, 21, 193-196 (1944).

[133] G. B. Bradshaw and W. C. Meuly (to E. I. du Pont de Nemours), U. S. Pat. 2,271,619 (Feb. 3, 1942).

[134] G. B. Bradshaw, *Soap Sanit. Chemicals*, 18 (No. 5), 23-24, 69-70 (1942).

Wright *et al.*[114] extended the method of Bradshaw and Meuly to include a variety of alcohols. They have described the general conditions for methanolysis and ethanolysis as follows. A typical reaction would require 1.6 equivalents of anhydrous alcohol per equivalent of neutral oil and as catalyst, 0.5% of sodium hydroxide on the basis of the oil used. The reaction may be carried out at ordinary or elevated temperatures. Separation of glycerol is apparent at the end of thirty minutes and is complete in one to two hours. The glycerol layer is withdrawn and the ester layer is acidified to decompose any soaps which may be present, and washed free of glycerol, alcohol, and salt.

When ethanol is used, the acid number of the oil must be below one. Excess alkali must be added if the acid number is above this value, otherwise insufficient alkali will be available for catalysis. However, when excess alkali is added the resulting soap produces emulsification of the ester and glycerol and the reaction mixture must be acidified to separate it into an alcohol–glycerol layer and an acid–ester layer. The total amount of water in the reaction mixture must be well below 0.3% and preferably below 0.1%, otherwise the alkali will be consumed in the formation of soaps, thereby resulting in incomplete ester formation or liberation of glycerol. An excess of alcohol or excess of alkali above that required for catalysis must be used to compensate for the presence of excessive water, but again acidification must be resorted to for the separation of glycerol.

Wright and co-workers, using cottonseed oil, demonstrated the effect of the variables, ethanol, water, and alkali, on the yield of glycerol. The highest yield (96.6%) was obtained under the following conditions: 100 g. of anhydrous cottonseed oil, 30 g. of ethanol (99.5%), 1.0 g. of sodium hydroxide, maximum concentration of water in mixture 0.11%. For coconut oil, the maximum yield (95.4%) of glycerol was obtained with the following conditions: 100 g. of anhydrous coconut oil, 30 g. of ethanol (99.5%), 2.0 g. of sodium hydroxide, maximum concentration of water in mixture 0.11%.

Normal propanol was found to be less reactive than either methanol or ethanol which could be compensated for in part by increasing the ratio of alcohol to oil. The reaction mixture must always be acidified when propanol is used in order to effect the separation of the glycerol and propyl esters. With peanut oil and *n*-propyl alcohol, a maximum yield (98.5%) of glycerol was obtained under the following conditions: 100 g. of peanut oil, 40 g. *n*-propanol (199% of theory), 2.0 g. of sodium hydroxide.

Isopropanol was found to be impractical from the commercial point of view owing to the necessity of removing its moisture by metallic sodium. Furfuryl alcohol and the Cellosolves were found to react, but required excessive ratios of alcohol to oil for even moderately complete reaction, and the glycerol did not separate from the reaction mixture.

Alcoholysis of Polyesters with Polyhydric Alcohols.—Interesterification between polyhydric alcohols and polyesters occurs in a manner analogous to that between monohydric alcohols and polyesters and may be carried out with any polyhydric alcohol and polyester. Although a reaction generally occurs with any combination of alcohol and ester, equilibrium may be established at concentrations of the products which are such as to make the reaction of little practical value. This is quite often the case when the displaced polyhydric alcohol cannot be readily removed from the reaction mixture owing to its high boiling point.

Few investigations have been devoted to the replacement of glycerol in triglycerides or natural fats with other polyhydric alcohols, primarily because of the difficulty of removing the high boiling glycerol (b.p. 290°C.). Only those polyhydric alcohols which are stable at temperatures of 200^{c} to 300°C. and have a boiling point above that of glycerol under the reaction conditions can be used. Such polyhydric alcohols include pentaerythritol, methyl and ethyl glucosides, mannitol, sorbitol, and the polyglycerols. The reaction is carried out with 1 to 1.5 equivalents of the polyhydric alcohol in the presence of 0.5 to 2.0% of lead or alkali salts as catalyst. If the reaction is carried out at atmospheric pressure, a temperature of 275° to 300°C. is required to remove the glycerol, consequently it is preferable to employ a vacuum of 40 to 300 mm. under which conditions the temperature can be reduced to 200° to 250°C. The reaction has also been carried out under other conditions, namely, with steam-vacuum distillation and by a continuous method employing a heated and evacuated column.[114]

Blagonravova[135] and also Burrell[136] compared the alcoholysis of refined linseed oil with glycol and with pentaerythritol and concluded among other things that pentaerythritol should not be present in great excess owing to the tendency of the polyhydric alcohol to carbonize. Best results were obtained with a maximum ratio of 2 moles of pentaerythritol per mole of oil. With increasing temperature from 220° to 270°C. the rate of alcoholysis increased. Mannitol has been employed to replace glycerol in tristearin and in olive oil under a relatively high vacuum (14 mm.), a temperature of 275°C., and the presence of sodium methylate as catalyst.[137–139] Sorbitol and pentaerythritol esters have been prepared in a similar manner.[140–142]

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[135] A. A. Blagonravova, M. A. Antipova, O. N. Savvina, and E. M. Svetlichnaya, *J. Applied Chem. U.S.S.R.*, 14, 192–197 (1941).

[136] H. Burrell, *Oil & Soap*, 21, 206–211 (1944).

[137] V. P. Golendeev, *J. Gen. Chem. U.S.S.R.*, 6, 1841–1846 (1936).

[138] J. C. Irvine and H. S. Gilchrist, *J. Chem. Soc.*, 125, 10–15 (1924).

[139] A. Lapworth and L. K. Pearson, *Biochem. J.*, 13, 296–300 (1919).

[140] J. A. Arvin (to E. I. du Pont de Nemours), U. S. Pat. 2,029,851 (Feb. 4, 1936).

[141] E. I. du Pont de Nemours, British Pat. 436,885 (Nov. 14, 1935).

[142] A. A. Blagonravova and M. A. Antipova, *Byull. Obmena Opyt. Lakokrasochnoĭ Prom.*, 1940, No. 10, 18–19.

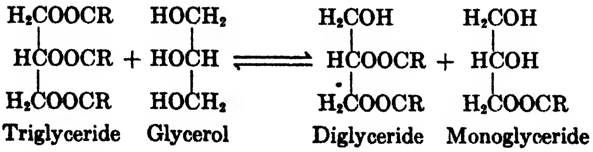
When it is not necessary to remove the glycerol from the reaction mixture or when either mixed alcohol esters or partially esterified mixed alcohol esters are desired, the reaction between natural fats and various polyhydric alcohols is of considerable importance. For industrial scale production of *completely esterified* polyhydric alcohols, direct reaction between the alcohol and acid is generally preferable to any other method. However, direct reactions of polyhydric alcohols with fatty acids for the production of *partially esterified* products possess the disadvantage that they cannot be made very specific with respect to the degree of esterification obtained. Regardless of the excess of alcohol used, a certain amount of complete esterification occurs. Also, because of the poor miscibility of fatty acids and many polyhydric alcohols, the fatty acids tend to react with the ester product which is first formed rather than with the alcohol, thereby increasing the degree of esterification beyond that which may be desired. For these reasons it is simpler and more practical to react a completely esterified ester with an excess of polyalcohol to produce the desired partially esterified product.

The reaction is of primary importance when applied to the interesterification of triglycerides, especially the natural fats. Numerous investigations of the reaction between polyalcohols and triglycerides have been made employing most of the available polyhydric alcohols under a wide range of conditions of pressure, temperature, catalyst and time of reaction.

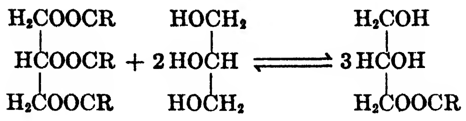
Although most of these reactions proceed in the absence of a catalyst they are greatly accelerated by certain catalytic agents. Generally, acidic substances are ineffective or very poor catalysts. The alkalies and their carbonates and alcoholates are most effective, and the oxides of calcium, magnesium, and lead are somewhat less so. Interesterification of most polyhydric alcohols and polyesters can be carried out at temperatures between 170° and 250°C., either at atmospheric pressure or under vacuum.

Production of Mono- and Diglycerides by Glycerolysis of Fats.—The reaction of glycerol with triglycerides for the production of mono- and diglycerides represents a special case of interesterification of polyhydric alcohols and polyesters which may be referred to as *glycerolysis*. The reaction is carried out industrially on a large scale for the production of a variety of partially esterified products.

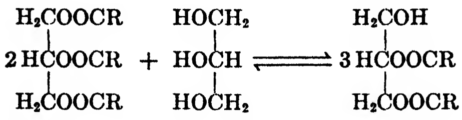
When a triglyceride is reacted with glycerol the reaction may occur in several different ways as illustrated in the following equations:



$$\begin{array}{ccccccc} H_2COOCR & & HOCH_2 & & H_2COH & & H_2COH \\ | & & | & & | & & | \\ HCOOCR & + & HOCH & \rightleftharpoons & HCOOCR & + & HCOH \\ | & & | & & | & & | \\ H_2COOCR & & HOCH_2 & & H_2COOCR & & H_2COOCR \\ \text{Triglyceride} & & \text{Glycerol} & & \text{Diglyceride} & & \text{Monoglyceride} \end{array}$$



$$\begin{array}{c}\mathrm{H_2COOCR}\\ |\\ \mathrm{HCOOCR}\\ |\\ \mathrm{H_2COOCR}\end{array} + 2\begin{array}{c}\mathrm{HOCH_2}\\ |\\ \mathrm{HOCH}\\ |\\ \mathrm{HOCH_2}\end{array} \rightleftharpoons 3\begin{array}{c}\mathrm{H_2COH}\\ |\\ \mathrm{HCOH}\\ |\\ \mathrm{H_2COOCR}\end{array}$$



$$2\begin{array}{c}\mathrm{H_2COOCR}\\ |\\ \mathrm{HCOOCR}\\ |\\ \mathrm{H_2COOCR}\end{array} + \begin{array}{c}\mathrm{HOCH_2}\\ |\\ \mathrm{HOCH}\\ |\\ \mathrm{HOCH_2}\end{array} \rightleftharpoons 3\begin{array}{c}\mathrm{H_2COH}\\ |\\ \mathrm{HCOOCR}\\ |\\ \mathrm{H_2COOCR}\end{array}$$

From these equations it is seen that theoretically, at least one mole of triglyceride can react with one-half, one, or two moles of glycerol to form, respectively, one and a half moles of diglyceride, one mole each of di- and monoglyceride, or three moles of monoglyceride. Assuming a mean molecular weight of 860 for the triglyceride and 92 as the molecular weight of glycerol, these three reactions would require for theoretical conversion, respectively, 5.3, 10.7, and 21.4% of glycerol on the basis of the weight of triglyceride. In actual practice all three glycerides generally coexist regardless of the ratio of triglyceride to glycerol employed, although conditions can be selected such that one of the glycerides may predominate and the proportion of triglyceride can be made relatively small.

A further difficulty in producing monoglycerides by interesterification of triglycerides and glycerol is the tendency of the monoglycerides to form diglycerides under the influence of alkali catalysts. Fischer and coworkers[143] observed that glycerol-α-monobenzoate or acetate, in ethereal solutions containing potassium carbonate as a catalyst, is moderately rapidly converted to a mixture of glycerol and glycerol dibenzoate or diacetate. Chloroform solutions of monobenzoylglycol undergo similar reactions to form dibenzoylglycol.

Tsuchiya and Akiyama[144] investigated the glycerolysis of hardened fish oil with respect to the effect of time, temperature, and ratio of glycerol. The highest acetyl value was obtained when the oil was heated for 0.5 hour at 270° to 280°C. with 25% to 100% of its weight of glycerol. Even the highest acetyl value obtained was lower than that corresponding to complete conversion to monoglyceride; hence, it was assumed diglycerides were present in the reaction product. Alkali carbonates, hydroxides, and the oxides of magnesium, calcium, and zinc accelerated the reaction and made possible a considerable decrease in the reaction temperature. Hardened soybean oil, tallow, coconut, olive, and castor oils, behaved similarly to fish oil with respect to glycerolysis. The higher molecular weight alcohols were readily liberated from sperm and hardened sperm oils by glycerolysis.

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[143] E. Fischer, E. Pfähler, and F. Brauns, *Ber.*, **53B**, 1634–1644 (1920).

[144] T. Tsuchiya and G. Akiyama, *J. Soc. Chem. Ind. Japan*, Suppl. bind., **36**, 233–234B (1933).

Kawai and Yamamoto[145] investigated the conditions requisite for the maximum production of monoglycerides of teaseed oil by interesterification with glycerol. Teaseed oil was heated to temperatures of 170° to 180°, 210° to 220°, and 240° to 250°C. with 1.4 times the amount of glycerol necessary to convert all of the triglycerides to monoglycerides. The reaction was carried out both in the presence and in the absence of a catalyst. Potassium carbonate, tin, zinc, and oleic acid, and combinations of these were used as catalysts. The acid, saponification, and hydroxyl values were determined at intervals on samples withdrawn from the reaction mixture. All of the catalysts, and especially the combination of metallic catalysts together with oleic acid, produced marked acceleration of the reaction. The product of highest hydroxyl value was calculated to contain 10% of triglyceride and 40% each of di- and monoglycerides.

A number of processes and procedures for the industrial production of mono- and diglycerides by glycerolysis are described in the patent and scientific literature. According to Bailey[146] the reaction is generally carried out at atmospheric pressure and a temperature of 200° to 235°C. in closed vessels constructed of aluminum or stainless steel and provided with mechanical agitation. About 0.05% to 0.20% of catalyst on the basis of the weight of fat is used. Various alkaline catalysts (caustic soda, caustic potash, sodium alcoholates) are employed with a reaction time of one to two hours. When the maximum production of monoglycerides is desired it is preferable to use the theoretical quantity of glycerol (about 20%). A greater excess is of no practical advantage since equilibrium occurs when about 13.5% of glycerol has reacted. In the absence of appreciable triglycerides, this glycerol consumption corresponds to the formation of a mixture of mono- and diglycerides in the proportion of 70 to 30. For further details concerning the commercial preparation of mono- and diglycerides the reader is referred to Bailey and the patents of Edeler and Richardson,[147] Eckey and Clark,[148] Richardson and Eckey,[149] Christensen,[150] and Hilditch and Rigg.[151]

European practice, according to Grün,[152] differs somewhat from that followed in the United States for the production of mono- and diglycerides.

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[145] S. Kawai and S. Yamamoto, *J. Soc. Chem. Ind. Japan*, Suppl. bind., **43**, 219–220B (1940).

[146] A. E. Bailey, *Industrial Oil and Fat Products.* Interscience, New York, 1945.p. 679.

[147] A. Edeler and A. S. Richardson (to Procter & Gamble), Canadian Pats. 340,803 to 340,805 (April 10, 1934).

[148] E. W. Eckey and C. C. Clark (to Procter & Gamble), U. S. Pat. 2,065,520 (Dec. 29, 1936).

[149] A. S. Richardson and E. W. Eckey (to Procter & Gamble), U. S. Pat. 2,132,437 (Oct. 11, 1938).

[150] C. W. Christensen (to Armour), U. S. Pat. 2,022,493 (Nov. 26, 1935).

[151] T. P. Hilditch and J. G. Rigg (to Imperial Chemical Industries), U. S. Pat. 2,073,-797 (March 16, 1937).

[152] A. Grün, in *Chemie und Technologie der Fette und Fettprodukte.* Vol. 1, G. Hefter and H. Schönfeld, eds., Springer, Vienna, 1936, pp. 276–278.

For maximum monoglyceride production 12% to 15% of glycerol is used on the basis of the weight of fat to be converted. The reaction is carried out *in vacuo* at a temperature of 170°C. in tin-lined vessels. For maximum diglyceride production 6% to 8% of glycerol is used with a reaction temperature above 180°C. and below 250°C. Also, according to Grün, at 180°C. disproportionation of monoglyceride to diglyceride and glycerol occurs, and above 250°C. interesterification occurs with the formation of triglycerides and glycerol. As the temperature increases glycerol tends to form di- and polyglycerols and their esters.

According to Grün, the earliest catalysts used in glycerolysis were minerals such as kieselguhr, which were superseded by metallic oxides such as titanium, thorium, and aluminum oxides.[153] These oxides were not very active, partly because of their conversion to metallic soaps, and they were in turn superseded by the oxides, carbonates, and especially the alcoholates of the alkali and alkaline earth metals. Zinc and tin,[154] particularly the latter, are preferred as catalysts since they are excellent accelerators and are readily recovered with little loss. When powdered catalysts are used the reaction mixture is cooled sufficiently to permit filtration or centrifugation to remove the suspended material after which it is washed with water to recover the unreacted glycerol. Because of the surface-modifying properties of mono- and diglycerides, water washing is a difficult operation and Grün does not state how this can be effectively accomplished. Grün claims that the commercial product, whether principally mono- or diglyceride, contains up to 10% or more of triglyceride and it is difficult to obtain more than 60% to 70% of either mono- or diglyceride, respectively, under any practical reaction conditions.

Ordinarily, the glyceride mixture thus obtained is used without separation of the components but where this is desired recourse is had to fractionation from alcohol. Mono-, di-, and triglycerides may be separated by means of alcohol of different strengths. Hot, undiluted alcohol extracts considerably more mono- and distearin than tristearin. On cooling the alcoholic extract, distearin is chiefly separated while the monostearin remains in solution. By repetition of this process reasonably pure distearin can be obtained. By concentration of the mother liquor and recrystallization of the residue from more dilute alcohol or dilute alcohol–glycerol solution, at least 90% of the monostearin can be recovered. For the direct separation of monostearin the crude reaction product is treated with 84% to 88% alcohol by volume.

(*b*) *Ester Interchange*

Ester interchange has generally been applied in the sense that the term interesterification has been used here, rather than in the restricted sense of

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[153] Anton Jurgens Vereenigde Fabrieken, German Pat. 277,641 (Sept. 7, 1914).

[154] G. Schicht A.-G. and A. Grün, German Pat. 402,121 (Sept. 13, 1924).

the exchange of acyl radicals between two or more esters. If two esters, such as ethyl acetate and methyl butyrate, are heated together in the presence of a catalyst they will interact to form an equilibrium mixture of ethyl butyrate, methyl acetate, and the original esters according to the following equation:

$$CH_3COOC_2H_5 + C_3H_7COOCH_3 \rightleftharpoons C_3H_7COOC_2H_5 + CH_3COOCH_3$$

Similar reactions occur with esters of the higher aliphatic acids of both monohydric and polyhydric alcohols.

The reaction illustrated in the equation given above is of no particular economic importance but similar reactions with polyesters, and especially those of the triglycerides, are the basis of a number of industrial processes. A more practical example of true ester interchange is represented by the reaction which occurs when ester gum (glyceryl abietate) is heated with linseed or other natural oil in the production of varnish. The rearrangement of the acyl groups in natural fats by heating them in the presence of a catalyst represents still another practical example of true ester interchange. Ester interchange reactions are entirely analogous to many other well known double decomposition reactions.

These ester interchange reactions have been the subject of numerous scientific investigations and many practical applications thereof are disclosed in the patent literature. For example, Normann[155] heated one part by weight of tristearin with two parts by weight of almond oil, and two moles of tristearin with one mole of triacetin without a catalyst, and in both cases ester interchange proceeded only to the extent of approximately 50% after 72 hours. With tin as a catalyst, ester interchange between a mixture of coconut oil and ethyl stearate was appreciably greater than 50% after 16 hours. Naphthalene-β-sulfonic acid and sodium ethylate were also found to be active catalysts for the reaction. Tristearin and coconut oil (1:4) were reacted in the presence of naphthalene-β-sulfonic acid and of sodium ethylate as catalysts. With 1% naphthalene-β-sulfonic acid, a reaction temperature of 250°C., a reaction time of 2.5 hours, and atmospheric pressure, the melting point of the tristearin dropped from 57.3° to 34.5°C. With 0.1% to 0.2% sodium ethylate, a temperature of 140°C., reaction time of 0.5 hour, and reduced pressure, the melting point of the tristearin dropped from 57.7° to 31.4°C. The reduction in the melting point is indicative of the degree of ester interchange which occurred in the two cases.

Grün[156] heated equimolar quantities of tricaprylin and tristearin in the presence of tin for three hours at 230°C. Analysis of the reaction mixture

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[155] Ölwerke Germania G.m.b.H. and W. Normann, German Pat. 417.215 (Sept. 7, 1925).

[156] A. Grün, *Z. angew. Chem.*, **38**, 827 (1925).

gave results indicating that the reaction product contained 9% of tricaprylin, 20% of tristearin, and 71% of caprylostearoglycerides, of which the major component was stated to be caprylodistearin. Further interesterification gave a product corresponding to a mixture of caprylodistearin, tricaprylin, and stearodicaprylin. Other pairs of glycerides, namely, tristearin and triolein, triolein and tricaprylin, tricaproin, tributyrin, etc., gave analogous results.

Konen, Clocker, and Cox[157] have indicated the utility of the ester interchange reaction in the preparation of the glyceryl esters of highly reactive acids such as elaeostearic. This acid cannot be directly esterified with glycerol by ordinary methods because polymerization (gelation) occurs long before esterification is complete. However, these authors were able to prepare the glyceryl ester of elaeostearic acid by reacting equivalent quantities of anhydrous glyceryl acetate and methyl elaeostearate in the presence of 0.05% of dry sodium methylate. The methyl acetate was removed by distillation under vacuum at a temperature of 60° to 100°C.

Many natural fats possess relatively specific molecular configurations with respect to the distribution of the acyl groups in their triglycerides. Artificial triglycerides prepared by esterification of glycerol and a mixture of fatty acids possess random arrangements of acyl groups owing to the fact that the reaction of any given hydroxyl group and acyl radical is a relatively statistical one. When a natural fat is subject to rearrangement under the influence of a catalyst, a mixture of glycerides is formed in which the distribution of acyl groups is similarly statistical.

Since the physical and chemical properties of the individual triglycerides depend on their molecular configurations, it is obvious these properties will be altered by shifting the configuration of a mixture of glycerides from a highly specific to a completely random distribution of acyl groups. For example, a mixture of equal parts of triolein and tristearin will have quite different properties from a mixture of monoleindistearins and monostearindioleins resulting from a random distribution of the acyl groups among the glycerol molecules. Completely random distribution of the acyl groups would result in four compounds having configurations corresponding to α-oleo-β,α'-distearin, α-stearo-β,α'-diolein, β-oleo-α,α'-distearin, and β-stearo-α,α'-diolein, in addition to the original two homotriglycerides.

As has been pointed out by Bailey,[146] lard consists of a mixture of more or less specifically oriented glycerides with respect to the distribution of acyl groups. This specificity in glyceride configuration is responsible for the formation of relatively large, coarse crystals on solidification of hydrogenated and unhydrogenated lards. When lard is subjected to ester interchange which produces a random distribution of the acyl groups, this tend-

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[157] J. C. Konen, E. T. Clocker, and R. P. Cox, *Oil & Soap*, **22**, 57–60 (1945).

ency to form large crystals disappears and the emulsifying properties of the rearranged product is enhanced.

The rearrangement of natural fats or artificial mixtures of triglycerides can be accomplished by heating them to 200°C. or higher in the presence of a small amount of glycerol, monoglyceride, or diglyceride[146] to initiate the reaction. It can be accomplished more readily, however, by the addition of a catalyst, such as sodium ethylate, stannous hydroxide,[158,158a] and sodium hydroxide.[146]

Interesterification affords a means of improving many natural fats which otherwise possess limited applications. Beef and mutton tallows, and very hard oils containing large percentages of tristearin, palmitodistearin, and other glycerides having melting points above body temperature are difficultly absorbed and digested by many animals. On the other hand, certain liquid fats are available which require hardening to produce desirable products. By mixing these hard and soft fats in proper proportions a product of butterlike consistency can be obtained but the digestibility of the high melting glycerides in the mixture remains unaltered. By interesterification in the presence of glycerol and a catalyst, mixed fats, relatively rich in high and low melting glycerides, respectively, can be converted to a fat of more acceptable consistency and utility. When tributyrin and other low molecular weight glycerides are added to the interesterification mixture, products similar in composition to natural butter can be produced. Many variations of this ester interchange reaction are possible with a corresponding diversity of end products.[159-161]

The process of ester interchange is equally applicable to the modification of drying oils. Scheiber[162] has described various improved drying oils obtained by reacting tung oil, linseed oil, fatty acids, and glycerol, or a mixture of linseed or soybean oils with tung oil fatty acids at a temperature of 200°C. Schwartz[163] described a similar product obtained by the reaction of castor oil and fatty acids.

Ester interchange, or a combination of esterification and ester interchange, is widely used in the manufacture of modified alkyd resins. Such resins are prepared by reacting glycerol, or other polyhydric alcohols, with

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[158] C. van Loon (to Anton Jurgens Margarinefabrieken), U. S. Pats. 1,873,513 (Aug. 23, 1932) and 1,744,596 (Jan. 21, 1930); Dutch Pat. 16,703 (Aug. 15, 1927); British Pat. 249,916 (Dec. 30, 1924). See also C. M. Gooding (to Best Foods, Inc.), U. S. Pat. 2,309,949 (Feb. 2, 1943).

[158a] F. A. Norris and K. F. Mattil, *Oil & Soap*, **23**, 289–291 (1946).

[159] G. Schicht A.-G. and A. Grün, Austrian Pat. 96,522 (April 1, 1924); British Pat. 160,840 (April 28, 1921).

[160] Ölwerke Germania G.m.b.H., German Pat. 357,877 (Sept. 1, 1922).

[161] O. Schmidt, German Pat. 102,539 (April 22, 1898).

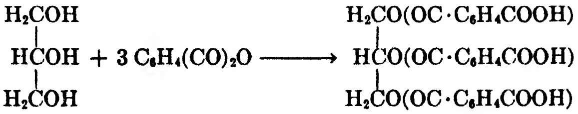
[162] J. Scheiber, German Pat. 513,309 (Nov. 26, 1930); 555,496 (July 26, 1932). See British Pat. 306,453 (April 17, 1929).

[163] G. L. Schwartz (to E. I. du Pont de Nemours), U. S. Pat. 1,558,299 (Oct. 20, 1925).

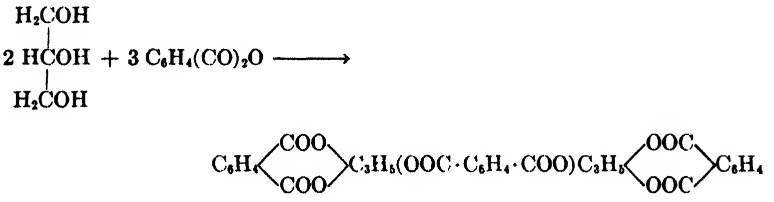
[164] E. A. Bevan, *J. Oil Colour Chem. Assoc.*, **26**, 155–168 (1943).

dibasic acids such as phthalic, maleic, succinic, sebacic, etc.[164] When polyhydric alcohols and polybasic acids are heated together a series of esterification and condensation reactions ensue which result in the formation of a mixture of products that have properties resembling those of natural resins.

With glycerol and phthalic anhydride, the reaction may be represented as occurring in two ways according to the following schemes:



$$\begin{matrix} H_2COH \\ | \\ HCOH \\ | \\ H_2COH \end{matrix} + 3\,C_6H_4(CO)_2O \longrightarrow \begin{matrix} H_2CO(OC\cdot C_6H_4COOH) \\ | \\ HCO(OC\cdot C_6H_4COOH) \\ | \\ H_2CO(OC\cdot C_6H_4COOH) \end{matrix}$$



$$2\begin{matrix} H_2COH \\ | \\ HCOH \\ | \\ H_2COH \end{matrix} + 3\,C_6H_4(CO)_2O \longrightarrow C_6H_4\begin{matrix} COO \\ COO \end{matrix}C_3H_5(OOC\cdot C_6H_4\cdot COO)C_3H_5\begin{matrix} OOC \\ OOC \end{matrix}C_6H_4$$

These products represent only the early stages of the reaction which are followed by further condensation and polymerization.

These unmodified alkyd resins have only limited use owing to certain inherent disadvantages. They are, therefore, modified by incorporation of various substances such as triglyceride oils, fatty acids of an oil, or other synthetic or natural resins. The number of possible modifications are extremely numerous since any vegetable oil, fatty acid, or mixture of fatty acids may be used in their production. As a consequence of the great diversity of modified alkyds which are possible with corresponding differences in properties, a voluminous patent and technical literature has appeared on the subject.[165]

One class of modified alkyd resins results from their interaction with nondrying oils or their derived fatty acids. In general, the incorporation of monobasic acids into alkyd resins increases their solubility. The short chain acids (acetic, butyric, etc.) cause considerable softening of the resin while the long chain acids, stearic, palmitic, oleic, ricinoleic, derived from nondrying oils result in increased flexibility. When drying oils or their fatty acids, *e. g.*, linoleic acid, are used as modification agents, the resulting resins harden rapidly at ordinary temperatures owing to the greater ease of oxidation and polymerization of the unsaturated acids.

Modified alkyd resins may be formed by several different methods as follows: (*1*) the monobasic fatty acid, glycerol, and dibasic acid, *e. g.*,

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[165] C. Ellis, *The Chemistry of Synthetic Resins.* 2 vols., Reinhold, New York, 1935.

phthalic acid, may be heated together; (*2*) mono- and diglycerides of the monobasic fatty acids may be condensed with the dibasic acid; (*3*) the polybasic acid or its anhydride may be heated with glycerol and a triglyceride oil. Depending on the reaction conditions, more or less interesterification will occur, especially in the early stages preceding the subsequent polymerization reactions.

(*c*) *Acidolysis*

Acidolysis is used here in a sense analogous to alcoholysis, *i. e.*, the replacement of an acyl group of an ester by an acyl group of a free fatty acid. If a fatty acid ester is heated with an excess of fatty acid in the presence of an esterification catalyst, an exchange of the acyl groups will occur between the free acid and ester. This tendency of one fatty acid to replace another is a function of their relative molecular weights. Low molecular weight acids tend to displace those of higher molecular weight. For example, formic, acetic, and propionic acids have been used to replace the fatty acids in coconut oil.

In the case of acetic acid and coconut oil, there results a mixture of laurodiacetin, myristodiacetin, etc., which is used as a plasticizing agent for nitrocellulose.[163] The reaction is, however, not confined to the replacement of high molecular weight acids. According to Barsky[166] the fatty acids derived from cottonseed and palm oils can replace those of coconut oil when the former are reacted with the latter at 260° to 300°C. even without a catalyst. Eckey[166a] was granted a patent covering the reaction of free fatty acids, as for example, oleic acid with triglycerides (tristearin) or natural fats (hydrogenated cottonseed oil) using water (0.25 to 10%) as catalyst.

Interesterification is presumed to occur between diterpenoid carboxylic acids and the triglycerides present in natural oils, although apparently under the conditions obtaining in the varnish kettle the degree of interchange between the acid radicals is not extensive. Investigations of the reactions of triglycerides with natural rosin or abietic acid have been conducted with a view to developing improved types of varnishes. According to the review of the subject by Ellis[165] little interchange occurs between the triglycerides and abietic acid. Tristearin and refined linseed oil were reacted with abietic acid by Pistor[167] but little reaction was observed under the conditions employed. Ragg[168] came to the same conclusion from similar experiments. Scheiber,[169] on the other hand, believed that some reaction occurred between rosin, Congo, and Manila resins and the triglycerides.

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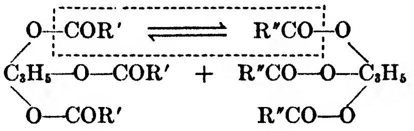
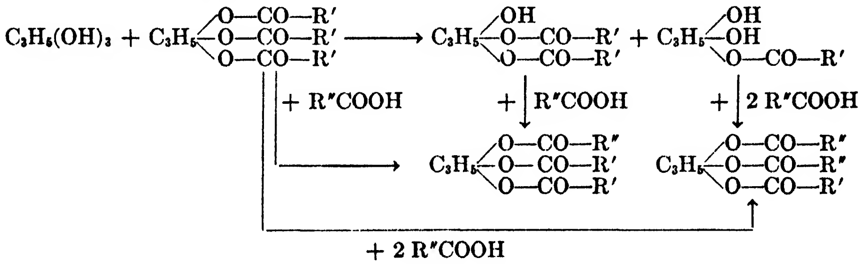
[166] G. Barsky (to Wecoline Products), U. S. Pat. 2,182,332 (Dec. 5, 1939).
[166a] E. W. Eckey (to Procter & Gamble), U. S. Pats. 2,378,005–7 (June 12, 1945).
[167] K. Pistor, *Farben.-Ztg.*, 30, 3056–3057 (1925); *Farbe u. Lack*, 1925, 456.
[168] M. Ragg, *Farben-Ztg.*, 26, 2335–2336 (1921).
[169] J. Scheiber, *Farbe u. Lack*, 1929, 393–394, 404–405, 418–419.

(*d*) *Mechanism of Interesterification*

It has been presumed that in ester interchange the acyl group of one glyceride molecule may be directly replaced by another acyl group from another glyceride molecule according to the following scheme:



In the presence of glycerol (alcoholysis), or of a small amount of glycerol and free fatty acid (acidolysis), interesterification may occur according to one of the following schemes:



Similar equations can be written for other alcohols whether mono- or polyhydric, and for any corresponding ester.

The nature of the various agents which effect ester interchange in natural fats are usually such as would tend to produce small initial amounts of mono- or diglycerides and it would, therefore, appear that the process is fundamentally one of alcoholysis in which glycerol, mono- or diglycerides are constantly generated and subsequently reacted to form new triglycerides. The reaction, when continued sufficiently long, will come to kinetic-equilibrium with attainment of a relatively high degree of randomness of the glyceride configurations. It is not improbable that even in the absence of a catalyst sufficient moisture may be present to produce the small amount of hydrolysis necessary to initiate the interesterification reaction.

The exact nature of the interesterification mechanism which obtains in the complex reactions involved, for example, in the modification of alkyd resins, is extremely difficult to determine. Flory[170] investigated the kinetics of less complex interesterification systems exemplified by decamethylene adipate polyesters and decamethylene glycol and lauric acid, and compared them with the kinetics of the esterification of diethylene glycol with adipic acid, and of decamethylene glycol and adipic acid. He found that

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[170] P. J. Flory, *J. Am. Chem. Soc.*, **58**, 1877–1885 (1936); **61**, 3334–3340 (1939); **62**, 2255–2261, 2261–2264 (1940).

the interesterification reaction was proportional to the acid catalyst present, but diminishes somewhat with an increase in the concentration of hydroxyl groups. The results obtained with both decamethylene glycol and lauryl alcohol agreed with the theory that the ester groups of the polymer molecules are attacked at random.

He also found that the rate of polyesterification with *p*-toluenesulfonic acid as catalyst, and a temperature of 109°C., was about eleven times as rapid as the corresponding alcoholysis reaction. In the uncatalyzed or carboxylic acid-catalyzed reaction, the rate constants were approximately the same for the same acid.

CHAPTER XI

ALKYLATION AND ALKOXYLATION

A variety of alkylation reagents and methods are available for the preparation of derivatives of fatty acids. The choice of methods necessarily depends on the derivative desired and the constitution of the reacting acid, *i. e.*, the nature of the substituent groups. The available alkylation reagents include diazomethane, dimethyl and diethyl sulfates, alkyl halides and metallic alcoholates, the last producing alkoxy derivatives. The products which may be produced include esters, ethers, ketones, extended normal hydrocarbon chains, and side chains.

1. Alkylation

Esters are normally prepared by direct esterification of acids and alcohols in the presence of a catalyst as has been previously described, but certain types of esters cannot be formed by this method. Very long chain acids cannot be readily esterified with very long chain alcohols but corresponding esters can be formed by the action of the acid chlorides with alcohols or sodium alcoholates.

Certain nonaliphatic acids, *e. g.*, ursolic, oleanolic, and other sapogenic acids, cannot be directly esterified even with low molecular weight alcohols, but on treatment with dimethyl sulfate, diazomethane, or by the action of methyl iodide on the silver salt, methyl esters of extreme stability can be prepared.[1] Higher homologous *n*-alkyl esters of these sapogenic acids can also be prepared by the reaction of the acid chloride with the appropriate alcohol, *e. g.*, propyl, butyl, etc. By this method, Sell and Kremers[2] introduced in turn all of the *n*-alkyl groups from C_2H_5 to C_8H_{17} into monoacetylursolic acid to form the corresponding alkyl esters. The acids cannot be regenerated from the esters by saponification with alcoholic alkali.

Ketones are formed by the reaction of acid chlorides with zinc alkyls or magnesium alkyl halides, in accordance with the equation:

$$2\,CH_3COCl + 2\,C_2H_5MgI \longrightarrow 2\,CH_3COC_2H_5 + MgCl_2 + MgI_2$$

This method is generally limited to ketones of low molecular weights. The higher ketones are generally produced by pyrolysis of the alkaline earth

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[1] H. M. Sell and R. E. Kremers, *J. Biol. Chem.*, **126**, 501–503 (1938).

[2] H. M. Sell and R. E. Kremers, *J. Biol. Chem.*, **125**, 451–453 (1938).

salts of the long chain fatty acids. The long chain symmetrical and unsymmetrical ketones are produced by a modification of the Robinson-Robinson synthesis.[3] A typical product is 12-nonacosanone, $\mathrm{CH_3(CH_2)_{10}CO(CH_2)_{16}}$-$\mathrm{CH_3}$, which is prepared from palmitic acid and dodecanoyl (lauroyl) chloride. Ethyl palmitate is reduced with sodium to *n*-hexadecanol and converted to *n*-hexadecyl iodide with iodine and red phosphorus. The iodide is reacted with the sodio salt of ethyl acetoacetate to form ethyl-2-acetyl-*n*-octadecanoate, $\mathrm{CH_3(CH_2)_{15}CHAcCOOEt}$. This compound is treated with sodium to form the sodio derivative and then with dodecanoyl chloride. The resulting 12-keto-13-acetyl-13-carbethoxy-*n*-nonacosane is then hydrolyzed to form the corresponding 12-nonacosanone. In this reaction the alkyl and acyl halides, namely, *n*-hexadecyl iodide and dodecanoyl chloride are introduced, successively, into ethyl acetoacetate to form the final reaction product.

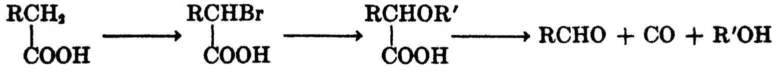
Ethers are formed when acids or esters containing hydroxyl groups in the carbon chain are treated with diazomethane or dimethyl sulfate. For example, ricinoleic acid esters are converted to the corresponding ethers by treatment with diazomethane according to the following equation:

$$\begin{matrix}\mathrm{CH_3(CH_2)_5CHOH} \\ | \\ \mathrm{ROOC(CH_2)_7CH{:}CHCH_2}\end{matrix} + \mathrm{CH_2N_2} \longrightarrow \begin{matrix}\mathrm{CH_3(CH_2)_5CHOCH_3} \\ | \\ \mathrm{ROOC(CH_2)_7CH{:}CHCH_2}\end{matrix} + \mathrm{N_2}$$

Smull and Saylor[4] carried out an alkylation reaction with the mixed methyl esters of linseed oil on the assumption that the $\mathrm{CH_2}$ group in $\mathrm{{=}CHCH_2CH{=}}$ of linoleic and linolenic acids would react similarly to malonic ester and cyclopentadiene. The esters were prepared from linseed oil by interesterification with methyl alcohol. The resulting esters were treated with sodium ethoxide in absolute ethanol, and then with ethyl iodide. The pure esters could not be isolated, but on the basis of analytical data it was concluded that alkylation had been fairly complete.

2. Alkoxylation

Alkoxylation has been employed by Darzens and co-workers to prepare a number of derivatives of the higher fatty acids. Darzens and Levy[5] employed the method of alkoxylation to prepare α-alkoxy fatty acids and various derivatives by treating the esters of α-bromo acids with various sodium alcoholates. The α-alkoxy fatty acid on heating in the presence of copper undergoes decomposition to the next lower aldehyde, carbon monoxide, and alcohol according to the following equations:



$$\begin{matrix}\mathrm{RCH_2} \\ | \\ \mathrm{COOH}\end{matrix} \longrightarrow \begin{matrix}\mathrm{RCHBr} \\ | \\ \mathrm{COOH}\end{matrix} \longrightarrow \begin{matrix}\mathrm{RCHOR'} \\ | \\ \mathrm{COOH}\end{matrix} \longrightarrow \mathrm{RCHO + CO + R'OH}$$

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[3] S. H. Piper, A. C. Chibnall, S. J. Hopkins, A. Pollard, J. A. B. Smith, and E. F. Williams, *Biochem. J.*, **25**, 2072–2094 (1931).

[4] J. G. Smull and J. S. Saylor, *J. Am. Chem. Soc.*, **64**, 3054 (1942).

[5] G. Darzens and A. Levy, *Compt. rend.*, **196**, 348–350 (1933).

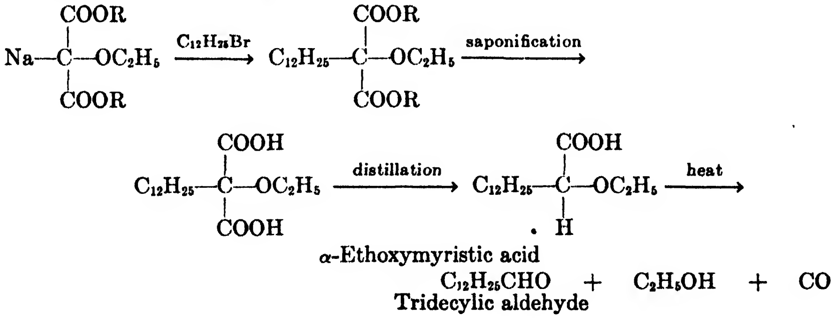
Saponification of the methyl ester of α-methoxyheptanoic acid prepared by this method gives the corresponding free acid which distills without decomposition at 122°C. at 15 mm. pressure. On distillation at atmospheric pressure in the presence of a little reduced copper, it undergoes decomposition with the formation of hexanal in 70% yield.

Saponification of the ester of α-methoxylauric acid gives the corresponding acid (m. p. 52°C.) which distills at 145°C. at 4 mm. pressure. On distillation at atmospheric pressure it undergoes decomposition with the formation of undecanal in 75% yield.

α-Methoxystearic acid (m.p. 62.5°C.) distills without decomposition at 190°C. at 5 mm. pressure. By heating for thirty minutes at 300°C., it decomposes with a theoretical yield of margaric aldehyde (heptadecanal).

Darzens and Meyer[6] have described another method for preparing long chain aliphatic aldehydes in the course of which α-ethoxy acids are prepared as intermediates. The method is a form of malonic ester synthesis in which an alkyl halide is reacted with sodioethoxymalonic ester to form the corresponding alkylethoxymalonic ester. The ester is saponified to give the dibasic acid which on distillation passes into the corresponding α-ethoxy acid and on further heating at 280° to 300°C. at atmospheric pressure, produces the corresponding aldehyde.

Lauryl alcohol on treatment with hydrobromic acid produces lauryl bromide and the latter when reacted with sodioethoxymalonic ester gives laurylethoxymalonic ester. The dibasic ethoxy acid which melts at 75°C. is obtained by saponification and when distilled gives α-ethoxymyristic acid. On further heating, the acid passes over to tridecylic aldehyde according to the following reactions:



$$\mathrm{Na{-}\overset{\displaystyle COOR}{\underset{\displaystyle COOR}{C}}{-}OC_2H_5} \xrightarrow{\mathrm{C_{12}H_{25}Br}} \mathrm{C_{12}H_{25}{-}\overset{\displaystyle COOR}{\underset{\displaystyle COOR}{C}}{-}OC_2H_5} \xrightarrow{\text{saponification}}$$

$$\mathrm{C_{12}H_{25}{-}\overset{\displaystyle COOH}{\underset{\displaystyle COOH}{C}}{-}OC_2H_5} \xrightarrow{\text{distillation}} \underset{\text{α-Ethoxymyristic acid}}{\mathrm{C_{12}H_{25}{-}\overset{\displaystyle COOH}{\underset{\displaystyle H}{C}}{-}OC_2H_5}} \xrightarrow{\text{heat}}$$

$$\underset{\text{Tridecylic aldehyde}}{\mathrm{C_{12}H_{25}CHO}} + \mathrm{C_2H_5OH} + \mathrm{CO}$$

Meyer[7] elaborated this method to include the preparation of α-ethoxy unsaturated acids of the general formula $\mathrm{RCH(OC_2H_5)COOH}$ by the action of ethylenic halides on sodioethoxymalonic ester. Ethoxymalonic ester is prepared by the condensation of malonic ester with ethyl orthoformate

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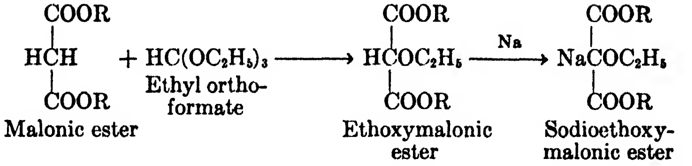
[6] G. Darzens and M. Meyer, *Compt. rend.*, **196**, 489–490 (1933).

[7] M. Meyer, *Compt. rend.*, **203**, 1074–1077 (1936).

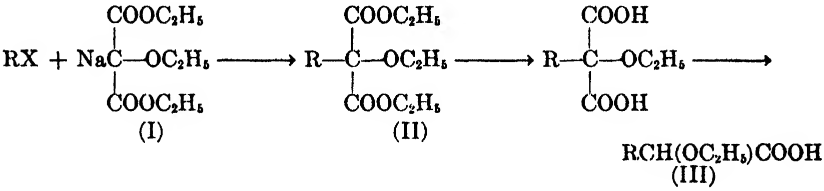
which in turn is treated with metallic sodium to produce sodioethoxymalonic ester according to the following equations:



$$\begin{array}{c}\mathrm{COOR}\\ |\\ \mathrm{HCH}\\ |\\ \mathrm{COOR}\end{array} + \mathrm{HC(OC_2H_5)_3} \longrightarrow \begin{array}{c}\mathrm{COOR}\\ |\\ \mathrm{HCOC_2H_5}\\ |\\ \mathrm{COOR}\end{array} \xrightarrow{\mathrm{Na}} \begin{array}{c}\mathrm{COOR}\\ |\\ \mathrm{NaCOC_2H_5}\\ |\\ \mathrm{COOR}\end{array}$$

Malonic ester; Ethyl orthoformate; Ethoxymalonic ester; Sodioethoxymalonic ester

Alkyl halides react with sodioethoxymalonic ester (I) to give the alkyl-substituted ethoxymalonic esters (II) which, on saponification and decarboxylation, yield α-ethoxyaliphatic acids (III) according to the following equations:



$$\mathrm{RX} + \underset{\text{(I)}}{\begin{array}{c}\mathrm{COOC_2H_5}\\ |\\ \mathrm{NaC{-}OC_2H_5}\\ |\\ \mathrm{COOC_2H_5}\end{array}} \longrightarrow \underset{\text{(II)}}{\begin{array}{c}\mathrm{COOC_2H_5}\\ |\\ \mathrm{R{-}C{-}OC_2H_5}\\ |\\ \mathrm{COOC_2H_5}\end{array}} \longrightarrow \begin{array}{c}\mathrm{COOH}\\ |\\ \mathrm{R{-}C{-}OC_2H_5}\\ |\\ \mathrm{COOH}\end{array} \longrightarrow \underset{\text{(III)}}{\mathrm{RCH(OC_2H_5)COOH}}$$

This method can be applied to the preparation of α-ethoxy acids not otherwise obtainable, and especially where R is an unsaturated radical of any chain length. For example, Meyer[7] prepared 2-ethoxy-$\Delta^{4,5}$-pentadecenoic acid, $CH_2{:}CHCH_2CH(OC_2H_5)COOH$, and 2-ethoxy-$\Delta^{12,13}$-tridecenoic acid, $CH_2{:}CH(CH_2)_9CH(OC_2H_5)COOH$, by this method. Both of these compounds which are liquids boiling at 120°C. at 15 mm., and 170°C. at 4 mm., respectively, were converted into the corresponding acid chlorides by treatment with thionyl chloride. The chlorides, boiling at 56°C. at 12 mm. pressure and 136°C. at 4 mm. pressure, respectively, on treatment with ammonia gave amides melting at 69.5°C. and 49°C., respectively.

CHAPTER XII

PYROLYSIS

Pyrolysis may be defined as the conversion of one substance into another by the agency of heat alone, or of heat with the aid of a catalyst. The conversion may consist of thermal decomposition whereby compounds of lower molecular weight are formed, or it may consist of thermal polymerization whereby compounds of higher molecular weight are formed from less complex molecules. Thus defined, pyrolysis includes such reactions as decarboxylation, dehydration, and polymerization, which are especially important in the field of fats and oils. Sometimes one, and sometimes two or more, of these reactions occur simultaneously or in sequence. Many fatty acids and their numerous derivatives have been subjected to pyrolysis as even a cursory examination of Hurd's[1] review of the subject will indicate.

1. Decarboxylation of Saturated Acids

The preparation of ketones by heating the calcium or barium salts of fatty acids is an old and well-known decarboxylation reaction.[2] The reaction is generally carried out by dry distillation of the salts using diminished pressure in the case of the longer chain acids. The same results may be accomplished by passing the vapors of the acids over heated zinc oxide or thoria. When the salts of a single acid are pyrolyzed, the resulting product is a symmetrical ketone, whereas a mixture of symmetrical and unsymmetrical ketones results on heating the salts of two different acids. If one of the salts of the mixed acids is calcium formate, an aldehyde[3] is obtained instead of a ketone. If, however, the calcium salt is heated with lime or other metallic hydroxide a hydrocarbon is obtained.[4] Each of these reactions may be considered as a process of removing a molecule of carbon dioxide from the acid in the form of calcium carbonate:

$$(R'COO)_2Ca + Ca(OOCR'')_2 \longrightarrow 2\ R'COR'' + 2\ CaCO_3$$

$$(RCOO)_2Ca + Ca(OCOH)_2 \longrightarrow 2\ RCHO + 2\ CaCO_3$$

$$(RCOO)_2Ca + Ca(OH)_2 \longrightarrow 2\ RH + 2\ CaCO_3$$

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[1] C. D. Hurd, *The Pyrolysis of Carbon Compounds*. Chemical Catalog Co., New York, 1929.

[2] A. Williamson, *Ann.*, **81**, 73–87 (1852). See C. Friedel, *Ann.*, **108**, 122–125 (1858); E. B. Ludlam, *J. Chem. Soc.*, **81**, 1185–1193 (1902).

[3] H. Limpricht, *Ann.*, **97**, 361–371 (1856).

[4] R. Piria, *Ann. chim. phys.*, **48**, 113–115 (1856).

When the calcium salts of the higher fatty acids, such as lauric, myristic, palmitic, or stearic are heated with calcium formate according to the method of Krafft,[5] dimeric aldehydes, $(RCHO)_2$, are produced but these can be readily depolymerized by vacuum distillation.[6] Dipropyl ketone has been prepared by the pyrolysis of calcium butyrate at 300° to 400°C.[7] The product, although consisting principally of butyrone, contains other ketones.[8] These mixed ketones have been used as a motor fuel under the trade name "Ketol." Calcium isobutyrate and isovalerate, when subjected to pyrolysis,[9-11] produce a mixture of ketones and aldehydes.

Pictet and Potok[12] claimed to have obtained a mixture of hydrocarbons, especially $C_{10}H_{22}$, $C_{14}H_{30}$, $C_{15}H_{32}$, and $C_{34}H_{70}$, by distilling sodium stearate at 13 to 15 mm. pressure, but Grün and Wirth[13] failed to observe the formation of high molecular weight paraffins when sodium stearate was pyrolyzed at 550° to 600°C. The principal product was found to consist of unsaturated hydrocarbons (60%) including an unidentified fraction melting at 50° to 55°C.

Laurone is produced by dry distillation of barium laurate and preferably by heating barium laurate with soda-lime, followed by distillation at 15 mm. pressure.[14] Myristone[15] and palmitone are produced by distilling the calcium and barium salts of myristic and palmitic acids. Stearone was prepared by Heintz[16] as early as 1855 by heating the calcium salt of stearic acid. Sato and co-workers[17,18] investigated the thermal decomposition of calcium and magnesium stearates and oleates, both as a function of time at a fixed temperature (400°C.), and also as a function of temperature (100° to 500°C.). The primary reaction products consisted of the corresponding ketones, the other products being carbon monoxide and unsaturated hydrocarbons.

The magnesium soaps of the acids were found to decompose more rapidly and at lower temperatures than did the corresponding calcium soaps. Decomposition of the magnesium salts begins at about 300°C. and becomes very rapid between 350° and 400°C. whereas decomposition of the calcium

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[5] F. Krafft, *Ber.*, **13**, 1413–1418 (1880).
[6] R. Feulgen and M. Behrens, *Z. physiol. Chem.*, **177**, 221–230 (1928).
[7] L. LeFranc, U. S. Pat. 1,656,488 (Jan. 17, 1928).
[8] E. Dépasse, *Bull. assoc. chim. sucr. dist.*, **43**, 409–414 (1926).
[9] G. A. Barbaglia and P. Gucci, *Ber.*, **13**, 1572–1573 (1880).
[10] C. Glücksmann, *Monatsh.*, **16**, 897–905 (1895).
[11] W. Dilthey, *Ber.*, **34**, 2115–2125 (1901).
[12] A. Pictet and J. Potok, *Helv. Chim. Acta*, **2**, 501–510 (1919).
[13] A. Grün and T. Wirth, *Ber.*, **53**, 1301–1312 (1920).
[14] F. Krafft, *Ber.*, **15**, 1711–1727 (1882).
[15] W. Delffs and A. Overbeck, *Ann. Physik*, **86**, 587–594 (1852).
[16] W. Heintz, *Jahresber. Chem.*, **8**, 514–517 (1855); *Ann. Physik*, **94**, 272–288 (1855); **96**, 65–80 (1855); *J. prakt. Chem.*, **64**, 413–415 (1855). See H. Rose, *J. prakt. Chem.*, **66**, 121–122 (1855).
[17] M. Sato, *J. Soc. Chem. Ind. Japan*, **30**, 252–260 (1927).
[18] M. Sato and C. Ito, *J. Soc. Chem. Ind. Japan*, **30**, 261–267 (1927).

salts begins at 350° to 400°C. and becomes rapid at 450° to 500°C. At 400°C. magnesium stearate forms approximately 80% of acetone-soluble products compared to about 30% for calcium stearate at 450°C.

Although the lower normal fatty acids may be readily distilled at ordinary pressures and the higher members in a vacuum, they can also be pyrolyzed under certain conditions. Ketonization of free fatty acids of low molecular weight occurs in the vapor state in the presence of various contact substances. Ketonization of the higher fatty acids usually does not occur in the presence of the same substances which generally produce cracking. For example, heating stearic acid for six hours at 300°C. in the presence of the oxides of silicon, titanium, thorium, copper, or zinc, produces not more than 6% or 7% of ketones; under the same conditions oxides of cadmium gave 13%, and oxides of iron, aluminum, and manganese on kieselgühr give about 17% to 24% of ketones. If the reaction is carried out in glass at 340° to 360°C., the yield can be raised to 30%.

On the other hand, when stearic acid is heated for four hours in iron reaction vessels on a commercial scale, yields of 91% of the corresponding ketone are obtained and further heating produces practically quantitative yields. According to Grün, Ulbrich, and Krczil,[19] the hot walls of the vessel are the best catalyst for this reaction, but addition of a small amount of commercial iron assists in the reaction. Grün *et al.* heated lauric, myristic, palmitic, stearic, and behenic acids under these conditions to temperatures of 270° to 300°C. for about three hours, whereupon the corresponding ketones were obtained in approximately quantitative yields. The melting points of the ketones were as follows: laurone, 70.3°; myristone, 76.5°; palmitone, 83°; stearone, 88.5°; and behenone, 92°C.

2. Pyrolytic Decomposition of Unsaturated Acids

Whereas the dry distillation of the alkaline earth salts of the saturated fatty acids produces primarily the corresponding ketones, similar treatment of the salts of unsaturated acids leads to more complex reactions. Easterfield and Taylor[20] distilled the barium salt of oleic acid in an atmosphere of hydrogen and obtained a greenish oil from which 2% of oleone separated on cooling. The unsaturated ketone melted at 58.5°C. and was identified by preparation of the corresponding oxime. The remaining portion was described as a viscous liquid whose analysis corresponded closely to that of oleone. When oleic acid was heated with iron filings, oleone (m.p. 59.5°C.) was obtained amounting to 10% on the basis of the oleic acid used. Elaidone (m.p. 70°C.) and brassidone (m.p. 80°C.) were obtained from elaidic and brassidic acids, respectively, when they were sim-

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[19] A. Grün, E. Ulbrich, and F. Krczil, *Z. angew. Chem.*, **39**, 421–428 (1926).
[20] T. H. Easterfield and C. M. Taylor, *J. Chem. Soc.*, **99**, 2298–2307 (1911).

ilarly heated with iron filings. Pure erucone could not be obtained from erucic acid under the same conditions.

Pictet and Potok[21] pyrolyzed sodium oleate *in vacuo* and obtained a greenish colored distillate which was found to consist principally of a mixture of olefins corresponding to C_9H_{18}, $C_{10}H_{20}$, $C_{11}H_{22}$, and $C_{13}H_{26}$. Breuer and Weinmann[22] investigated the pyrolysis of the calcium salts of oleic and undecenoic acids. Vacuum distillation of a mixture of calcium oleate and lime gave a clear yellow liquid which on standing precipitated a colorless crystalline product. Analysis of this product indicated that it consisted principally of hydroxyoleones admixed with oleone, and some hydroxystearic and oleic acids. The latter substances were presumed to be derived from the impurities present in the original oleic acid. The mother liquor, which had an iodine value corresponding to oleone, after standing a week precipitated a white crystalline product melting at 58.5°C. and was otherwise similar to Easterfield and Taylor's oleone. The oily residue, after separation of the solid oleone, gave on vacuum distillation a yellow oil which by analysis and preparation of the oxime corresponded to oleone. The principal products obtained by pyrolysis of calcium oleate appear, therefore, to consist largely of liquid oleone, a small amount of solid oleone probably a *trans*-isomer of the liquid product—and a small amount of hydroxyoleone.

Vacuum distillation of calcium undecenoate gave an oily liquid which deposited white crystals melting at 51°C. and corresponding in composition to undecylenone. Ruzicka and co-workers[23] distilled undecenoic acid with iron filings and obtained an undecylenone melting at 42°C.

Neuberg[24] heated a mixture of valeric and oleic acids (1:8) for 16 hours at 350°C. in sealed tubes with a view to obtaining information on the relation of this reaction to the genesis of petroleum. The tubes were opened periodically to release the pressure and at the end of the reaction the mixture was examined to determine the nature of the products which were formed. A light yellow oil was obtained which, after removal of free acids, aldehydes, and ketones, was found to be optically active, possessed a naphtha-like odor and apparently consisted of a mixture of hydrocarbons.

Barium ricinoleate on dry distillation *in vacuo* yields methylhexylketone as a distillate and an isomeric ricinoleate as a residue.[25]

3. Pyrolytic Decomposition of Mixed Fatty Acids

In countries lacking adequate supplies of petroleum oil but possessing

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[21] A. Pictet and J. Potok, *Helv. Chim. Acta*, **2**, 501–510 (1919).

[22] G. Breuer and K. Weinmann, *Sitzber. Akad. Wiss. Wien, Math. naturw. Klasse, Abt. IIb*, **144**, 616–624 (1935); *Monatsh.*, **67**, 42–50 (1935).

[23] L. Ruzicka, M. Stoll, W. Scherrer, H. Schinz, and C. F. Seidel, *Helv. Chim. Acta*, **15**, 1459–1467 (1932).

[24] C. Neuberg, *Biochem. Z.*, **7**, 199–212 (1908).

[25] F. Krafft, *Ber.*, **21**, 2730–2737 (1888).

a large actual or potential production of vegetable oils, the pyrolysis of the latter has always offered attractive possibilities for the production of both lubricating oils and fuel oils of the Diesel type. Considerable work on the pyrolysis of vegetable oils has been carried out in China and Japan as well as other countries lacking in natural deposits of petroleum.

Various species of vegetable oils, as well as the soaps of their derived fatty acids, have been subjected to pyrolysis for the production of hydrocarbons. Hirose and Yamada[26] pyrolyzed the sodium soaps of the mixed fatty acids of herring oil and obtained approximately 53% of oil and an appreciable yield of hydrocarbon gas, rich in methane. Although the oil was highly unsaturated (iodine value, 117.9), no naphthenic hydrocarbons appeared to be produced.

Sato and co-workers[27,28] investigated the pyrolysis and subsequent hydrogenation of the calcium and magnesium soaps of the mixed fatty acids derived from soybean oil. The maximum yield of oil was obtained by heating the calcium or magnesium soaps below 450°C. for several hours followed by distillation above 500°C. The distillation time was shorter, and the specific gravity of the oil was higher, in the case of the magnesium soaps when the cracking and distillation were carried out at the same temperature. The crude product was fractionated to produce a light oil (100° to 175°C.), a middle oil (175° to 300°C.), and a residue. The first fraction was hydrogenated both in the vapor and liquid phases, and the middle oil in the liquid phase using a nickel catalyst in all cases.

Heptane, octane, and nonane were isolated from the hydrogenated light oil fraction. The hydrogenated middle oil gave constituents whose boiling points and ultimate compositions corresponded to $C_{11}H_{24}$, $C_{13}H_{28}$, and $C_{14}H_{30}$ but the specific gravities were higher than the known values for these paraffins. It was inferred from these results that the light oil consisted entirely of straight chain hydrocarbons, whereas the middle oil probably contained naphthenic hydrocarbons as well as paraffins.

In 1937 China turned to tung and other vegetable oils as a source of fuels and since that time has erected several plants for cracking them into gasoline and other liquid fuels. According to Cheng,[29] two processes are used, employing respectively, high pressure and atmospheric pressure cracking.

In the pressure process, oil is pumped to a constant-level vessel from which it is sprayed through nozzles into the cracking still under pressure of 50 to 150 lbs. per sq. in. and a temperature of 400° to 500°C. When the proper temperature and pressure are attained a release valve is opened to the distillate receiver. The cracking rate is controlled by regulating the

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[26] M. Hirose and C. Yamada, *J. Chem. Ind. Japan*, **25**, 1428–1438 (1922).

[27] M. Sato, *J. Soc. Chem. Ind. Japan*, **30**, 242–245 (1927).

[28] M. Sato and H. Matsumoto, *J. Soc. Chem. Ind. Japan*, **30**, 245–252 (1927).

[29] F.-W. Cheng, *Chem. & Met. Eng.*, **52**, No. 1, 99 (1945).

temperature and opening of the release valve. The optimum cracking temperature was found to be about 450°C. although distillation begins about 400°C. The crude product, resembling crude oil, is produced at the rate of 75 lbs. for every 100 lbs. of charging stock. Half of this product yields a light spirit on refining and the other half kerosene, diesel oil, and lubricating oil fractions.

In the atmospheric cracking process the vegetable oil is first saponified by lime and the lime soaps catalytically cracked, preferably with aluminum chloride. The yield of crude oil is only 55% by weight in this process compared to 75% by the pressure method.

4. Pyrolytic Decomposition of Monoesters

The products of pyrolysis of the fatty acid esters depend primarily on the nature of the ester radical. The normal aliphatic esters yield acids and olefins on pyrolysis, whereas in the case of the phenyl esters, the phenyl group cannot be separated as an unsaturated hydrocarbon. The first of these reactions may be illustrated by the following equation:

$$RCOOCH_2CH_2R' \longrightarrow RCOOH + CH_2{:}CHR'$$

This reaction has been known for a long time. Heintz[30] showed that the pyrolysis of cetyl palmitate led to the formation of palmitic acid and hexadecene according to the equation:

$$C_{15}H_{31}COOC_{16}H_{33} \longrightarrow C_{15}H_{31}COOH + C_{16}H_{32}$$

Krafft[31] established the reaction as a method for the preparation of α-unsaturated hydrocarbons. With reduced pressure (300 to 400 mm.), the formation of secondary reaction products is minimized and distillation is practically complete. Gault and Altchidjian[32] obtained a yield of 25% of pure hexadecene by pyrolyzing cetyl palmitate under the above-mentioned conditions.

Octadecyl palmitate undergoes pyrolysis when it is distilled at 120 to 140 mm. pressure with the production of palmitic acid and α-octadecene, $C_{16}H_{33}CH{:}CH_2$; tetradecyl palmitate pyrolyzed at 500 mm. pressure yields the corresponding tetradecene, $C_{14}H_{28}$, while dodecyl palmitate yields dodecene, $C_{12}H_{24}$. Since dodecyl palmitate is itself readily distillable at low pressure, it is necessary to carry out the pyrolysis at about 600 mm. pressure. However, at high pressures there is a tendency to form ketones. As a practical method it is necessarily confined to esters of relatively long chain acids and long chain alcohols, although other esters behave in an

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[30] W. Heintz, *Ann. Physik*, **93**, 481–506 (1854).

[31] F. Krafft, *Ber.*, **16**, 3018–3024 (1883); **19**, 2218–2223 (1886).

[32] H. Gault and Y. Altchidjian, *Ann. chim.*, **2**, 209–268 (1924). See H. Gault and F. A. Hessel, *ibid.*, **2**, 319–377 (1924).

analogous manner. For example, ethyl stearate slowly decomposes when heated to 300°C. in a sealed tube to form stearic acid and ethylene.

The aromatic esters such as phenyl palmitate and phenyl stearate behave quite differently compared with the aliphatic esters since, as was previously mentioned, the phenyl group cannot be removed in the form of unsaturated hydrocarbon. When these two phenyl esters are heated at 300° to 320°C. under pressure in the presence of nitrogen, tridecane and pentadecane, respectively, are obtained,[33] which should leave phenyl acrylate as the other product of pyrolysis. However, the phenyl acrylate, which no doubt is formed, undergoes further pyrolysis to acetylene and phenyl formate together with a small amount of phenol. The over-all reaction appears to be as follows:

$$RCH_2CH_2COOC_6H_5 \longrightarrow RH + [CH_2{:}CHCOOC_6H_5] \longrightarrow$$

$$CH{:}CH + HCOOC_6H_5 \longrightarrow CO + C_6H_5OH$$

If phenyl stearate is pyrolyzed at 320°C. at atmospheric pressure, neither acetylene nor ethylene is evolved and no other hydrocarbon appears to form despite the fact that carbon monoxide and phenol are produced in accordance with the equation just given. Phenyl laurate likewise produces phenol when pyrolyzed at 300° to 320°C.

5. Pyrolytic Dehydration

Dehydration reactions may occur in compounds which contain a hydroxyl radical and an adjacent hydrogen atom which can be removed in the form of a molecule of water. They may also occur between two molecules of the same or different substances where one molecule contains a hydroxyl group and the other a removable hydrogen. These dehydration reactions may be brought about by the action of heat alone, by a dehydrating agent, or a combination of the two, either with or without the aid of a catalyst. Pyrolytic dehydration may be accompanied by other reactions such as decarboxylation, polymerization, etc. In some cases, these simultaneous or subsequent reactions cannot be separated while in others, one or the other can be made to predominate.

Few natural higher fatty acids are known which contain hydroxyl groups, but a number of them have been prepared artificially from ordinary fatty acids. The best known natural hydroxy acids of high molecular weight are ricinoleic and dihydroxystearic, both of which occur in castor oil.

(a) Dehydration of Saturated Hydroxy Acids

The α-hydroxy acids undergo two types of pyrolytic reactions one of which results in the formation of aldehydes and ketones, and the other

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[33] S. Skraup and F. Nieten, *Ber.*, **57**, 1294–1310 (1924).

yields unsaturated acids. These two reactions may be represented by the following equations:

(*1*) $RCH_2CHOHCOOH \longrightarrow RCH_2CHO + CO + H_2O$

(*2*) $RCH_2CHOHCOOH \longrightarrow RCH{:}CHCOOH + H_2O$

Blaise[34] showed that the distillation of lactides led to the formation of aldehydes in 50% to 60% yield and it is apparent that α-hydroxy acids when heated to distillation temperatures pass to the corresponding lactides, after which the lactide loses carbon monoxide in accordance with equation (*1*). As was pointed out by Blaise, this reaction makes it possible to pass in a stepwise manner from a higher fatty acid to the next lower acid, and by repetition of the process descend the entire series. The steps involved are as follows: (*a*) Preparation of the α-bromo derivative of the normal acid; (*b*) conversion of the bromo acid to the corresponding α-hydroxy acid; (*c*) pyrolysis of the α-hydroxy acid to form the lactide, and distillation of the lactide to form the aldehyde containing one less carbon atom than the original acid; and (*d*) oxidation of the aldehyde to the corresponding acid and repetition of the process.

These reactions have been applied to caproic, nonanoic (pelargonic), lauric, myristic, and palmitic acids. For example, Bagard[35] obtained a 50% yield of caproic aldehyde by pyrolytic distillation of α-hydroxyheptanoic acid, together with various other reaction products such as butyl ethylene, heptenoic acid, and α-hydroxyheptanolactide. By conversion of the heptanoic acid to α-acetyoxyheptanoic acid followed by pyrolysis, the yield of aldehyde can be increased to approximately 70%. Bagard also obtained nonaldehyde in 70% yield by distillation of α-hydroxycapric acid. α-Hydroxyundecanoic acid gave 52% of capric aldehyde.

Pyrolysis of α-hydroxypalmitic acid at 170°C. and 20–25 mm. pressure yields pentadecyl aldehyde.[36] Pyrolysis of α-hydroxystearic acid at 270°C. produces heptadecyl aldehyde in 50% to 60% yield. According to Le Sueur,[37] heptadecyl aldehyde is formed both directly from α-hydroxystearic acid and from its lactide. Yields of 50% of heptadecyl aldehyde are obtained by heating α-hydroxystearic acid at 240° to 250°C. and very slowly at 270° to 280°C. because of intermediate formation of lactides.

By heating β-hydroxy acids to high temperatures, they are generally converted to α,β-unsaturated acids according to the following equation:

$$RCHOHCH_2COOH \longrightarrow RCH{:}CHCOOH + H_2O$$

Both normal and iso acids form α,β-unsaturated acids when subjected to pyrolytic distillation. The reaction has been applied to a number of the

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[34] E. E. Blaise, *Compt. rend.*, **138**, 697–699 (1904).

[35] M. P. Bagard, *Bull. soc. chim.*, **1**, 307–320 (1907).

[36] S. Landa, *Chem. Listy*, **19**, 264–267 (1925).

[37] H. R. Le Sueur, *J. Chem. Soc.*, **85**, 827–838 (1904); **87**, 1888–1906 (1905).

lower acids, including β-hydroxybutyric,[38,39] β-hydroxyvaleric, and β-hydroxyisocaproic,[40] but does not appear to have been applied to the higher β-hydroxy acids.

The γ- and δ-hydroxy acids pass so readily to lactones that any pyrolytic action occurring must be attributed to the lactone rather than the hydroxy acid. Few high molecular weight γ- or δ-hydroxy acids have been subjected to pyrolysis reactions. δ-Hydroxy-*n*-valeric acid has been obtained as an oily liquid which on distillation at 110° to 120°C. at 13 to 14 mm. pressure passes to a polymer of δ-valerolactone.

(b) *Dehydration of Ricinoleic Acid*

The pyrolysis of ricinoleic acid, its salts, and esters, is of considerable industrial importance because of the variety and utility of the end products which are obtained by variations in the reaction conditions.

Goldsobel[41] and Vernon and Ross[42] reported that destructive distillation of the sodium or calcium salt of ricinoleic acid resulted in the production of heptanal and $\Delta^{10,11}$-undecenoic acid. Similarly, Perkins and Cruz[43] have shown that the *in vacuo* pyrolysis of castor oil, which consists of about 80% of triricinolein, produces heptanal and undecenoic acid, and forms a ready source of both of these products. The distillation is carried out rapidly at a relatively high temperature.

Pyrolysis of sodium ricinoleate in the presence of sodium hydroxide and a supply of oxygen produces principally a capryl alcohol, or octanol-2, and sebacic acid according to the following equation:

$$\underset{\text{Sodium ricinoleate}}{CH_3(CH_2)_5CHOHCH_2CH{:}CH(CH_2)_7COONa} \xrightarrow[\Delta, O_2]{NaOH}$$

$$\underset{\substack{\textit{sec}\text{-Capryl alcohol}\\ \text{(octanol-2)}}}{CH_3(CH_2)_5CHOHCH_3} + \underset{\text{Sebacic acid}}{HOOC(CH_2)_8COOH}$$

The production of sebacic acid on an industrial scale is accomplished by this reaction.

The most important pyrolytic reaction of ricinoleic acid and its esters is that of dehydration to produce octadecadienoic acids. The dehydration of castor oil involves dehydration of the ricinoleic acid and dihydroxystearic acid residues which comprise approximately 80% and 2%, respectively, of the fatty acids of this oil. This dehydration was carried out practically as long ago as 1898 without any knowledge of the actual reac-

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[38] W. Moldenhauer, *Ann.*, **131**, 323–343 (1864).
[39] R. Fittig and J. G. Spenzer, *Ann.*, **283**, 66–79 (1894).
[40] L. Braun, *Monatsh.*, **17**, 207–224 (1896).
[41] A. G. Goldsobel, *Ber.*, **27**, 3121–3129 (1894).
[42] A. A. Vernon and H. K. Ross, *J. Am. Chem. Soc.*, **58**, 2430–2433 (1936).
[43] G. A. Perkins and A. O. Cruz, *J. Am. Chem. Soc.*, **49**, 1070–1077 (1927).

tion which occurred. Two German patents[44,45] described a process for solubilizing castor oil in mineral oil and for preparing a substitute for linseed oil by heating the former to 300°C. until it had lost 10% of its volume.

Subsequently, Fokin[46] described the action of various dehydrating agents, including oxalic acid, phosphoric anhydride, and zinc chloride, on ricinoleic and hydroxystearic acids and their glycerides. He showed that these dehydrating agents acted to remove from hydroxy acids the elements of water in the form of the hydroxyl group and an adjacent hydrogen atom. In the case of monohydroxystearic acid there results on dehydration, a monounsaturated acid, while in the case of ricinoleic acid, which already contains one double bond, there results a diunsaturated acid. Since the hydroxyl group can combine with a hydrogen atom on either adjacent carbon atom, it is obvious that a mixture of isomeric unsaturated acids will be formed by dehydration. These reactions may be illustrated by the following formulas:

$$\underset{\text{10-Hydroxystearic acid}}{CH_3(CH_2)_6CH_2CHOHCH_2(CH_2)_7COOH} \longrightarrow \begin{cases} \longrightarrow \underset{\Delta^{9,10}\text{-Octadecenoic acid}}{CH_3(CH_2)_7CH{:}CH(CH_2)_7COOH} \\ \longrightarrow \underset{\Delta^{10,11}\text{-Octadecenoic acid}}{CH_3(CH_2)_6CH{:}CH(CH_2)_8COOH} \end{cases}$$

$$\underset{\text{Ricinoleic acid}}{CH_3(CH_2)_4CH_2CHOHCH_2CH{:}CH(CH_2)_7COOH} \begin{cases} \rightarrow \underset{\Delta^{9,10,12,13}\text{-Octadecadienoic acid}}{CH_3(CH_2)_4CH{:}CHCH_2CH{:}CH(CH_2)_7COOH} \\ \rightarrow \underset{\Delta^{9,10,11,12}\text{-Octadecadienoic acid}}{CH_3(CH_2)_5CH{:}CHCH{:}CH(CH_2)_7COOH} \end{cases}$$

In the case of ricinoleic acid, one of the resulting octadecadienoic acids will contain a system of isolated double bonds, whereas the other will contain a system of conjugated double bonds. If the dehydration were quantitative and equal amounts of conjugated and nonconjugated octadecadienoic acids were formed, it might be expected that the product would have drying properties intermediate between linoleic and linolenic acids on the one hand, and elaeostearic acid on the other. In actual practice the dehydration is probably neither quantitative nor the ratio of isomeric acids exactly 1:1. Nevertheless, when applied to castor oil, the process leads to the formation of a product with excellent drying characteristics and is an acceptable substitute for, and in some uses superior to, tung oil.

The dehydration of ricinoleic acid or its glycerides may be carried out under a variety of conditions which have been described in various pat-

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[44] H. Nördlinger (to Chemische Fabrik Flörsheim), German Pat. 104,499 (Feb. 18, 1898).

[45] H. Nördlinger (to Chemische Fabrik Flörsheim), German Pat. 131,964 (Aug. 9, 1901).

[46] S. Fokin, *J. Russ. Phys.-Chem. Soc.*, **46**, 224–226, 1027–1042 (1914).

ents[47–56] and literature[57–60] on the subject. Since both conjugated and nonconjugated bonds are produced as a result of dehydration, it is evident that the dehydration reaction will be accompanied by more or less polymerization, and unless protected by an inert gas or vacuum, by a certain amount of oxidation. The principal differences revealed by the various patents applicable to this reaction are the nature of the catalyst and the temperature and time of the reaction. The variations in these conditions affect the extent of the dehydration and the subsequent polymerization. The catalysts and dehydrating agents which have been used and claimed to be effective in promoting dehydration include phosphorus pentoxide,[46] acid clays,[51,57,60] various metallic oxides including oxides of tungsten, thorium, uranium, molybdenum,[49,55,60] silicotungstic, phosphotungstic, borotungstic acids,[55] acetic anhydride,[53] silica gel,[56,60] potassium persulfate and pyrosulfate,[52] and many other sulfates and oxides.[56] The optimum temperature for maximum dehydration appears to lie between 225° and 240°,[60] although temperatures from 170° to 310°C. have been employed.[54,60] Carbon dioxide, nitrogen, and vacuum have been used to minimize oxidation.

6. Polymerization of Fatty Acids and Monoesters

Generally, polymerization phenomena have been of importance primarily in the case of the fatty oils rather than their derived acids, and only recently has attention been given to the polymerization of the free acids and their monoesters. Heat polymerization of fatty oils to produce bodied oils has been practiced for many years, whereas heat polymerization of fatty acids is of very recent practice. Interest was stimulated in the phenomenon of heat polymerization of fatty acids to a considerable extent by Bradley's[61–65] development of the theory of functionality as applied to

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[47] H. Ufer (to I. G. Farbenindustrie), U. S. Pat. 1,892,258 (Dec. 27, 1932).

[48] J. Scheiber, U. S. Pats. 1,942,778 (Jan. 9, 1934); 1,979,495 (Nov. 6, 1934).

[49] F. Münzel, Swiss Pat. 193,931 (April 1, 1938); French Pat. 830,494 (Aug. 1, 1938).

[50] P. Rizzi, Italian Pat. 356,438 (Nov. 12, 1937); French Pat. 845,929 (Sept. 5, 1939).

[51] A. Schwarzman (to Spencer Kellogg and Sons), U. S. Pat. 2,140,271 (Dec. 13, 1938).

[52] Koninklijke Industrieele Maatschappij voorheen Noury & van der Lande N. V., British Pat. 508,516 (July 3, 1939).

[53] J. S. Brod, U. S. Pat. 2,212,385 (Aug. 20, 1940).

[54] F. G. Nessler (to Sherwin-Williams), U. S. Pat. 2,336,186 (Dec. 7, 1943).

[55] A. E. Rheineck and S. B. Crecelius (to Devoe and Reynolds), U. S. Pat. 2,345,358 (March 28, 1944).

[56] H. S. Miller (to Air Reduction Co.), U. S. Pat. 2,351,444 (June 13, 1944).

[57] T. Yamada, *J. Soc. Chem. Ind. Japan*, Suppl. binding, **38**, 120–123 (1935).

[58] A. V. Blom, *Farben-Ztg.*, **44**, 901–902 (1939); *Paint Oil Chem. Rev.*, **101**, No. 15, 9, 28 (1939).

[59] J. Scheiber, *Angew. Chem.*, **46**, 643–647 (1933).

[60] W. C. Forbes and H. A. Neville, *Ind. Eng. Chem.*, **32**, 555–558 (1940).

[61] T. F. Bradley, *Ind. Eng. Chem.*, **29**, 440–445, 579–584 (1937).

[62] T. F. Bradley, E. L. Kropa, and W. B. Johnston, *Ind. Eng. Chem.*, **29**, 1270–1276 (1937).

[63] T. F. Bradley, *Ind. Eng. Chem.*, **30**, 689–696 (1938).

[64] E. L. Kropa and T. F. Bradley, *Ind. Eng. Chem.*, **31**, 1512–1516 (1939).

film formation, production of synthetic resins, oil bodying, and related phenomena. According to Bradley's theory of functionality, which is an extension of the work and theories of Carothers,[66,67] Kienle,[68–71] and Staudinger,[72–74] a minimum number of functional groups are required to be present in the reacting substance in order that polymer formation may occur. In the case of the fatty acids the functional groups may be unsaturated linkages, hydroxyl groups, and carboxyl groups, two or more of which must be present in heat polymerization reactions. Thus, the saturated acids are incapable of undergoing heat polymerization *per se*. However, if only double bonds are present then only addition polymerizations are possible, and if only hydroxyl and carboxyl groups are present, only condensation reactions are possible. When both types of functional groups are present both types of polymerization can occur.

When certain types of unsaturated fatty acids are heated under conditions which result in polymerization, the unsaturation decreases with the formation of essentially dimeric products by the process of ring closure. Such a reaction occurs, for example, when elaeostearic acid or its esters are heat polymerized. In this case the reaction occurs through a diene reaction to produce a substituted six-membered hydroaromatic ring system.[75–79]

The mechanism of heat polymerization of the nonconjugated fatty acids, such as linoleic and linolenic, cannot occur through a diene mechanism unless a previous shift of isolated to conjugated double bonds occurs. However, all existing evidence points to the formation of a dimer as the first product of heat polymerization in these acids. According to Bradley[61] the fatty acids of the natural drying oils possess a normal functionality of but two, one function resulting from the presence of the carboxyl group and the second from the entire system of unsaturated carbon-to-carbon double bonds.

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[65] T. F. Bradley and W. B. Johnston, *Ind. Eng. Chem.*, **32**, 802–809 (1940); **33**, 86–89 (1941). See T. F. Bradley and D. Richardson, *ibid.*, **34**, 237–242 (1942).

[66] W. H. Carothers, *J. Am. Chem. Soc.*, **51**, 2548–2559 (1929); *Chem. Revs.*, **8**, 353–426 (1931).

[67] W. H. Carothers and J. A. Arvin, *J. Am. Chem. Soc.*, **51**, 2560–2570 (1929).

[68] R. H. Kienle, *Ind. Eng. Chem.*, **22**, 590–594 (1930).

[69] R. H. Kienle and C. S. Ferguson, *Ind. Eng. Chem.*, **21**, 349–352 (1929).

[70] R. H. Kienle and A. G. Hovey, *J. Am. Chem. Soc.*, **51**, 509–519 (1929); **52**, 3636–3645 (1930).

[71] R. H. Kienle, *Ind. Eng. Chem.*, **23**, 1260–1261 (1931). See R. H. Kienle and P. F. Schlingman, *ibid.*, **25**, 971–975 (1933).

[72] H. Staudinger and E. Huseman, *Ber.*, **68**, 1618–1634 (1935).

[73] H. Staudinger and W. Heuer, *Ber.*, **67**, 1164–1172 (1934).

[74] H. Staudinger, W. Heuer, and E. Huseman, *Trans. Faraday Soc.*, **32**, 323–335 (1936)

[75] E. E. Ware and C. L. Schumann, *J. Ind. Eng. Chem.*, **7**, 571–573 (1915).

[76] C. L. Schumann, *J. Ind. Eng. Chem.*, **8**, 5–15 (1916).

[77] R. S. Morrell, *J. Soc. Chem. Ind.*, **34**, 105–109 (1915).

[78] E. Rossmann, *Fettchem. Umschau*, **40**, 96–123 (1933).

[79] L. A. Jordan, *J. Oil Colour Chem. Assoc.*, **17**, 47–66 (1934).

Bradley and Johnston[65] experimentally investigated a large number of monoesters of unsaturated fatty acids and showed that on heating these substances to 300°C. polymerization occurred with the formation of dimers as the primary reaction product. The conclusions of these authors are of such fundamental significance that they are reproduced in part as follows:

(*1*) The predominant reaction is polymerization by the bimolecular addition of unsaturated fatty acid radicals leading to the production of dibasic acid esters in yields ranging as high as 60% to 70%. Such yields are difficult to attain within short periods unless the reactants are conjugated.

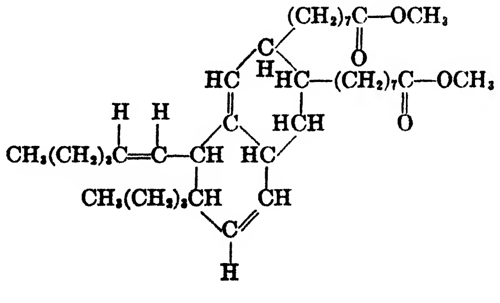
(*2*) The dimerized esters are not identical but may be classified in three groups according to their densities which, in turn, are determined by the original degree of unsaturation and ultimately from structural differences.

(*3*) The physical and chemical constants strongly favor a bicyclic structure for the dimers which are derived from the octadecatrienates and a monocyclic structure for those which are derived from the octadecadienates. Although these nonvolatile dimers vary somewhat as a result of certain impurities, the best preparations show a surprising degree of conformity with the theoretical constants of the postulated structures.

(*4*) The observed constants denote that the polyene esters yield entirely analogous (isomeric) and possibly identical dimers, regardless of whether they originate from conjugated or nonconjugated esters. This supports the isomerization theory of Scheiber[80] and the conclusions of Brod, France, and Evans.[81]

(*5*) On the basis of the present data and pertinent considerations involved, it is postulated that the conjugated and nonconjugated methyl octadecatrienates polymerize by a bimolecular addition which is followed by, or which also involves, an additional intramolecular ring closure, leading to a compound of the structure shown in Formula I or to isomers of it:

(I)



(*6*) The present data support the prior conclusions of others that the octadecadienate esters dimerize by a 1,4-diene addition, leading to compounds having the structure shown in Formula II or isomers of it:

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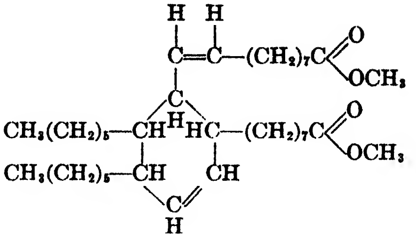
[80] J. Scheiber, *Farbe u. Lack,* 1929, 585–587.

[81] J. S. Brod, W. G. France, and W. L. Evans, *Ind. Eng. Chem.*, 31, 114–118 (1939).



(II)

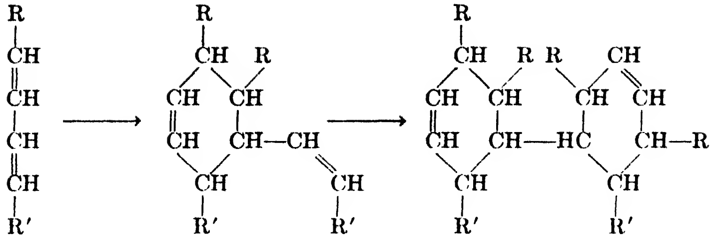
(*7*) During the thermal treatment of these esters, reactions other than the normal diene additions occur. One of the most prominent and important of these side reactions has been recognized to involve the thermal decomposition of a portion of the reactants, which leads to the formation of unsaturated hydrocarbons and esters of low molecular weight. These reactions increase as the time of thermal treatment is extended and therefore become most prominent in the case of the nonconjugated esters.

(*8*) The decomposition reactions create fragments which are indicated to unite and form polymers of lower density and molecular weight than the dimeric ester polymers. Such variations as occur in the physical and chemical constants of the dimers are attributed to the presence of the abnormal polymeric impurities which originate from certain of the decomposition products. The low saponification numbers are due to this cause.

(*9*) Monomeric products of reduced unsaturation and of high density have been detected in the case of the tung and linseed esters to the extent of about 10%. Such cyclized monomers have been detected previously by others. Their lack of conjugation and low degree of unsaturation do not conform with suggested structures.

(*10*) Methyl oleate has been indicated to undergo polymerization at 300°C. since the methyl esters of the acids of olive oil have been shown to form 20% of polymers of which several distill within the range of 200° to 220°C. at 1 mm.

In a subsequent publication, Bradley and Johnston[65] reported on the nature of the product produced by polymerizing at 300°C., a mixture of $\Delta^{9,10,11,12}$- and $\Delta^{9,10,12,13}$-methyl linoleates obtained by methanolysis from dehydrated castor oil. They found that ordinary vacuum distillation removed the unreacted monomeric ester and that the residue completely volatilized in the molecular still. The distilled polymer had a molecular weight less than 1000 and consisted predominantly of a dimer with only a small amount of a trimer. They concluded that $\Delta^{9,10,11,12}$-linoleic acid and its esters should produce a dimer as the predominant polymerization product and that polymerization should cease at the trimeric stage because of the nature of the terminal substituents and the loss of conjugation as illustrated by:



Thermal polymerization of methyl-9,11-octadecadienate where R = $CH_3(CH)_5$— and R′ = —$(CH_2)_7COOCH_3$.

Prior to the publication of Bradley's work on polymerization of the fatty acids and monoesters, the production and utilization of these products was patented by Hill and Walker.[82] Their patents covered the polymerization of the fatty acids and monoesters of a wide variety of fatty oils (linseed, tung, perilla, chia, oiticica, soybean, poppyseed, sunflowerseed, hempseed, rubber seed, maize, wheat, menhaden, and sardine oils), separation of the unreacted monomer by distillation, and esterification of the polymer with glycols, glycerol, pentaerythritol, mannitol, and other polyhydroxy alcohols to produce synthetic fats or stand oils. A modification of the process consists in polymerizing the alkyl esters, distilling off the unpolymerized portion, and saponifying the residue to produce the polymerized acids.

Cowan and Falkenburg[83] have described the preparation and properties of various synthetic oils made from the dimeric and trimeric fatty acids of soybean oil and various polyalcohols such as glycerol, pentaerythritol, and mannitol either *per se* or modified with polybasic anhydrides.

7. Polymerization of Dibasic Acids

The cyclization or polymerization of the dibasic acids is important from the standpoint of the development of synthetic resins and fibers. The presence of two carboxyl groups in the dibasic acids renders possible the formation of cyclic anhydrides by dehydration. However, the first two members of the series, namely, oxalic and malonic acids, do not form cyclic anhydrides on heating, but undergo decarboxylation instead. When, however, succinic and glutaric acids are heated above their melting points for some time they form anhydrides having the formulas shown in III and IV. These anhydrides are more conveniently prepared by heating the acid with acetic anhydride or chloride.

Adipic acid, the next higher homolog in the series of dibasic acids, is converted by refluxing it with acetic anhydride into a microcrystalline poly-

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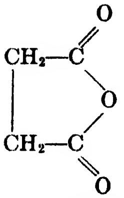
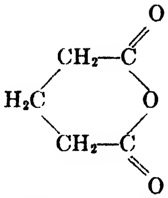
[82] A. Hill and E. E. Walker (to Imperial Chemical Industries), British Pat. 428,864 (May 15, 1935); French Pat. 781,293 (May 11, 1935).

[83] J. C. Cowan and L. B. Falkenburg, *Oil & Soap*, **20**, 153–157 (1943).

(III)



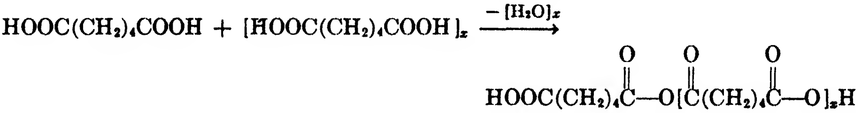
Succinic anhydride
(m.p. 120°C.)



(IV)

Glutaric anhydride
(m.p. 57°C.)

meric anhydride melting at 70° to 85°C. The product appears to be a mixture of linear polymers of varying chain lengths:



$$HOOC(CH_2)_4COOH + [HOOC(CH_2)_4COOH]_x \xrightarrow{-[H_2O]_x} HOOC(CH_2)_4\overset{O}{\overset{\|}{C}}-O[\overset{O}{\overset{\|}{C}}(CH_2)_4\overset{O}{\overset{\|}{C}}-O]_xH$$

Instead of intramolecular condensation occurring to form a heterocyclic ring with seven atoms in the ring, similar to the five- and six-membered rings formed by succinic and glutaric acids, an intermolecular reaction occurs with different molecules to form polymers of various chain lengths. This tendency toward intermolecular reaction or polymer formation increases with increasing numbers of methylene groups in the chain of the dibasic acid. Pimelic and suberic acids containing five and eight methylene groups, respectively, yield similar linear polymers.

Adipic acid forms similar polymers which on heating in a high vacuum produce a distillate consisting of the normal cyclic anhydride, thus indicating the polymerization is reversible. The monomer distills from the equilibrium mixture and is a stable but reactive substance which can be repolymerized by the catalytic action of a trace of water.

CHAPTER XIII

HALOGENATION

1. Introduction

The halogen derivatives of fatty acids are of importance in fat chemistry because they serve as intermediates in the preparation of desirable derivatives and because they provide a means of separating and identifying the components in mixtures of unsaturated acids. Few systematic investigations have been made of the halogenation products of fatty acids and no very extensive homologous series of halogen derivatives has been prepared and investigated in detail. Not a few of the halogen derivatives of the fatty acids which have been prepared and described in the literature are of dubious purity owing to lack of homogeneity of the parent acid or because of contamination with secondary reaction products.

Halogenation is one of the more frequently applied reactions in fat chemistry, at least on the laboratory scale, primarily because it provides the basis for several analytical methods used for determining the degree of unsaturation of fatty acids and glycerides. These methods involve the addition of iodine, chlorine, or bromine to the double bonds which are present in the reacting acid or ester. Addition reactions are, however, not the only halogenation reactions which these substances can undergo, and free halogens are not the only halogenating agents which are used. Besides addition reactions, fatty acids undergo substitution reactions, both in the carboxyl radical and in the carbon chain. In addition to the free halogens, other halogenation reagents such as thionyl chloride, sulfur monochloride, phosphorus trichloride, phosphorus pentachloride, phosphorus oxychloride, halogen hydrides, hypochlorous acid, oxalyl chloride, and phosgene are used to introduce halogens into various types of fatty acids.

2. Addition Reactions

(a) *Halogen Addition to Monoethenoid Acids*

The free halogens—chlorine, bromine, and iodine—as well as iodine monobromide and iodine monochloride, generally add to the double bonds of unsaturated acids. The rate and extent of the reaction depend on the halogenating agent, the conditions under which the reaction is carried out, and the constitution of the unsaturated acid. In decreasing order of activity, the halogens are chlorine, bromine, and iodine.

The relative rates of halogen addition are a function of the structure of the monoethenoid acids as was demonstrated by Ponzio and Gastaldi[1] by means of iodine absorption. As indicated in Table 113, relatively little addition of halogen occurs at the double bond in the proximity of the carboxyl group, whereas relatively complete addition occurs at remote double bonds whether located near the center of a long aliphatic chain or at a terminal methylene group. Ponzio and Gastaldi observed that even when the reaction time was extended to 70 and more hours, the addition of halogen to $\Delta^{2,3}$-octadecenoic acid was only about 50% of the theoretical.

TABLE 113

RELATIVE REACTIVITY OF MONOETHENOID ACIDS WITH VARIOUS HALOGENATION AGENTS

Acid	Iodine value			
	Calcd.	Hübl (4 hrs.)	Wijs (0.5 hr.)	Hanus (0.5 hr.)
$CH_3CH:CHCOOH$	295.0	17.4	10.3	4.3
$CH_3(CH_2)_{12}CH:CHCOOH$	99.8	6.6	20.4	1.9
$CH_3(CH_2)_{14}CH:CHCOOH$	89.7	8.7	18.0	3.0
$CH_3(CH_2)_7CH:CH(CH_2)_7COOH$	89.7	Theoretical		
$CH_2:CH(CH_2)_8COOH$	137.8	135.1	137.3	...

The increasing ease of halogen addition with increasing distance of the double bond from the carboxyl group was even more strikingly demonstrated by Eckert and Halla[2] who found the iodine value of $\Delta^{2,3}$-, $\Delta^{3,4}$-, and $\Delta^{4,5}$-octadecenoic acids (oleic acids) by the Hübl method to be 9.04, 16.27, and 26.96, respectively, compared to 89.87 required by theory.

If the concentration of halogen, reaction temperature, or reaction time is excessive, some substitution in the hydrocarbon chain occurs. Therefore, both in the quantitative determination of unsaturation and in the preparation of derivatives, these conditions must be rigidly controlled. In the quantitative determination of unsaturation, dilute solutions of the halogenation reagent are used at room temperature for a specified time. For the preparation of derivatives, *e. g.*, bromo addition products, the halogen is added very slowly at low temperatures, 0° to −10°C. The rate of reaction is also affected by light of various wave lengths and catalysts, such as mercuric chloride and mercuric acetate.[3,4]

The naturally occurring monoethenoid acids generally add halogens normally to produce dihalogenated derivatives. The lower members of the

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[1] G. Ponzio and C. Gastaldi, *Gazz. chim. ital.*, **42**, II, 92–95 (1912).

[2] A. Eckert and O. Halla, *Monatsh.*, **34**, 1815–1824 (1913).

[3] H. D. Hoffman and C. E. Green, *Oil & Soap*, **16**, 236–238 (1939).

[4] F. A. Norris and R. J. Buswell, *Ind. Eng. Chem., Anal. Ed.*, **15**, 258–259 (1943).

series are liquids at room temperature and few of their melting and freezing points or other properties have been determined. In the case of the positionally isomeric, halogen-substituted, long chain, monoethenoid acids, the melting point decreases as the distance of the halogen from the carboxyl group increases. In the case of *cis-trans*-isomers the halogen-substituted *trans*-isomers melt above those of the corresponding *cis*-isomers. These melting point relationships are illustrated in Table 114.

TABLE 114

MELTING POINTS OF THE DIBROMO DERIVATIVES OF SOME MONOETHENOID ACIDS

Halogenated acid	M.p., °C.	Reported by
$\Delta^{9,10}$-Dibromopalmitic	29	Bömer and Grossfeld[5]
$\Delta^{3,4}$-Dibromostearic	71–72, 67	Ponzio[6] Eckert and Halla[2]
$\Delta^{4,5}$-Dibromostearic	62	Eckert and Halla[2]
$\Delta^{9,10}$-Dibromostearic (*cis*)	28.5–29	Holde and Gorgas[7]
$\Delta^{9,10}$-Dibromostearic (*trans*)	29–30	Holde and Gorgas[7]
$\Delta^{11,12}$-Dibromostearic (*trans*)	33	Bertram[8]
$\Delta^{12,13}$-Dibromostearic (*cis*)	liq. at −20	Grün and Czerny[9]
$\Delta^{13,14}$-Dibromobehenic (*cis*)	46.5	Lewkowitsch[10]
$\Delta^{13,14}$-Dibromobehenic (*trans*).	54	Holt[11]

(b) *Halogen Addition to Nonconjugated Polyethenoid Acids*

Most polyunsaturated acids having all of their double bonds in nonconjugated positions add halogen normally with the production of a mixture of stereoisomers. For example, halogens add rapidly and smoothly to $\Delta^{9,10,12,13}$-linoleic acid, but it has generally been assumed that the addition occurs in two stages, first at the 9,10-double bond and then at the 12,13-double bond. Toyama and Tsuchiya[12] investigated the addition of bromine and thiocyanogen to linoleic acid and found that in the case of thiocyanogen, addition actually occurred in this manner. However, just the reverse order of addition was observed to occur in the case of bromine, the 12,13-double bond of linoleic acid was first saturated followed by saturation of the 9,10-double bond.

The position at which halogen addition occurred was established by treating linoleic acid with one mole of bromine and subjecting the reac-

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[5] A. Bömer and J. Grossfeld, in *Handbuch der Lebensmittel-Chemie,* Vol. IV, A Juckenack *et al.*, eds., Springer, Berlin, 1939, p. 218.

[6] G. Ponzio, *Atti accad. sci. Torino,* **39,** 552–560 (1903–1904).

[7] D. Holde and A. Gorgas, *Z. angew. Chem.,* **39,** 1443–1446 (1926).

[8] S. H. Bertram, *Biochem. Z.,* **197,** 433–441 (1928).

[9] A. Grün and W. Czerny, *Ber.,* **59,** 54–63 (1926).

[10] J. Lewkowitsch, *Chemical Technology and Analysis of Oils, Fats, and Waxes.* Vol. I, 6th ed., Macmillan, 1921–1923, p. 580.

[11] A. Holt, *Ber.,* **24,** 4120–4129 (1891).

[12] Y. Toyama and T. Tsuchiya, *J. Soc. Chem. Ind. Japan,* Suppl. binding, **38,** 36–38B (1935).

tion product to ozonolysis. Azelaic acid, $HOOC(CH_2)_7COOH$, and a bromo derivative were obtained. On debromination and reduction the bromo derivative gave nonanoic (pelargonic) acid. These results indicate that the dibromo addition product of linoleic acid is 12,13-dibromo-$\Delta^{9,10}$-octadecenoic acid. When linoleic acid was treated with one mole of iodine chloride, ICl, and the iodochlorooctadecenoic acid isolated and subjected to ozonolysis, it was found that the halogen had also added to the 12,13-double bond forming 12,13-chloroiodo-$\Delta^{9,10}$-octadecenoic acid[13] which is in agreement with the behavior of linoleic acid with bromine.

The partial halogenation of linolenic acid with one mole of bromine, and subsequently with two moles of bromine, followed at each step by ozonolysis, indicated that addition occurred first at the 15,16-double bond, followed by addition at the 12,13-double bond. When linolenic acid was treated with one mole and then with two moles of iodine chloride and subjected to ozonolysis at each stage, it was found that addition occurred first at the 15,16-double bond and then at the 12,13-double bond.[14] This method of partial halogenation followed by ozonolysis was applied by Toyama and Tsuchiya[14] to the determination of the structure of clupanodonic acid.

(c) *Halogen Addition to Conjugated Polyethenoid Acids*

If the double bonds present in unsaturated fatty acids are conjugated, halogen addition is generally erratic and incomplete under the same conditions in which nonconjugated acids react normally. Whereas $\Delta^{9,10,12,13}$-linoleic acid adds two moles of halogen, $\Delta^{9,10,11,12}$-linoleic acid adds one mole of halogen normally, but the second mole adds slowly and incompletely even after many hours. It has generally been assumed that halogen adds rapidly to the 9,10-double bond followed by slow addition to the 11,12-double bond. However, the behavior of $\Delta^{9,10,11,12}$-linoleic acid with respect to halogen addition is very suggestive of the 1,4-addition observed with many dienes. It has been repeatedly observed that in many dienes containing the group —CH:CH—CH:CH—, halogen addition occurs first at the 1,4-positions with the simultaneous formation of a new double bond at the 2,3-position. Thus, addition of bromine to $\Delta^{2,3;4,5}$-hexadiene results in the formation of 2,5-dibromo-$\Delta^{3,4}$-hexene according to the equation:

$$CH_3CH{:}CHCH{:}CHCH_3 + Br_2 \longrightarrow CH_3CHBrCH{:}CHCHBrCH_3$$

It is not improbable that 1,4-addition occurs in the case of aliphatic acids containing two double bonds in conjugated positions.

In the case of doubly-conjugated acids, *e. g.*, elaeostearic acid, halogen adds normally to two of the three double bonds but with considerable

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[13] Y. Toyama and T. Tsuchiya, *J. Soc. Chem. Ind. Japan*, Suppl. binding, **39**, 219–220B (1936).

[14] Y. Toyama and T. Tsuchiya, *Bull. Chem. Soc. Japan*, **10**, 441–443 (1935).

difficulty, or not at all, to the third double bond. Two assumptions have been made to explain this observation, namely, that addition occurs first at the 9,10-double bond followed by addition at the 11,12-double bond, while the 13,14-double bond reacts very slowly or not at all, or alternatively that normal addition occurs at the two extreme double bonds while the central or 11,12-double bond is unreactive. Actually, the order of addition has not been established exactly, but it is not unlikely that 1,4-addition occurs in the case of doubly conjugated double bonds. For example, in the case of elaeostearic and similarly conjugated acids, 1,4-addition may occur with either pair of conjugated double bonds with formation of a new double bond which does not add halogen. The dihalogenated acid thus formed would then contain two double bonds in isolated positions, one of which is an original double bond. The original double bond farthest removed from the halogen may then be saturated leaving the other double bond unsaturated. Such a mechanism would produce a mixture of tetrahalogenated acids.

If addition of bromine to elaeostearic acid occurred in this manner, two positionally isomeric tetrabromo acids would be formed in which the remaining double bond would occupy the 10,11- and the 12,13-positions, respectively. On bromination of elaeostearic acid and its naturally occurring isomers, punicic and trichosanic acids, in petroleum ether solution, all three acids form crystalline tetrabromides melting at 113.5–114°C.[15] The fact that all three of these acids form tetrabromides of the same melting point might be considered as evidence against 1,4-addition. However, by subjecting these tetrabromo derivatives to ozonolysis the position of the remaining double bond could be determined and the mode of halogen addition established.

(*d*) *Halogen Addition to Ethinoid Acids*

Stearolic, behenolic, and similar acids which contain a triple bond add only one molecule of halogen[16] according to the following equation:

$$CH_3(CH_2)_7C{:}C(CH_2)_7COOH + Br_2 \longrightarrow CH_3(CH_2)_7BrC{:}CBr(CH_2)_7COOH$$

$\Delta^{10,11}$-Undecinoic acid, $CH{:}C(CH_2)_8COOH$, adds only one mole of halogen by the Hanŭs iodine method.[17]

(*e*) *Halogen Hydride Addition to Unsaturated Acids*

Halogen acids of the hydride type, HX, add to the double bonds of monounsaturated fatty acids under certain conditions to form monohalogen

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[15] Y. Toyama and T. Tsuchiya, *J. Soc. Chem. Ind. Japan*, Suppl. binding, **38**, 182–185B (1935).

[16] A. Grün, *Analyse der Fette und Wachse*. 2 vols., Springer, Berlin, 1925–1929.

[17] P. L. Harris and J. C. Smith, *J. Chem. Soc.*, **1935**, 1572–1576.

derivatives of the corresponding saturated acids. The halogen hydrides are considerably less reactive in this respect than are the halogens themselves or the oxygenated halogen acids, HOX. Owing to the lesser.activity of halogen hydrides, their reactions may be more readily controlled. The ease of addition depends on the number, kind, and location of the double bonds in the unsaturated acid chain, as well as on the presence of catalysts and orienting substances in the reaction mixture.

Addition of the halogen atom may occur statistically at either carbon atom connected by the double bond or specifically at one or the other. Relatively little systematic work has been reported on the rate and specificity of the addition of the halogen hydrides as a function of the position of the double bond in the carbon chain. On the basis of such information as is available, addition at the double bond adjacent to the carboxyl group and at the double bond of the terminal methylene group of the hydrocarbon chain probably occurs at quite different reaction rates with the formation of differently oriented end products. Addition at any intermediately located double bond will vary from the extremes observed in the two types of terminal addition in proportion to the distance of the double bond from the carboxyl and the terminal methyl group.

The older literature contains frequent references to the preparation of the monohalogen derivatives of various fatty acids by addition of halogen hydrides. For example, Piotrowski[18] reported the preparation of monochlorostearic acid from oleic and elaidic acids. The unsaturated acids were dissolved in four times their weight of acetic acid and saturated with dry hydrochloric acid at 0°C. After standing four days, water was added to precipitate the chlorostearic acid which in both instances melted at 38°C. Albitzky[19] was unable to prepare chlorostearic acids by this method and therefore resorted to heating an acetic acid solution of oleic and elaidic acids, saturated with hydrochloric acid, to 150°C. in a sealed tube. According to Albitzky, both acids gave the same monochlorostearic acid which melted at 38–41°C., solidified at 12–13°C. and remelted at 20–22°C. When heated in a sealed tube at 170°C. for six to seven hours with aqueous potassium hydroxide, the chlorostearic acids from either source were converted to the same hydroxystearic acid. However, the melting and freezing points of all the products varied considerably, and it is probable that none of them was of high purity. In the light of more recent work, it can be safely assumed that these early preparations represented mixtures of positional isomers and, in some cases, of both geometrical and positional isomers.

Addition of halogen at a double bond adjacent to the carboxyl group and at a terminal methylene group appears to occur more specifically than at

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[18] S. Piotrowski, *Ber.*, **23**, 2531–2533 (1890).

[19] A. Albitzky, *J. prakt. Chem.*, **61**, 94–98 (1900).

an intermediate double bond. According to Ponzio,[20] hydrobromic acid adds to $\Delta^{2,3}$-octadecenoic acid, and forms 2-bromostearic acid melting at 54°C. .

Eckert and Halla[2] prepared a series of monoiodostearic acids by treating $\Delta^{2,3}$-octadecenoic acid with hydriodic acid and then treating the monohalogenated acid with alcoholic potassium hydroxide to produce $\Delta^{3,4}$-octadecenoic acid. By the same sequence of reactions, the $\Delta^{4,5}$-octadecenoic acid was produced from $\Delta^{3,4}$-octadecenoic acid, and from it, by treatment with hydriodic acid, the corresponding iodostearic acid was prepared. The melting points of the 2-, 3-, and 4-iodostearic acids prepared in this manner were found to be 54°, 57°, and 58.5°C., respectively.

Halogen Halide Addition at Terminal Methylene Bonds.—The addition of halogen acids to unsaturated fatty acids containing a terminal methylene group has been investigated in some detail by J. C. Smith and co-workers. As a result of this work, the mechanism of the addition of hydrogen bromide, chloride, and iodide to the double bond of undecenoic and related acids is now fairly well understood. Prior to the work of Ashton and Smith,[21] it was observed that addition of hydrogen bromide to $\Delta^{10,11}$-undecenoic acid, $CH_2{:}CH(CH_2)_8COOH$, occurred nonspecifically to produce either 10- or 11-bromoundecanoic acid. These authors found that, in *any solvent* and in the *absence of air*, addition of hydrogen bromide to undecenoic acid produced primarily 10-bromoundecanoic acid, CH_3-$CHBr(CH_2)_8COOH$, m.p. 35.1°C., in accordance with the Markownikoff rule of halogen addition. In the *presence of air* the reaction product was found to *vary with the solvent*, some solvents enhancing and some hindering the so-called *peroxide effect*. The 11-bromoundecanoic acid, CH_2BrCH_2-$(CH_2)_8COOH$, m. p. 51°C., was the principal product of reaction when undecenoic acid was treated with hydrogen bromide in petroleum naphtha solution in the presence of air.

Ashton and Smith[22] found that the addition of hydrogen bromide to ethyl undecenoate was entirely analogous to the addition which occurred in the case of the unesterified acid, *i. e.*, formation of ethyl 10-bromoundecanoate which is in contrast to the *peroxide-catalyzed* addition which gave ethyl 11-bromoundecanoate. Esterification of the carboxyl group was, therefore, without effect on the orientation in the addition reaction. When the corresponding alcohol, undecenol, was halogenated, no *peroxide effect* was observed and the product obtained was found to be 10-bromoundecanol. However, when the terminal hydroxy group was blocked by formation of the corresponding acetate, the use of a peroxide catalyst with hydrogen bromide resulted in the formation of the 11-bromoundecanol. This

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[20] G. Ponzio, *Atti accad. sci. Torino*, 40, 970–973 (1905).

[21] R. Ashton and J. C. Smith, *J. Chem. Soc.*, 1934, 435–440.

[22] R. Ashton and J. C. Smith, *J. Chem. Soc.*, 1934, 1308–1310.

reaction is of importance in the preparation of dicarboxylic acids by way of the bromo alcohol.

Abraham and Smith[23] investigated the addition of hydrogen chloride to $\Delta^{10,11}$-undecenoic acid. Hydrogen chloride was allowed to react with undecenoic acid in benzene solution both with and without a catalyst and in the presence and absence of air. In every case the main product was found to be 10-chloroundecanoic acid, m.p. 32°C. The same product was produced by treating 10-hydroxyundecanoic acid (m.p. 49–49.5°C.) with phosphorus pentachloride followed by hydrolysis of the chloro-acid chloride. When 11-hydroxyundecanoic acid was treated in the same manner, 11-chloroundecanoic acid, m.p. 40.5°C., was obtained. 10-Iodoundecanoic acid, m.p. 22–23°C., was prepared by the addition of hydrogen iodide to $\Delta^{10,11}$-undecenoic acid and by treatment of 10-bromoundecanoic acid with sodium iodide in acetone. The isomeric 11-iodoundecanoic acid, prepared by Ashton and Smith,[22] melted at 66°C.

It is apparent from the work of Smith *et al.* that hydrogen bromide differs from hydrogen chloride and iodide in its reactivity with unsaturated fatty acids and other olefins containing a terminal methylene group, by the fact that addition may be accelerated and the orientation reversed in the presence of oxidative catalysts in the former, but not in the latter.

It should be mentioned here that ω-bromo derivatives of the normal fatty acids can be prepared by a method which leaves no doubt as to the position occupied by the halogen. This method, which was used by Chuit and Hausser[24] to prepare all the ω-bromo aliphatic acids from C_8 to C_{21}, consists in the direct replacement of a terminal hydroxyl group with a halogen. Under these conditions no isomeric derivatives can be formed.

Harris and Smith[25] investigated the reaction of hydrogen bromide with fatty acids containing a terminal triple bond. In the case of the addition of hydrogen bromide to $\Delta^{10,11}$-undecinoic acid, $CH{\vdots}C(CH_2)_8COOH$, m.p. 43°C., it was found that the reaction was not subject to a *peroxide or oxidant* effect. $\Delta^{10,11}$-Undecinoic acid in the presence of perbenzoic acid was found to add one mole of hydrogen bromide to form monobromoundecenoic acid melting at 18.6°C. In the presence of diphenylamine (antioxidant) the same acid added hydrogen bromide to form a monobromoundecenoic acid melting at 12.1°C. Both reaction products apparently were mixtures of 10- and 11-bromoundecenoic acid, but the predominant bromo derivative obtained in the presence of perbenzoic acid was 11-bromo-$\Delta^{10,11}$-undecenoic acid, $BrHC{:}CH(CH_2)_8COOH$, while that obtained by reaction in the presence of diphenylamine was predominantly 10-bromo-$\Delta^{10,11}$-undecenoic acid, $CH_2{:}CBr(CH_2)_8COOH$.

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[23] E. P. Abraham and J. C. Smith, *J. Chem. Soc.*, 1936, 1605–1607.

[24] P. Chuit and J. Hausser, *Helv. Chim. Acta*, 12, 463–492 (1929).

[25] P. L. Harris and J. C. Smith, *J. Chem. Soc.*, 1935, 1572–1576.

Harris and Smith also prepared a bromo-$\Delta^{10,11}$-undecenoic acid, m.p. 41–42°C., which was previously prepared by Krafft[26] as a by-product of the action of alcoholic potassium hydroxide solution on 10,11-dibromoundecanoic acid. Krafft suggested that his acid was *trans*-11-bromo-$\Delta^{10,11}$-undecenoic acid. Harris and Smith, on the basis of the results of the catalytic reduction of their acid, concur in the assumption that the acid is 11-bromo-$\Delta^{10,11}$-undecenoic acid, but that it possesses a *cis*- rather than the *trans*-configuration.

Proof of the randomness of halogen halide addition in the case of nonterminal methylene groups was obtained by Harris and Smith[27] and by Abraham, Mowat, and Smith,[28] who observed that HBr added to $\Delta^{9,10}$-undecenoic acid, $CH_3CH{:}CH(CH_2)_7COOH$, to give equal amounts of 9- and 10-bromoundecanoic acids. The equilibrium ratio of the two positional isomers was unaffected by the presence of catalysts or solvent, but the rate of reaction was found to be affected by the solvent used. If the amide or corresponding alcohol was used instead of the acid, the proportion of 9- and 10-bromo compounds remained unchanged. It may be inferred on the basis of this work that, when the double bond is situated at a distance of more than one carbon atom from the terminal methyl group, addition of hydrogen bromide is statistical and at equilibrium a mixture of the two bromo acids is produced in a ratio of 1:1.

(*f*) *Addition of Oxygenated Halogen Acids to Unsaturated Acids*

Hypochlorous and hypobromous acids add to the double bonds of unsaturated fatty acids to form chlorohydrins or bromohydrins. Under proper conditions, chlorohydrins may also be prepared from unsaturated acids by reaction with chlorine. Except as intermediates for the preparation of polyhydroxy acids, the halohydrins have been of no great practical value and consequently little attention has been afforded these reactions. Most of the investigators of the addition products of the higher unsaturated acids with hypochlorous and hypobromous acids have been concerned with problems of isomerism.

The most extensive investigation of these reactions was reported by Albitzky[29,30] more than forty years ago. He prepared a series of addition products of oleic, elaidic, erucic, and brassidic acids from which, in turn, were prepared the corresponding dihydroxy acids and the mono- and diacetyl derivatives.

The work of Albitzky, although comprehensive, is vitiated by the fact that the unsaturated acids which he used were not very pure, their correct

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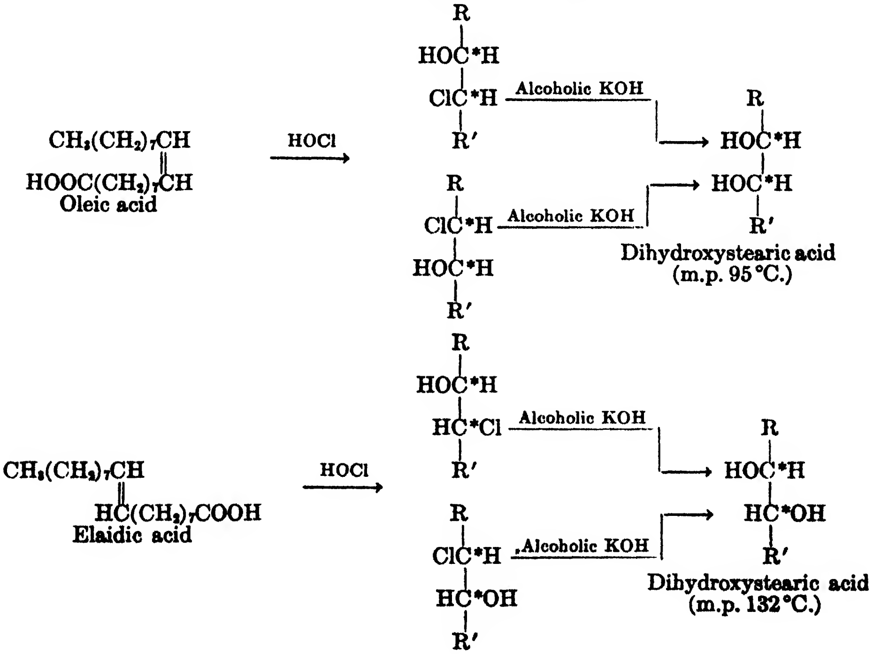
[26] F. Krafft, *Ber.*, **29**, 2232–2240 (1896).
[27] P. L. Harris and J. C. Smith, *J. Chem. Soc.*, **1935**, 1108–1111.
[28] E. P. Abraham, E. L. R. Mowat, and J. C. Smith, *J. Chem. Soc.*, **1937**, 948–954.
[29] A. Albitzky, *J. Russ. Phys.-Chem. Soc.*, **31**, 76–100 (1899); **34**, 788–810 (1902).
[30] A. Albitzky, *J. prakt. Chem.*, **61**, 65–94 (1900).

configurations were unknown at the time, and the nature of some of the reaction products was not recognized. For example, he assumed a *trans*-configuration for oleic and erucic acids and a *cis*-configuration for elaidic and brassidic acids, whereas the reverse configurations are now known to be correct. Consideration was not given the fact that the hydroxyl group and halogen atom of hypochlorous acid can add to oleic acid at either the ninth or tenth carbon atom to give a mixture of *cis*-9-hydroxy-10-chloro- and *cis*-9-chloro-10-hydroxystearic acids, and that similar additions occur with elaidic acid to give two *trans*-chlorohydroxystearic acids. The addition products of each acid represent pairs of positional isomers and they may also represent different stereoisomers as well. However, when the chlorine atoms are replaced by hydroxyl groups, the same positional isomers are produced in all cases, and the stereoisomerism evidént in these compounds corresponds to the *cis*- and *trans*-configurations of the parent acids.

Furthermore, all four of the chlorohydroxystearic acids, and both of the dihydroxystearic acids contain two asymmetric carbon atoms; therefore four optically active dihydroxystearic acids are theoretically possible, two of which represent *cis*-, and the other two *trans*-, configurations. These relationships are indicated in the following accompanying schemes in which the asymmetric carbon atoms are indicated by asterisks.



Albitzky prepared his halohydroxylated acids by the addition of hypochlorous or hypobromous acid to the alkali salt of the unsaturated acid dissolved in a large volume of water. The excess reagent was destroyed by addition of sulfurous acid, and the halohydroxy acid which was formed was precipitated by addition of dilute sulfuric acid. The resulting halohydrins generally comprised viscous oily liquids which were not completely characterized, but such analytical data and description as Albitzky gives seems to indicate that the products were not very pure. According to Nicolet and Poulter,[31] chlorohydrins of oleic and elaidic acids can be prepared by carefully controlled action of chlorine on solutions of their potassium salts containing potassium carbonate. The chlorohydrins obtained in this manner are uncrystallizable viscous oils and were considered by Nicolet and Poulter to be similar to those obtained by Albitzky by addition of hypochlorous acid.

In order to discuss the probable identity of the chlorohydrins, it is necessary to refer to their epoxy and dihydroxy conversion products. The halohydrins which Albitzky prepared were converted into dihydroxy acids by reacting them with potassium, barium, and silver hydroxides. The reaction conditions in all cases were relatively severe. For example, the reaction with potassium hydroxide was carried out by dissolving an equal weight of the halohydroxy acid and alkali in water or alcohol and heating the solution in a sealed tube at a temperature of about 150°C. for eight hours. When barium hydroxide was used, the halohydrin was dissolved in five volumes of alcohol to which was added twice the weight of alkali dissolved in the minimum amount of water, and the solution refluxed for two days. When silver oxide was used, one part of the halohydrin was stirred with three parts of the oxide and heated to the melting point until the reaction was completed, after which it was boiled with hydrochloric acid, filtered, and extracted with alcohol.

In view of the severity of the reaction conditions, it is not surprising that the yields of dihydroxy acids were low, often less than ten per cent, and it is not unlikely that they were accompanied by a variety of side reaction products. On the basis of the melting points of the various fractions which were obtained, Albitzky concluded that treatment of the chlorohydrin obtained from oleic acid by the action of alkali produced only the low melting dihydroxystearic acid (m.p. 95°C.), and that the same treatment of the chlorohydrin of elaidic acid produced the corresponding high melting dihydroxystearic acid (m.p. 132°C.).

When the same products were prepared by treatment of the two chlorohydrins with silver oxide, the melting points of the dihydroxystearic acids were found to be reversed and corresponded to those obtained by direct oxidation of oleic and elaidic acids with alkaline permanganate, *i. e.*, the high melting hydroxy acid was obtained from the chlorohydrin of oleic

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[31] B. H. Nicolet and T. C. Poulter, *J. Am. Chem. Soc.*, **52**, 1186–1191 (1930).

acid and the low melting one from the chlorohydrin of elaidic acid. It was also observed that the dichlorostearic acids prepared from oleic and elaidic acids gave, on treatment with potassium hydroxide, the low melting dihydroxystearic acid from oleic acid and the high melting acid from elaidic acid. It was, therefore, postulated by Albitzky that treatment of the chlorohydrin with alcoholic potassium hydroxide removed the halogen with simultaneous inversion of the acid, whereas silver oxide removed the chlorine without inversion. These postulates were generalized to include the bromohydrins and other pairs of isomeric acids such as erucic and brassidic.

However, when the data of Albitzky are critically examined, the evidence for his conclusions is not too convincing. As mentioned before, the yields of dihydroxy acids were generally quite low and the melting points of the fractions varied over wide limits. In the case of the bromohydrins obtained from oleic and elaidic acids, the melting point data seem to indicate that both dihydroxystearic acids were obtained regardless of which isomer was used. In fact, Albitzky concluded that both high and low melting dihydroxystearic acids were obtained when bromohydroxystearic acid prepared from oleic acid was treated with silver oxide. Moreover, he reported that saponification with alcoholic potassium hydroxide of the monoacetyl derivative of chlorohydroxystearic acid obtained from elaidic acid gave both high and low melting dihydroxystearic acids in almost equal amounts.

Theoretically, at least, there appears to be no reason for assuming that hypochlorous or hypobromous acids should add to the double bond of oleic or elaidic acid preferentially to produce specifically either the 9-halo-10-hydroxy- or the 10-halo-9-hydroxystearic acids; also theoretically, at least, it should be possible to replace the halogen of either acid by a hydroxyl group without alteration of the stereo-configuration.

In light of the present knowledge of the configurations of oleic and elaidic acid, the assumption that inversion occurred when the halogen was removed by potassium and barium hydroxides, and that inversion did not occur when silver oxide was used to remove the halogen, probably needs to be revised. It appears that the low melting *cis*-oleic acid actually gave the low melting dihydroxystearic acid and the high melting *trans*-elaidic acid gave the high melting dihydroxystearic acid as would be expected if the various addition and substitution reactions occurred without concomitant alteration of the geometrical configurations of the respective acids.

It is necessary, therefore, to assume that the treatment of the halohydrins with potassium and barium hydroxides did not cause inversion, but that treatment with silver oxide did. It must also be assumed that mild oxidation by alkaline permanganate is accompanied by inversion since oleic and elaidic acids produce the high melting (132°C.) and the low melting (95°C.) dihydroxystearic acids, respectively, by this treatment.

In contrast to the conditions employed by Albitzky, Nicolet and Poulter[31] refluxed the chlorohydrins of oleic and elaidic acids for two hours with an excess of sodium ethylate in 95% alcohol, whereby the acids were converted into the corresponding epoxides in 45% and 75% yields, respectively. Both epoxides were solids melting at 53.8°C., but apparently were not identical as their mixture melted at 45–47°C. Treatment of the epoxides with aqueous alkali or acid resulted in slow hydrolysis to produce dihydroxy acids. Only the low melting dihydroxystearic acid was obtained from the oleic epoxide and only the high melting dihydroxystearic acid was obtained from the elaidic epoxide.

Treatment of the epoxides of oleic and elaidic acids with dry hydrogen chloride in dry ether resulted in the regeneration of chlorohydrins, but unlike the original chlorohydrins from which the epoxides were formed, they were obtained as solids melting at 35° and 50°C., respectively. Nicolet and Poulter, therefore, concluded that the original chlorohydrins were 9-chloro-10-hydroxystearic acids, while those regenerated by way of the epoxide were 9-hydroxy-10-chlorostearic acids. According to Nicolet and Poulter, the epoxides are formed quite readily when the chlorohydrins are treated with alkali, whereas the dihydroxystearic acids are formed from the epoxides with considerable difficulty. Likewise, the chlorohydrins are readily regenerated from the epoxides; in fact they can be quantitatively determined by means of this reaction. All of these reactions appear to occur without inversion, the *cis*-acids giving only *cis*-derivatives, and the *trans*-acids giving only *trans*-derivatives.

The observations of Albitzky and of Nicolet and Poulter may perhaps be interpreted by assuming that hypochlorous acid adds to the double bonds of monounsaturated aliphatic acids to form a mixture of isomeric chlorohydrins which on treatment with alcoholic potassium hydroxide are converted first to epoxides and then to dihydroxy acids. In contrast to the original acids which form oily mixtures of isomeric chlorohydrins when treated with hypochlorous acid, the epoxides when treated with hydrogen chloride form specific chlorohydrins having definite melting points.

These reactions may be represented by the equations on page 347 in which oleic acid is used as the prototype to which other similar acids may be referred. All of the products are presumed to possess a *cis*-configuration, whereas all of the corresponding products from elaidic acid are presumed to possess a *trans*-configuration.

Nicolet and Cox[32] prepared the dichlorodihydroxy- and dibromodihydroxystearic acids by treatment of linoleic acid with potassium hypochlorite and hypobromite, respectively. The linoleic acid was prepared by bromination of the fatty acids of cottonseed oil and separation of the

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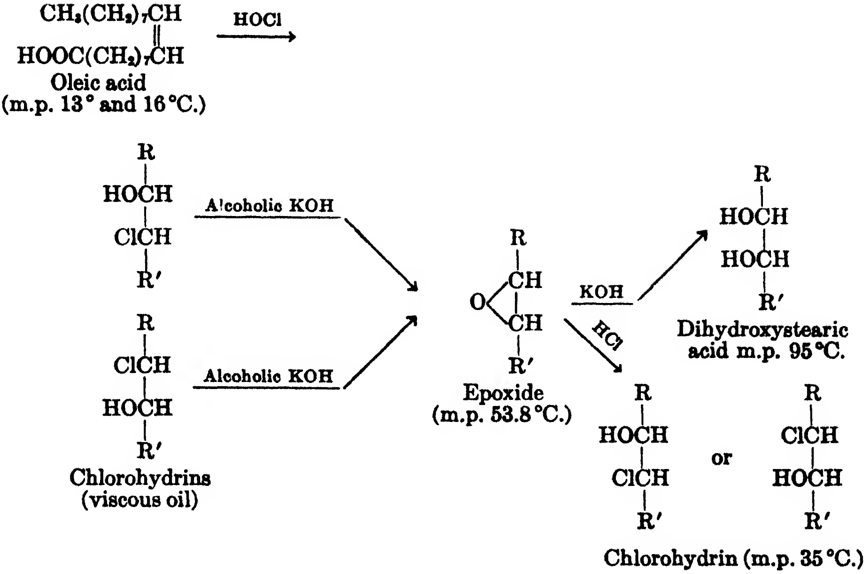
[32] B. H. Nicolet and H. L. Cox, *J. Am. Chem. Soc.*, **44**, 144–152 (1922).



tetrabromides followed by debromination to regenerate the linoleic acid. The reactions were carried out by dissolving the acid in a 1% solution of potassium hydroxide and adding two moles of 2 *N* hypochlorite or hypobromite. The reaction products were precipitated by passing into the solution a stream of carbon dioxide. They were obtained as light brown viscous oils which could not be crystallized or distilled at a pressure as low as 10 mm.

Since it is possible for the halogen and hydroxyl group to add at both the 9,10 and the 12,13 double bonds of linoleic acid in two different orientations, the product obtained by the reaction of linoleic acid and hypochlorous acid or hypobromous acid should be a mixture of four positional isomers. As such, they are of little practical value except as intermediates in the production of tetrahydroxy acids into which they can be converted by treatment with alkali, as has been discussed under the corresponding halohydrins of the monoethenoid acids.

3. Substitution Reactions

(a) *Substitution of Halogen for Hydrogen in the Hydrocarbon Chain*

Several types of substitution reactions are possible when the higher aliphatic acids are reacted with halogenating reagents. Free halogens may replace one or more hydrogens in the hydrocarbon chain; halogen derived from thionyl chloride, phosphorus pentachloride, and other halogenating agents may replace a hydroxyl group in the carboxyl radical or elsewhere in the carbon chain of hydroxy acids.

The first type of halogen substitution is difficult to control with respect to the number and position of the replaceable hydrogens. Precautions must be taken in the quantitative determination of unsaturation to avoid simultaneous or subsequent replacement of hydrogen in the hydrocarbon chain. Chlorine is much more reactive in this respect than iodine or bromine, and its activity is more readily affected by concentration, time, temperature, light, catalysts, etc.[32a]

The hydrogen atoms attached to the carbon atom adjacent to a carboxyl group are more susceptible to substitution than those farther removed. This activity is partially explained on the basis of the enolization of the carbonyl group of the carboxyl radical. Alpha-substitution of the lower members of the aliphatic acid series is readily accomplished by treatment of the acid with halogen in the presence of a catalyst. The alpha-halogenation of acid chlorides and esters occurs more readily than in the case of the free acids. The α-chloro and α-bromo acids may be prepared by the action of dry chlorine or bromine on the anhydrous acid in the presence of phosphorus. All of the α-chloro and α-bromo acids from acetic to stearic have been prepared in this manner.

Hell and co-workers[33-35] prepared the α-monobromo derivatives of myristic, palmitic, and stearic acids by reacting the free acids with bromine in the presence of amorphous phosphorus and subsequently hydrolyzing the α-monobromoacyl bromide to the corresponding acid according to the following scheme:

$$RCH_2COOH \xrightarrow[P]{Br_2} RCHBrCOBr \xrightarrow{H_2O} RCHBrCOOH$$

The method of preparation follows. Dry stearic acid, for example, is thoroughly mixed with dry amorphous phosphorus in a flask fitted with a reflux condenser and dropping funnel. Bromine is admitted slowly to the reaction mixture which is warmed on the steam bath. The reaction, which is violent at first, soon subsides with further addition of bromine. When the reaction is complete, the mixture is slowly poured into water whereupon the α-bromostearic acid is regenerated from the corresponding bromoacyl bromide. It is washed with water by decantation and dissolved in petroleum ether from which solvent the monobromostearic acid crystallizes on standing.

Mendel and Coops[36] used a very similar method of preparing methyl

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[32a] H. H. Guest and C. M. Goddard, Jr., *J. Am. Chem. Soc.*, **66**, 2074–2075 (1944).
[33] C. Hell and S. Twerdomedoff, *Ber.*, **22**, 1745–1748 (1889).
[34] C. Hell and C. Jordanoff, *Ber.*, **24**, 936–943 (1891).
[35] C. Hell and J. Sadomsky, *Ber.*, **24**, 2388–2396 (1891).
[36] H. Mendel and J. Coops, *Rec. trav. chim.*, **58**, 1133–1143 (1939).

α-bromopalmitate and α-bromostearate prior to their conversion into the corresponding α-hydroxy acids.

The higher α-monobromo acids are soluble in the usual fat solvents and are readily esterified with ethyl alcohol. When refluxed with alcoholic alkalies they are converted into the corresponding α-monohydroxy acids. These α-hydroxy acids, like the bromo acids from which they are prepared, are soluble in ether, benzene, chloroform, hot alcohol, and acetic acid.

(*b*) *Preparation of Acyl Halides*

The acyl or fatty acid halides are derived from the acids by replacement of the hydroxyl of the carboxyl group by a halogen. The preparation and reactions of the acyl halides are important in fatty acid chemistry primarily because the reaction products are essential intermediates in the preparation of pure synthetic glycerides and other esters of known constitution. Although any of the halogens may be substituted for the hydroxyl group, only the chlorides have been extensively prepared and used. In the case of the lower members of the aliphatic acid series (acetic to butyric) the fluorides, chlorides, bromides, and iodides have been prepared. All are liquids having relatively low boiling points. The boiling points increase as the molecular weights of the halogens increase from fluorine to iodine and as the homologous series is ascended. Alternation does not occur in the boiling points as it does in the melting points of the ascending series of acids.

Acid chlorides may be prepared by any of the reactions illustrated in equations (*1*) to (*7*).

(*1*) $RCOOH + PCl_5 \longrightarrow RCOCl + HCl + POCl_3$

(*2*) $3\,RCOOH + PCl_3 \longrightarrow 3\,RCOCl + H_3PO_3$

(*3*) $2\,RCOONa + POCl_3 \longrightarrow 2\,RCOCl + NaPO_3 + NaCl$

(*4*) $RCOOH + SOCl_2 \longrightarrow RCOCl + SO_2 + HCl$

(*5*) $RCOOH + SO_2Cl_2 \longrightarrow RCOCl + HCl + SO_3$

(*6*) $RCOOH + (COCl)_2 \longrightarrow RCOCl + CO_2 + CO + HCl$

(*7*) $RCOOH + COCl_2 \longrightarrow RCOCl + CO_2 + HCl$

One of the earliest methods,[37] but now little used, consisted of the treatment of the salt of the acid with phosphorus oxychloride (see Eq. *3*). Treatment of the salt with half the theoretical amount of oxychloride results in the formation of the corresponding acid anhydride according to equation (*8*).

(*8*) $6\,RCOONa + POCl_3 \longrightarrow 3\,(RCO)_2O + 3\,NaCl + Na_3PO_4$

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[37] C. Gerhardt, *Ann.* 87, 57–84 (1853).

Bauer[38] reported a comprehensive and systematic investigation of the preparation of the higher fatty acid chlorides by all of the reactions mentioned above save those involving sulfuryl chloride and phosphorus oxychloride. Acid chlorides were prepared from lauric, myristic, palmitic, stearic, oleic, elaidic, and linoleic acids. He concluded on the basis of yields, ease of handling, and cost of reagent, that phosphorus tri- and pentachlorides are superior to other chlorinating agents for the preparation of pure saturated acid chlorides, and that oxalyl chloride was preferable for use in preparing unsaturated acid chlorides.

The acyl bromides can be prepared by treating the aliphatic acids with phosphorus bromides in the same manner used in preparing acyl chlorides. The acyl iodides are usually prepared from the anhydrides or salts of the aliphatic acids by the action of phosphorus iodide or preferably by the action of calcium iodide on the acid chlorides. Acyl fluorides are produced when the corresponding chloride is treated with silver fluoride, anhydrous zinc fluoride, or potassium fluoride.

Reactions of Fatty Acids with Phosphorus Chlorides.—Phosphorus trichloride and phosphorus pentachloride have been generally employed for replacing specific hydroxyl groups with chlorine and especially for the preparation of acid chlorides. More recently, thionyl chloride and oxalyl chloride have been used extensively for this purpose, but they have not entirely superseded the use of either phosphorus trichloride or phosphorus pentachloride. In fact, advantages and disadvantages as well as variable yields have been claimed for each of these chlorinating agents in the hands of different workers.

Krafft and Tritschler[39] described a number of monounsaturated acid chlorides, *e. g.*, undecenoyl, oleoyl, elaidoyl, and brassidoyl chlorides, which were prepared by treatment of the free acid with phosphorus pentachloride. The general method of preparation consisted in cooling the acid to a low temperature (ice) and treating it with slightly more than an equimolar quantity of phosphorus pentachloride, then heating the mixture slightly to complete the reaction. The phosphorus oxychloride formed in the reaction was removed by distillation under reduced pressure and the acid chloride purified by several distillations. Nearly quantitative yields were claimed. The corresponding anhydrides, nitriles, amides, and benzoyl derivatives were prepared from the acid chlorides.

The method of Krafft and Tritschler has been followed by later workers, especially for the preparation of oleoyl chloride. Sulzberger[40] prepared oleoyl chloride by treatment of oleic acid with phosphorus pentachloride and with thionyl chloride obtaining identical yields (75%) by both methods.

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[38] S. T. Bauer, *Oil & Soap*, **23**, 1–5 (1946). See R. R. Ackley and G. C. Tesoro, *Ind. Eng. Chem., Anal. Ed.*, **18**, 444–445 (1946).

[39] F. Krafft and F. Tritschler, *Ber.*, **33**, 3580–3585 (1900).

[40] N. Sulzberger, *Z. angew. Chem.*, **27**, 40 (1914).

The reaction with phosphorus pentachloride was carried out by adding pure oleic acid (15 g.), divided into three or four portions, to one mole of finely powdered phosphorus pentachloride. On the addition of the first portion of the acid at room temperature instantaneous evolution of hydrochloric acid occurs which continues as long as the acid is added. The mixture, which warms only slightly during the reaction, is allowed to stand until the evolution of hydrochloric acid is complete, whereupon the oily reaction product is poured off from the excess phosphorus pentachloride. The product is distilled *in vacuo* to separate the oleoyl chloride from the phosphorus oxychloride.

Täufel and Künkele[41] prepared oleoyl chloride both by means of phosphorus trichloride and phosphorus pentachloride. Thionyl chloride was also used, but its use was considered to be unsatisfactory for reasons which will be mentioned later. Täufel and Künkele employed moderately large quantities of oleic acid but the yields obtained were low, 48% with phosphorus pentachloride and 46% with phosphorus trichloride. According to their method, 200 g. of oleic acid was cooled with ice water and continuously shaken, while about 150 g. of phosphorus pentachloride was added in small amounts at about ten-minute intervals or until no further reaction was evident. The liquid was separated from solid unreacted pentachloride and distilled. The phosphorus oxychloride distilled over first, followed by the oleoyl chloride at a temperature of 180°C. and a pressure of 8 mm.

Chlorination with phosphorus trichloride was carried out by Täufel and Künkele in a manner similar to that described by Aschan[42] using relatively small amounts of oleic acid. Five grams of phosphorus trichloride was added to 20 g. of ice-cold oleic acid. The mixture was maintained in an ice bath for one-half hour and then shaken for the same length of time at room temperature followed by warming at 60°C. in a water bath for 10 minutes. The reaction mixture was then cooled again in ice to bring about separation of the oleoyl chloride and phosphorous acid (H_3PO_3). The oleoyl chloride was decanted and distilled *in vacuo*. Fractional distillation, followed by analysis of the fractions and comparison of the boiling points with the boiling point–composition curve of oleic acid and oleoyl chloride at 6 mm. pressure, indicated that the reaction products obtained by Täufel and Künkele were mixtures of oleic acid (40%) and oleoyl chloride (60%). The boiling points at 6 mm. for oleic acid and oleoyl chloride were found to be 204° and 170°C., respectively.

Bömer and co-workers[43,44] found that the method of Krafft and Tritschler

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[41] K. Täufel and F. Künkele, *Fettchem. Umschau*, **42**, 27–29 (1935).

[42] O. Aschan, *Ber.*, **31**, 2344–50 (1898). See H. Richet, *Bull. soc. chim.*, **1946**, 52–54.

[43] A. Bömer and W. Kappeller, *Fette u. Seifen*, **44**, 340–343 (1937).

[44] A. Bömer and J. Stather, *Fette u. Seifen*, **44**, 29–31 (1937).

was applicable to the preparation of elaidoyl chloride. Twenty grams of cold elaidic acid was reacted with a molar quantity of phosphorus pentachloride (14.6 g.) added in small portions. The reaction mixture was warmed to about 45°C. and allowed to stand one-half hour before distilling off the phosphorus oxychloride *in vacuo*. After removal of the phosphorus oxychloride, the temperature was raised to 90° and the colorless elaidoyl chloride distilled. When the temperature was allowed to rise above 130° the acid chloride underwent decomposition and became brown. This change also occurs on long standing at lower temperatures. According to Bömer and Kappeller, this method results in a yield of 98% of elaidoyl chloride which is in agreement with the observations of Krafft and Tritschler.

Reactions of Fatty Acids with Thionyl Chloride.—Thionyl chloride, $SOCl_2$, is a useful reagent for the introduction of chlorine in place of various groups, *e. g.*, OH, SH, NO_2, SO_3H, or of hydrogen or oxygen.[45] It may also be used as a dehydrating agent, polymerization catalyst, etc. In the chemistry of fatty acids it is principally of value for introducing chlorine in the place of the hydroxyl group to form acid chlorides.

The reagent, when pure, is a colorless liquid, fuming in air and boiling at 78.8°C. At about 150° it decomposes into a mixture of sulfur chloride, sulfur dioxide, and chlorine. It often contains traces of phosphoryl chloride, stannic chloride, and oxides of sulfur. Tests for these impurities and methods of removal are described by Silberrad.[45] Verkade[46] claims that prior purification of thionyl chloride by distillation over quinoline or boiled linseed oil is essential to the prevention of the formation of tarry reaction products when oleic acid is reacted with thionyl chloride.

The frequent use of thionyl chloride for the preparation of acid chlorides is due primarily to the fact that it is easier to handle than phosphorus pentachloride and the end products of the reaction are volatile and therefore easy to remove. The preparation of many acid chlorides by the action of thionyl chloride on free acids or their alkali salts has been described, but few of them pertain to long chain aliphatic acids.

The usual method is to heat the pure dry acid or the sodium salt with an excess of thionyl chloride at the boiling point of the latter, followed by distillation of the excess thionyl chloride. In some cases it is unnecessary to heat the reaction mixture except to remove the excess thionyl chloride. Meyer,[47] for example, prepared a number of acid chlorides by reaction of the acid with a large excess of thionyl chloride in the cold for 24 hours and then removed the excess reagent by distillation. By treatment of the acid chloride with ammonia, he prepared the corresponding amides.

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[45] C. A. Silberrad, *Chemistry & Industry* in *J. Soc. Chem. Ind.*, **45**, 36–38, 55–57 (1926).
[46] P. E. Verkade, *Rec. trav. chim.*, **62**, 393–397 (1943)
[47] M. Meyer, *Compt. rend.*, **203**, 1074–1077 (1936).

McMaster and Ahmann[48] reported an investigation of the action of thionyl chloride on organic acids in which sixteen acids were reacted with thionyl chloride. None of the normal aliphatic acids was included although the method described is stated to be generally applicable for the preparation of the aliphatic acid chlorides. According to the method of McMaster and Ahmann, 15 to 25 g. of purified acid is treated with two to three times this weight of thionyl chloride. In some cases reaction occurs spontaneously but generally it is necessary to reflux the mixture to complete the reaction. Where the acid is insoluble in thionyl chloride, a solvent such as benzene, naphtha, or pyridine may be used. The by-products of the reaction are generally volatile and are removed when the excess thionyl chloride is removed by distillation from the reaction mixture. Daubert, Fricke, and Longenecker[49] found the method of McMaster and Ahmann to be quite satisfactory for the preparation of the saturated acid chlorides but they preferred the use of oxalyl chloride for the preparation of oleoyl chloride.

Carré and Libermann[50] found that many acids which react with difficulty or not at all with thionyl chloride do so readily when the reaction is carried out in the presence of pyridine. When the reaction is carried out in anhydrous ether, pyridine, equivalent to one mole of the free acid, is added; when carried out in pyridine alone, two to three moles of pyridine are used for each mole of acid. Pyridine hydrochloride separates from the ether solution as the reaction proceeds and at the end of the reaction an ethereal solution of hydrochloric acid is added to precipitate the excess pyridine which is filtered off. These authors observed that when monobasic anhydrides were treated with thionyl chloride they were easily and quantitatively converted into acid chlorides according to the equation:

$$(RCO)_2O + SOCl_2 \longrightarrow SO_2 + 2\,RCOCl$$

Black and Overley[51] prepared 9,10,12,13-tetrabromostearoyl chloride from the corresponding tetrabromostearic acid by treatment of the latter with thionyl chloride. A slight excess of thionyl chloride was added in small portions to tetrabromostearic acid heated to 120°C. After the reaction was completed, the mixture was cooled to room temperature and dissolved in anhydrous petroleum naphtha, and then cooled to −26°. The acid chloride, which was separated by filtration, melted at 59.5–60°C.

Täufel and Künkele[41] attempted to prepare oleoyl chloride with thionyl chloride and stated that although they varied the reaction conditions over wide limits, they were not successful. Among other products, they gener-

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[48] L. McMaster and F. F. Ahmann, *J. Am. Chem. Soc.*, **50**, 145–149 (1928).

[49] B. F. Daubert, H. H. Fricke, and H. E. Longenecker, *J. Am. Chem. Soc.*, **65**, 2124–2144 (1943). See H. Richet, *Bull. soc. chim.*, 1946, 52–54.

[50] P. Carré and D. Libermann, *Compt. rend.*, **199**, 1422–1423 (1934).

[51] H. C. Black and C. A. Overley, *J. Am. Chem. Soc.*, **61**, 3051–3052 (1939).

ally obtained a substance which melted at 50°C. It contained no chlorine and had an iodine number of 90.4 and a saponification number of 191. It apparently consisted principally of an iso-oleic acid of unknown configuration. A similar chlorine-free product melting at 38°C. and having an iodine number of 86.7 was obtained when the chlorination was carried out with an insufficient amount of phosphorus pentachloride.

These results are in contrast to those of Sulzberger[40] who prepared oleoyl chloride by warming oleic acid on a water bath with a small excess of thionyl chloride. The mixture was distilled to remove the excess thionyl chloride after which the temperature rose to 190°C. whereupon the oleoyl chloride distilled under a pressure of 9 mm. Analyses indicated that the product, which was obtained in 75% yield, was relatively pure.

Verkade[46] obtained oleoyl chloride in 90% yield by reaction of thionyl chloride with oleic acid, but only when the inorganic chloride was first distilled over quinoline and boiled linseed oil to remove impurities.

The reaction of thionyl chloride with long chain hydroxy acids does not appear to have been extensively investigated. Apparently a variety of reactions occur depending on conditions. These include, besides formation of the acid chloride, addition of SOCl in place of the hydrogen of the hydroxyl group in the carbon chain, replacement of the hydroxyl group of the carbon chain with chlorine, and formation of various condensation and polymerization products.

Reactions of Fatty Acids with Oxalyl Chloride.—Oxalyl chloride, $(COCl)_2$, has been extensively used for preparing acid chlorides. Staudinger[52,53] described a convenient method for the preparation of pure oxalyl chloride and investigated many of its reactions. Adams and co-workers[54-56] extended these investigations to various types of alcohols, phenols, and acids, especially in the presence of pyridine, and included also an investigation of the use of oxalyl bromide. Adams and Ulich[57] found that aliphatic acids, either alone or in benzene solution, when warmed with two moles of oxalyl chloride were converted quickly and almost quantitatively into the corresponding acid chlorides. When the sodium salt was used, these authors found that one mole of the salt reacted with 1 to 1.5 moles of oxalyl chloride in benzene to give sodium chloride and the corresponding acid chloride in practically quantitative yields. The latter method is of more general applicability and requires less oxalyl chloride to give the desired acid chloride. The acid anhydride may be used in the place of the free acid or sodium salt, likewise, with an almost quantitative yield of the

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[52] H. Staudinger, *Ber.*, **41**, 3558–3566 (1908).
[53] H. Staudinger and E. Anthes, *Ber.*, **46**, 1426–1437 (1913).
[54] R. Adams and H. Gilman, *J. Am. Chem. Soc.*, **37**, 2716–2720 (1915).
[55] R. Adams and L. F. Weeks, *J. Am. Chem. Soc.*, **38**, 2514–2519 (1916).
[56] R. Adams, W. V. Wirth, and H. E. French, *J. Am. Chem. Soc.*, **40**, 424–431 (1918).
[57] R. Adams and L. H. Ulich, *J. Am. Chem. Soc.*, **42**, 599–611 (1920).

corresponding acid chloride. On the other hand, acid anhydrides may be formed from the acid by the reaction of one mole of oxalyl chloride on two or more moles of the sodium salt of the acid suspended in benzene solution.

The mechanism of the formation of the acid chlorides is explained by the assumption that treatment of the aliphatic acid with oxalyl chloride results in the formation of a double anhydride, followed by its decomposition into a simple anhydride and conversion of this anhydride into the corresponding chloride by the following reactions:

$$2\,RCOOH + (COCl)_2 \longrightarrow (RCOOCO)_2 + 2\,HCl$$

$$(RCOOCO)_2 \longrightarrow (RCO)_2O + CO_2 + CO$$

$$(RCO)_2O + (COCl)_2 \longrightarrow 2\,RCOCl + CO_2 + CO$$

Lauroyl chloride is prepared according to the general method of Adams as follows: 25 g. of lauric acid and 40 g. of oxalyl chloride are placed in a round bottom flask connected with a ground-in glass condenser and warmed slightly to start the reaction, after which it is allowed to proceed spontaneously for 15 to 20 minutes. After this period, the mixture is refluxed for about two hours, followed by distillation of the reaction mixture at atmospheric pressure until the excess oxalyl chloride is collected. Then the chloride of the aliphatic acid is distilled under diminished pressure. The yield of lauroyl chloride (b.p. 145–147°C. at 20 mm.) by this method was found to be 27 g. or 99% of the theoretical.

Oxalyl bromide was found to react exactly like oxalyl chloride to produce the corresponding acid bromides. When aromatic acids were added to phosphorus pentabromide suspended in benzene and refluxed for one to two hours, the corresponding acid bromides were produced but the yield was only about 50% of theory. The use of the sodium salt in place of the free acid gave larger yields.

Averill, Roche, and King[58] prepared a number of fatty acid chlorides for use as intermediates in the synthesis of pure glycerides of known constitution, by reacting higher saturated acids with oxalyl chloride according to the method of Adams and Ulich. Wood *et al.*[59] found the thionyl chloride method unsatisfactory for the preparation of unsaturated fatty acid chlorides. However, application of the method of Adams and Ulich to the preparation of oleoyl, elaidoyl, linoleoyl, and linolenoyl chlorides was considered satisfactory although the only yield reported was that for linoleoyl chloride (82%).

Reactions of Fatty Acids with Phosgene.—In 1870, Kempf[60] found that acetyl chloride was formed when acetic acid was treated with phosgene at

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[58] H. P. Averill, J. N. Roche, and C. G. King, *J. Am. Chem. Soc.*, 51, 866–872 (1929).

[59] T. R. Wood, F. L. Jackson, A. R. Baldwin, and H. E. Longenecker, *J. Am. Chem. Soc.*, 66, 287–289 (1944).

[60] T. Kempf, *J. prakt. Chem.*, 1, 402–415 (1870).

110–120°C. Later, Hentschel[61] noted that treatment of the sodium salts of the lower fatty acids converted them into mixtures of acid chlorides and anhydrides. The reaction does not seem to have found much favor as a laboratory method of preparing acid chlorides but several patents[62–64] have been issued which describe the preparation of the fatty acid chlorides by the action of phosgene on the corresponding acids.

The earliest of these patents was issued to Hochstetter[62] and describes generally the vapor phase reaction of phosgene and acid in contact with a porous surface contained in an externally heated chamber, and specifically, the reaction at 200°C. of phosgene and chloroacetic acid in contact with charcoal to form chloroacetyl chloride. A British patent[63] describes the preparation of higher fatty acid chlorides by reaction of fatty acids and phosgene in the presence of specially activated charcoal. According to the claims of the patent, the method obviates the use of solvents and produces pure chlorides in practically quantitative yields. The process is claimed to be extremely simple and can be applied in the preparation of both saturated and unsaturated acid chlorides. An example is cited in which 145 to 150 parts of stearic or oleic acid is heated to about 150°C. in the presence of 1.5 to 3.0 parts of finely divided activated charcoal and the stirred mixture treated with phosgene until evolution of hydrochloric acid ceases, after which the pure, colorless chloride is separated by filtration. A more recent disclosure, contained in a Swiss patent,[64] describes the preparation of palmitoyl and stearoyl chlorides by reaction of palmitic or stearic acid with phosgene at a temperature above 140°C. in the presence of a small quantity of a tertiary amine salt, such as pyridine hydrochloride.

Prat and Étienne[65] described the preparation of lauroyl, palmitoyl, stearoyl, and oleoyl chlorides by reaction of phosgene and the corresponding fatty acids at temperatures of 140–145°C. in the absence of a catalyst. They used a reaction vessel having a fritted glass bottom to admit the phosgene in a finely divided form into the acid heated to the reaction temperature. The authors investigated a variety of reaction conditions including the influence of inert and activated dispersing media (broken glass, pumice, activated carbon), solvents (toluene and xylene), temperature, and flow of phosgene through the acid. The presence of solvents at reflux temperature resulted in a slow rate of reaction. At temperatures between 120° and 160°C., a flow rate of 10 g. per hr. of phosgene through the fatty acid (120 g.) gave an increased reaction rate which reached a maximum with a flow rate of 60 g. per hr. With lauric acid, a flow rate of 60 g. per hr. and a temperature of 150° gave a maximum production (about 94%) of

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[61] W. Hentschel, *Ber.*, 17, 1284–1289 (1884).
[62] A. Hochstetter, German Pat. 283,896 (April 27, 1915).
[63] I. G. Farbenindustrie A.-G., British Pat. 515,963 (Dec. 19, 1939).
[64] Société pour l'industrie chimique à Bâle, Swiss Pat. 213,047 (April 16, 1941).
[65] J. Prat and A. Étienne, *Bull. soc. chim.*, 11, 30–34 (1944).

lauroyl chloride in four hours and only slightly less (about 90%) in three hours. At 160° and the same flow rate, oleic acid gave a maximum yield (85%) of oleoyl chloride in two hours. With palmitic and stearic acids, under the same conditions, 70% to 75% yields of acid chlorides were obtained.

Bauer[66] was unable to prepare saturated acid chlorides by reaction of fatty acids and phosgene. For example, little reaction occurred by heating stearic acid for six hours at a temperature of 150°C., either with or without a catalyst, when phosgene was passed into the reaction mixture at a slow rate. The use of a solvent for either the fatty acid or the phosgene failed to effect appreciable reaction. The use of xylene boiling at 140° failed to increase the reaction between myristic acid and phosgene. Bauer concluded that excessive amounts of phosgene were required for chlorination and the use of this reagent for laboratory preparation of acid chlorides was not practical owing to the necessity for recycling the reagent.

(c) *Properties and Reactions of Acid Chlorides*

The normal aliphatic acid chlorides are generally liquids at room temperature, and possess a pungent odor and fume in contact with air owing

TABLE 115

PHYSICAL PROPERTIES OF THE FATTY ACID CHLORIDES[a]

Chloride	Formula	M.p., °C.	B.p., °C.	d_4^{20}
Ethanoyl (acetyl)	CH_3COCl	−112	51–52	1.104
Propionoyl	C_2H_5COCl	− 94	78–80	1.065
Butyroyl	C_3H_7COCl	− 89	101–102	1.028
Valeroyl	C_4H_9COCl	...	128	1.016^{15}
Caproyl	$C_5H_{11}COCl$	...	152–153	...
Heptanoyl	$C_6H_{13}COCl$	...	175	...
Capryloyl	$C_7H_{15}COCl$	...	195	...
Nonanoyl	$C_8H_{17}COCl$	...	220	...
Capryl	$C_9H_{19}COCl$	...	114^{15}	...
Lauroyl	$C_{11}H_{23}COCl$	− 17	142^{15}	...
Myristoyl	$C_{13}H_{27}COCl$	− 1	168^{15}	...
Palmitoyl	$C_{15}H_{31}COCl$	12	192^{15}	...
Stearoyl	$C_{17}H_{35}COCl$	23	215^{15}	...
Undecenoyl	$C_{10}H_{19}COCl$	...	128.5^{14}	...
Oleoyl	$C_{17}H_{33}COCl$	...	213^{13}	...
Elaidoyl	$C_{17}H_{33}COCl$	...	216^{13}	...
Brassidoyl	$C_{21}H_{41}COCl$	...	...	...

[a] The nomenclature of the acid chlorides is confused by the use of two different suffixes, -yl and -oyl. The first is intended to apply with the common names of the acids (*e.g.*, acetyl, capryl, oleyl, etc.), the other with the Geneva names (*e.g.*, ethanoyl, decanoyl, octadecenoyl, etc.). The Geneva system makes no provision for the use of the -oyl suffix with common names. There is a growing tendency, however, to use the -oyl suffix with the common names of acids, which has been done here with the exception of caproic and capric acids, whose chlorides would be indistinguishable under this system. See paragraph 140 of "Introduction, With Key and Discussion of the Naming of Chemical Compounds for Indexing," *Chem. Abstracts*, **39**, 5891 (1945).

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[66] S. T. Bauer, *Oil & Soap*, **23**, 1–5 (1946).

to their ready hydrolysis in contact with water. Some of their properties are given in Table 115.

Owing to the great lability of the chlorine atom in the acyl chlorides, these substances are useful intermediates in the synthesis of glycerides and in other reactions. The halogen atom is readily replaced by HO, C_2H_5O, NH_2, NHOH, $NHNH_2$, N_3, etc., as indicated in the following reactions of fatty acid chlorides:

(1) $RCOCl + H_2O \longrightarrow RCOOH + HCl$

(2) $RCOCl + HOR \longrightarrow RCOOR + HCl$

(3) $RCOCl + NH_3 \longrightarrow RCONH_2 + HCl$

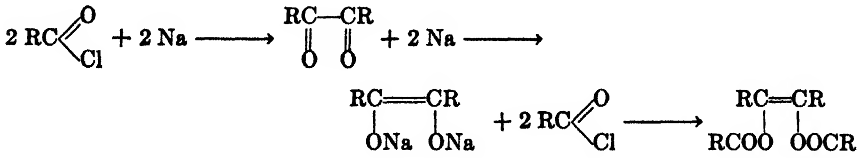
(4) $RCOCl + NH_2R \longrightarrow RCONHR + HCl$

(5) $RCOCl + HNR_2 \longrightarrow RCONR_2 + HCl$

(6) $RCOCl + NaOCOR \longrightarrow RCOOCOR + NaCl$

As indicated by these reactions, it is possible to form esters (*2*), amides (*3*), alkylamides (*4*), dialkyamides (*5*), and anhydrides (*6*) by reaction of acid chlorides and the corresponding alcohol (*2*), amino compound, or salt of a fatty acid (*6*), respectively.

Ralston and Selby[67] investigated the reaction of sodium on the higher aliphatic acid chlorides in ether solution. They found that lauroyl, myristoyl, palmitoyl, and stearoyl chlorides reacted smoothly at the boiling point of ether to give the corresponding diesters of the unsaturated diols in 60% to 70% yields. This observation is contrary to those of previous workers who found that the lower aliphatic acid chlorides yield diacyls (RCOCOR) and that benzoyl chloride yields ethyl benzoate[68] when treated with sodium in anhydrous ether. Ralston and Selby postulated the following mechanism to explain the formation of the diesters of unsaturated diols by the action of sodium on acid chlorides:



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[67] A. W. Ralston and W. M. Selby, *J. Am. Chem. Soc.*, **61**, 1019–1020 (1939).

[68] I. A. Pearl, T. W. Evans, and W. M. Dehn, *J. Am. Chem. Soc.*, **60**, 2478–2480 (1938).

CHAPTER XIV

HYDROGENATION AND HYDROGENOLYSIS

1. Introduction

Hydrogenation reactions are of paramount importance in the chemistry of fats and oils and many of their derived products. Various processes based on these reactions are conducted on a large scale to produce annually millions of pounds of solid or plastic fats from liquid oils for use in products such as shortening, margarine oils, hardened soap stock, and for such purposes as improving the hardness, plasticity, and stability of lard. Hydrogenation is also applied to the reduction of carbonyl groups in fatty acid esters and glycerides to produce fatty alcohols for use as intermediates in the manufacture of detergents, wetting agents, and other products possessing surface-modifying properties.

In the laboratory, hydrogenation processes are applied to saturate the double bonds of unsaturated acids, esters, glycerides, and natural oils; for the reduction of carbonyl groups including reduction of esters to alcohols and the reduction of keto acids to hydroxy and normal acids; for the reduction of hydroxyl groups; and for the preparation of fatty acid amines from nitriles. Hydrogenation involving reduction rather than addition to unsaturated linkages is sometimes referred to as hydrogenolysis to distinguish the two types of reactions.

Various reducing agents and methods are available for accomplishing these reactions, the foremost of which comprises the action of molecular hydrogen in the presence of a suitable catalyst. Other methods involve the use of metals such as sodium and zinc, or agents such as hydrazine, hydriodic acid, etc. The function of sodium, zinc, and other metals is generally to produce nascent or atomic hydrogen by their action on alcohols or weak acids. Certain types of hydrogenation reactions which require high pressures or temperatures when molecular hydrogen is used, proceed smoothly and rapidly at atmospheric pressure and low temperatures in the presence of atomic hydrogen. Consequently, molecular hydrogen in the presence of a catalyst is generally employed industrially, while in the laboratory the use of nascent hydrogen in the absence of a catalyst is quite frequently preferred. However, both practices are carried out in the laboratory and the method used is oftentimes a matter of choice or availability of facilities. In other cases where the structure of a compound is being investigated and preferential action is required, a specific method of reduction may have to be employed, thus precluding the use of less selective methods.

Although reactions involving catalytic hydrogenation of organic substances were known prior to 1897, it was the classical work of Sabatier[1] and his associates which led to the general introduction of this method into industry and in laboratory research. Great impetus was given industrial hydrogenation by the discovery in 1903 by Normann,[2] that liquid marine and vegetable oils could be converted by this method into hard white fats. A year later, Ipatieff discovered that the application of high pressures led to hydrogenation reactions not possible at atmospheric or moderately low pressures. Within a few years following the discoveries of Normann and Ipatieff, most of the useful applications and methods of hydrogenation were brought to a high state of development for both industrial and laboratory use.

It is obvious that a process of such economic importance and practical application as a research tool would result in a flood of publications which has grown beyond all possibility of reviewing and cataloguing. Important applications, especially to the research worker, are often difficult or impossible to locate owing to the fact that they may be described incidentally to an investigation in which it was merely the means of obtaining some intermediate for the preparation of a desired product. Many reviews, as well as monographs, varying from a few to nearly a thousand pages have been written on the subject of catalytic hydrogenation and the reader is referred to them for both historical and practical treatments of the subject. These include the classical work of Sabatier translated by Reid,[1] Ellis's comprehensive survey,[3] and Adkins'[4] practical treatment from the standpoint of the research chemist. Reference should also be made to the reviews of Armstrong and Williams,[5] Wurster,[6] Mitchell,[7] and especially to the critical and practical description of hydrogenation processes by Bailey.[8]

Despite the vast amount of work and the flood of publications, only four catalysts for the reaction of hydrogen have found a permanent place in industry and in the laboratory. These are platinum, palladium, nickel,

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[1] P. Sabatier, *Catalysis in Organic Chemistry.* Trans. by E. E. Reid, Van Nostrand, New York, 1922.

[2] W. Normann, British Pat. 1515 (Jan. 21, 1903). See Herforder Maschinenfett-und Ölfabrik, Leprince Siveke, German Pat. 141,029 (April 4, 1903).

[3] C. Ellis, *Hydrogenation of Organic Substances*, 3rd ed., Van Nostrand, New York, 1930. See H. W. Lohse, *Catalytic Chemistry*, Chemical Pub. Co., Brooklyn, 1945.

[4] H. Adkins, *Reactions of Hydrogen with Organic Compounds over Copper-Chromium Oxide and Nickel Catalysts.* Univ. of Wisconsin Press, Madison, 1937.

[5] E. F. Armstrong and K. A. Williams, *Chemistry & Industry*, **59**, 3–9 (1940); *Chem. Age London*, **41**, 271–272, 285–288 (1939).

[6] O. H. Wurster, *Ind. Eng. Chem.*, **32**, 1193–1199 (1940).

[7] H. R. Mitchell, *Food Manufacture*, **18**, 369–373, 401–404 (1943); *Chem. Age London*, **48**, 471–475, 495–499 (1943).

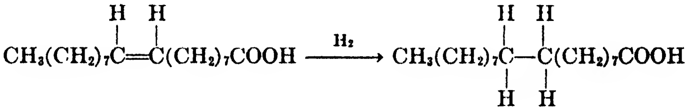
[8] A. E. Bailey, *Industrial Oil and Fat Products.* Interscience, New York, 1945.

and copper chromite, of which only the last two are of primary importance in industry. All of these metals may be treated in various ways to improve their catalytic activity so that the actual number of catalysts in use is considerably larger than the number of metals might indicate. Reaction pressures vary from atmospheric to 400 atmospheres and reaction temperatures from room temperature to 400°C. Generally speaking, the use of higher pressures is preferred to higher temperatures.

For the saturation of double bonds of fatty acids and oils, nickel catalyst, molecular hydrogen, and low temperatures and pressures are generally used; while, for the reduction of carbonyl groups, copper chromite catalyst and moderately high pressures and temperatures are employed industrially and in some laboratory operations. However, the use of sodium and alcohol is much more generally used for the reduction of carbonyl and nitrile linkages on a laboratory scale. The methods of preparation and industrial use of nickel catalysts are described and comprehensively discussed by Bailey,[8] and both nickel and copper chromite catalysts for laboratory use are similarly described and discussed by Adkins[4] and are therefore omitted here.

2. Saturation of Double Bonds by Hydrogenation

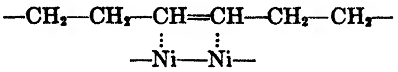
Hydrogenation for the purpose of reducing double bonds consists simply of adding one molecule of hydrogen to each double bond in the compound undergoing reduction to produce a completely or partially saturated product. In the case of oleic acid this reaction consists of the addition of one mole of hydrogen to a molar quantity of the acid to produce a mole of stearic acid according to the following equation:



$$CH_3(CH_2)_7\overset{H}{C}=\overset{H}{C}(CH_2)_7COOH \xrightarrow{H_2} CH_3(CH_2)_7\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}(CH_2)_7COOH$$

This reaction is generally uncomplicated by side reactions since the final product is completely saturated and entirely symmetrical with respect to the orientation of the hydrogen atoms of the methylene groups. Both oleic acid, which has a *cis*-configuration, and elaidic acid, which has a *trans*-configuration, are reduced to the same stearic acid. However, complications arise as soon as a second double bond is present in the molecule which is subjected to reduction and still greater complications arise in the presence of a third or a fourth double bond, a hydroxy or other reducible group.

Despite a vast amount of work on the subject, the exact mechanism of the hydrogenation reaction is not known. A number of theories have been proposed to explain the various steps in the over-all reaction but none of them has been proved unequivocably. It is generally assumed that reaction first occurs between the catalyst and the unsaturated compound to form an adsorption complex or intermediate at the surface of the catalyst. This adsorption complex:



$$\begin{array}{c} -CH_2-CH_2-CH{=}CH-CH_2-CH_2- \\ \vdots \quad \vdots \\ -Ni-Ni- \end{array}$$

then reacts with hydrogen to form the corresponding saturated bond and simultaneously regenerates the catalyst with liberation of heat.

It has been experimentally observed that the addition of hydrogen, short of complete saturation, to polyunsaturated acids or esters produces a variety of end products including so-called iso acids. In order to account for the appearance of these iso acids several theories have been advanced, namely: (*1*) Addition of hydrogen occurs randomly at all of the double bonds of a polyunsaturated acid; (*2*) polyunsaturated acids are hydrogenated preferentially in a progressive or stepwise manner; (*3*) hydrogen is not only added at the double bonds but at high temperatures in heterogeneous media, dehydrogenation also occurs; (*4*) hydrogenation is accompanied by wandering of double bonds; (*5*) any one or all of these reactions may occur simultaneously or successively depending on the conditions of hydrogenation.

Although unequivocal proof for any of these assumptions is lacking, available experimental evidence indicates that certain of them are reasonably valid as indicated in the following discussion.

If one mole of hydrogen added randomly to a mole of linolenic acid, there would be produced a mixture of three isomeric forms of linoleic acid, namely, $\Delta^{9,10,12,13}$-, $\Delta^{12,13,15,16}$-, and $\Delta^{9,10,15,16}$-linoleic acid. If in the course of the hydrogenation geometric isomerization occurred, the number of isomers formed would be correspondingly increased since four geometric isomers are possible for each positional isomer. As will be pointed out later, evidence exists that such geometric isomers are actually formed during the hydrogenation of the esters or acids derived from certain oils.

Random addition of a second molecule of hydrogen to the three positionally isomeric linoleic acids mentioned above would yield three positionally isomeric oleic acids, namely, $\Delta^{9,10}$-, $\Delta^{12,13}$-, and $\Delta^{15,16}$-oleic acid, and since each of these can occur in either *cis*- or *trans*-modifications a total of six isomeric oleic acids are therefore possible. Thus, on the assumption that hydrogen adds in a random or statistical manner in the partial hydrogenation of a fat containing linolenic acid, it is theoretically possible to have twelve linoleic acids and six oleic acids in the mixture.

In contrast to the assumption of random addition, it has been assumed that the hydrogen adds preferentially to a particular double bond at such a rate (or for some other reason) that this bond is completely saturated in a large number of molecules before a second bond is attacked. This preferential addition to a specific double bond reduces the number of isomers formed from linolenic acid to one specific positionally isomeric or, if inversion also occurs, to two geometrically isomeric linoleic acids. Further hydrogenation, if also specific, then leads to only two oleic acids, one *cis* and the other *trans*.

The third assumption to be considered is the preferential hydrogenation of specific bonds to produce relatively simple mixtures of the reduction products, but accompanied by dehydrogenation to produce unsaturated acids similar to those which would be produced by purely random addition of hydrogen.

Experimental evidence appears to indicate that all of the double bonds in the hydrocarbon chain of unsaturated fatty acids are dissimilar with respect to their energy of activation and hence, rates of reactivity, since they apparently do not add hydrogen with the same ease. On the basis of this evidence it appears that the saturation of double bonds in long chain fatty acids occurs preferentially. This preferential addition of hydrogen to specific double bonds is sometimes referred to as *selectivity*, although the word has also been applied to the relative production of geometrical isomers of the *cis*-*trans*-type.

Selectivity has also been used to refer to preferential hydrogenation as a function of molecular weight. Ueno[9] found that the higher molecular weight fatty acids (C_{20} and C_{22}) of sardine oils are more slowly reduced than those of lower molecular weight (C_{18}), and he therefore considers the hydrogenation reaction as being selective with respect to the reduction of lower as compared to higher molecular weight acids of the same degree of unsaturation.

Whenever the subject of selective hydrogenation is discussed, reference is invariably made to the formation of iso acids, especially isolinoleic and iso-oleic acids. Oftentimes it is not clear whether the authors refer to positional isomers or geometric isomers or to both.

This lack of specificity with reference to the kind of iso acids which are meant has led to much confusion. Unfortunately the various positional and geometric isomers which are probably produced on partial hydrogenation of a highly unsaturated acid have seldom been prepared in pure form and therefore their properties have not been determined.

$\Delta^{9,10}$-Oleic and elaidic acids have been prepared in pure form and their melting points, solubilities, and other properties of the acids, esters, and common salts are known. On the other hand, little or nothing is known concerning the corresponding $\Delta^{8,9}$- and $\Delta^{10,11}$-oleic acids. It may be surmised that the *cis*-forms of these positional isomers are liquids like $\Delta^{9,10}$-oleic acid and that their properties are rather similar. The corresponding *trans*-acids are probably solids and their properties similar to elaidic acid.

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[9] S.-I. Ueno, *J. Soc. Chem. Ind. Japan*, **28**, 1235–1239 (1925).

It may be further surmised that ordinary oleic, *cis*-$\Delta^{8,9}$-oleic, and *cis*-$\Delta^{10,11}$-oleic acids add halogens and hydrogen under similar conditions at about the same rates and that their lead salts have relatively similar solubilities; also that ordinary elaidic acid, *trans*-$\Delta^{8,9}$-oleic, and *trans*-$\Delta^{10,11}$-oleic acids yield insoluble lead salts and react with halogens and hydrogen quite similarly. If these assumptions are correct, the *cis*- and *trans*-acids can be separated and distinguished from each other as a group, but the components of each group will be difficult or impossible to separate and identify.

Similar assumptions may be made with regard to ordinary linoleic and linolelaidic acids, *i. e.*, all of the *cis-cis*-acids having two unconjugated double bonds in the vicinity of those present in ordinary linoleic acid will be liquids having soluble lead salts and other similar properties. The corresponding linolelaidic or *trans-trans* positional isomers may be expected to have higher melting points and somewhat less soluble lead salts. The isomerization of the linoleic acids is, however, much more complicated because two other geometric isomers are possible for each positional isomer, namely a *cis-trans*- and a *trans-cis*-isomer. It would not be unexpected if the chemical and physical properties of these two geometric isomers were found to be intermediate between those of the *cis-cis*- or ordinary linoleic acid and the *trans-trans*- or linolelaidic acid.

The difficulties of distinguishing between the various possible positional and geometric isomers of linoleic acid which may be postulated as products of hydrogenation of more highly unsaturated acids are almost insuperable in the present state of development of our analytical methods. However, the above possibilities should be borne in mind in any discussion of selective hydrogenation until unequivocal proof is at hand regarding the specific isomers which are actually present in any given type of hydrogenated oil.

(a) *Hydrogenation of Linoleic and Other Polyethenoid Acids*

The selectivity of the hydrogenation reaction was first pointed out in 1917 by Moore, Richter, and Van Arsdel,[10] and was confirmed by Richardson, Knuth, and Milligan,[11] Hilditch and Moore,[12] and others.[13] According to these early workers linoleic acid, *cis-cis*-$\Delta^{9,10,12,13}$-octadecadienoic acid, or its esters, is practically completely converted to oleic acid or its esters before saturation of the second double bond occurs. Hilditch and Vidyarthi[14] state that on hydrogenation of methyl linoleate or methyl linolenate "no

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[10] H. K. Moore, G. A. Richter, and W. B. Van Arsdel, *J. Ind. Eng. Chem.*, **9**, 451–462 (1917).

[11] A. S. Richardson, C. A. Knuth, and C. H. Milligan, *Ind. Eng. Chem.*, **16**, 519–522 (1924); **17**, 80–83 (1925).

[12] T. P. Hilditch and C. W. Moore, *J. Soc. Chem. Ind.*, **42**, 15–17T (1923).

[13] D. R. Dhingra, T. P. Hilditch, and A. J. Rhead, *J. Soc. Chem. Ind.*, **51**, 195–198T (1932). See T. P. Hilditch and A. J. Rhead, *ibid.*, **51**, 198–202T (1932); T. P. Hilditch and E. C. Jones, *ibid.*, **51**, 202–203T (1932).

[14] T. P. Hilditch and N. L. Vidyarthi, *Proc. Roy. Soc. London*, **A122**, 563–570 (1929).

fully-saturated ester is produced until nearly 90% of the polyethylenic ester has been transformed into monoethylenic compounds (*i. e.*, methyl oleate and iso-oleates)." Hilditch and Moore[12] have shown this to be true for a considerable number of natural oils as well as the monoesters prepared from them. This probability was also pointed out by Armstrong and Hilditch[15] as early as 1919.

Such specific action is difficult to explain except on the assumption that a preferential orientation occurs at the instant the catalyst–reactant complex is formed at the catalyst surface which involves only the 12,13-double bond. But, if the complex dis-associates after saturation of the double bond, it is difficult to understand why no new complex would be formed involving the monoethenoid compound until after all, or nearly all (90%), of the dienoic acid is hydrogenated to the monoethenoid stage. This preferential or selective action appears to be independent of the nature of the catalyst as it has been observed to occur with a variety of catalysts and conditions of hydrogenation. For example, Suzuki and Inoue[16] found that methyl linoleate was reduced in two stages when hydrogenated in tetralin in the presence of palladium–barium sulfate catalyst. After one mole of hydrogen was consumed the product was subjected to oxidation whereupon fission occurred at the 9,10-double bond to produce pelargonic acid, $CH_3(CH_2)_7COOH$, and azelaic acid, $COOH(CH_2)_7COOH$.

These authors obtained identical results in the case of an isolinoleic acid isolated from silk worm pupa.[17] This acid was shown to be a $\Delta^{9,10,12,13}$-octadecadienoic acid but it was not identical with ordinary linoleic acid since on bromination it gave no solid tetrabromide. Nevertheless, the partially reduced isolinoleic acid gave pelargonic and azelaic acids when oxidatively cleaved at the remaining double bond. The velocity of the hydrogenation reactions of linoleic and the isolinoleic acids were measured and it was found that in both stages normal linoleic acid hydrogenated more rapidly than the iso acid. It should be borne in mind that oxidative cleavage provides no information regarding the geometric configuration of the acid, and all four geometric isomers of ordinary linoleic acid would give the same oxidation products on complete fission.

It has been postulated that if linolenic acid, $\Delta^{9,10,12,13,15,16}$-octadecatrienoic acid, is substituted for linoleic acid in the reaction, saturation of the 15,16-double bond occurs almost exclusively prior to addition at either the 12,13- or the 9,10-double bonds. Moore[18] found that catalytic hydrogenation of tung oil or the elaeostearic acid thereof resulted in a decrease of the maximum absorption at 2700 Å. and a corresponding increase in the ab-

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[15] E. F. Armstrong and T. P. Hilditch, *Proc. Roy. Soc. London*, **A96**, 137–146 (1919).
[16] B. Suzuki and Y. Inoue, *Proc. Imp. Acad. Tokyo*, **6**, 266–268 (1930).
[17] Y. Inoue and B. Suzuki, *Proc. Imp. Acad. Tokyo*, **7**, 15–18 (1931).
[18] T. Moore, *Biochem. J.*, **33**, 1635–1638 (1939).

sorption at 2300 Å. This change in absorption is produced by a disappearance of triene conjugation and an increase in diene conjugation, which can occur only as a result of the saturation of the 9,10- or 13,14-double bond of eleaostearic acid. Saturation of the middle or 11,12 double bond would produce an acid absorbing at neither 2700 Å. nor 2300 Å.

In contrast to the behavior of elaeostearic acid, van der Veen[19] reported that the hydrogenation of methyl linolenate with one mole of hydrogen at 180°C. and 1.0 to 1.5% of nickel–kieselguhr catalyst (0.2% to 0.3% nickel) resulted in addition first at the 12,13- or middle double bond to form $\Delta^{9,10,15,16}$-linoleic acid. This acid isomerized in part to form some $\Delta^{10,11,14,15}$-linoleic acid. Subsequent hydrogenation with a second mole of hydrogen resulted in the formation of $\Delta^{10,11}$-elaidic acid, several positionally isomeric ($\Delta^{8,9}$- and $\Delta^{10,11}$-oleic) acids, and stearic acid.

The composition of the reaction mixture and constitutions of the component acids were established by determination of iodine and thiocyanogen values, the percentage of saturated acids by the Bertram oxidation method, and by ozonization. The formation of the end products of hydrogenation were explained by assuming that the $\Delta^{9,10,15,16}$-linoleic acid which first formed underwent partial isomerization to form some $\Delta^{10,11,14,15}$-linoleic acid. The latter product then underwent hydrogenation at the 14,15-double bond and simultaneous elaidinization to form $\Delta^{10,11}$-elaidic acid. The $\Delta^{9,10,15,16}$-linoleic acid underwent hydrogenation at the 15,16-double bond and shifting of the 9,10-double bond to the 8,9- and, to a lesser extent, to the 10,11-position without formation of normal oleic acid.

The conclusions of van der Veen were substantiated in part by Lemon[20] who showed by alkali isomerization and absorption spectra techniques that linolenic acid on partial hydrogenation produced $\Delta^{9,10,15,16}$-linoleic acid whose double bonds could not be shifted to form a conjugated system.

The observations of van der Veen and Lemon were confirmed and extended by Bailey and Fisher,[20a] who hydrogenated cottonseed, soybean, and linseed oils under selective conditions, after which they determined the composition of the products in terms of the component fatty acids. The data thus obtained were applied in calculating the relative reactivities of the component fatty acids toward hydrogenation, which were found to be in the ratios of the following whole numbers: oleic acid, 1; iso-oleic acid, 1; isolinoleic ($\Delta^{9,10,15,16}$-linoleic) acid, 3; linoleic acid, 20; linolenic acid, 40.

Gunstone and Hilditch[20b] and Hilditch[20c] reported that the relative rates of oxidation of methyl oleate, linoleate, and linolenate were approximately in the ratio of 1:12:25, and Hilditch[20c] pointed out that in both hydro-

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[19] H. van der Veen, *Chem. Umschau Fette Öle Wachse Harze*, **38**, 89–96, 219 (1931).
[20] H. W. Lemon, *Can. J. Research*, **F22**, 191–198 (1944).
[20a] A. E. Bailey and G. S. Fisher, *Oil & Soap*, **23**, 14–18 (1946).
[20b] F. D. Gunstone and T. P. Hilditch, *J. Chem. Soc.*, **1945**, 836–841.
[20c] T. P. Hilditch, *Nature* **157**, 586 (1946).

genation and oxidation the effect of the $\mathrm{-CH{:}CHCH_2CH{:}CH-}$ group is to increase the rate of reaction 12–20 times over that for the monoethenoid system, and that the introduction of a second reactive $\mathrm{-CH_2}$ group doubled the rate again.

Much less is known concerning the hydrogenation of acids containing more than three double bonds. According to Ubbelohde and Savanoe,[21] clupanodonic acid absorbs sufficient hydrogen to pass directly to linoleic acid without the intermediate formation of linolenic acid. On bromination of progressively hydrogenated whale oil, these authors[22] were able to isolate octabromides and tetrabromides from the hardened oil but did not observe the formation of any hexabromides.

Toyama and Tsuchiya[23] observed that the methyl esters of the highly unsaturated acids obtained from Japanese sardine oil were also preferentially and stepwise hydrogenated in the presence of nickel under ordinary pressure and at temperatures of 185° to 210°C. The original mixed esters of fatty acids containing up to four double bonds had an iodine value of 350.6 and the acids gave 127.1% of ether-insoluble bromides. During the course of the hydrogenation in which the iodine value of the acids was reduced to 173.1, the amount of ether-insoluble bromides was reduced to 1.67% and still later when the iodine value was reduced to 134.9 no ether-insoluble bromide was found. No solid acids were formed up to this point but immediately afterward solid fatty acids were formed in substantial amounts. It is thus apparent that, up to the point of disappearance of acids giving an ether-insoluble bromide, only hydrogenation of the polyethenoid and diethenoid (linoleic) acids occurred. Following the completion of this stage of the hydrogenation, the diethenoid acids were then further hydrogenated to monoethenoid (oleic) acids, and no doubt to saturated acids.

As mentioned above, solid acids formed rapidly at or just below an iodine value of 134.9 and evidence was obtained that at least part of these acids contained two double bonds probably as a result of the formation of geometric isomerides having a *trans*-configuration at one or both of the double bonds.

(*b*) *Hydrogenation of Oleic and Other Monoethenoid Acids*

Formation of Positional Isomers.—Pigulevskiĭ and Artamonov,[24] using platinum black as a catalyst, hydrogenated a series of octadecenoic (oleic) acids in which the double bond occupied different positions in the hydrocarbon chain. They found that the highest rate of hydrogenation occurred

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[21] L. Ubbelohde and T. Savanoe, *Z. angew. Chem.*, **32**, I, 257–262, 269–272, 276–280 (1919).

[22] L. Ubbelohde and T. Savanoe, *Seifensieder-Ztg.*, **46**, 681 (1919).

[23] Y. Toyama and T. Tsuchiya, *J. Soc. Chem. Ind. Japan*, **28**, 1079–1087 (1925).

[24] G. V. Pigulevskiĭ and P. A. Artamonov, *J. Gen. Chem. U.S.S.R.*, **12**, 510–517 (1942).

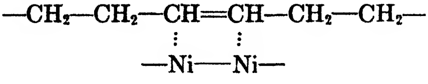
with the double bond in the 9,10-position and the lowest rate when the bond was in the 2,3-position, which is in accord with the observation of Ponzio and Gastaldi[25] and others regarding the relative rates of absorption of halogens by these double bonds.

It has been held by various investigators that hydrogenation is probably accompanied by dehydrogenation, at least under certain conditions, primarily because hydrogenation–dehydrogenation is an equilibrium reaction which, however, is generally carried out in such a manner that the equilibrium is always far to the right. In fact, Sabatier, on purely theoretical grounds, concluded that the action of nickel catalyst is reversible and confirmed this conclusion experimentally. Subsequent investigators have contributed confirmatory evidence relative to the dehydrogenation reaction.

As early as 1921, Levey[26] indicated in a patent that the dehydrogenation of oleic acid was entirely practical but Suzuki and Kurita[27] were unable to substantiate this claim regardless of the type of catalyst or reaction conditions which were used. A year later, Hilditch and Vidyarthi[28] found that hydrogenation of methyl oleate, methyl palmitoleate, and methyl erucate, when carried out to reduce the iodine value about 30%, resulted in the formation of both positional and geometric isomers. Hydrogenation of methyl oleate at different temperatures (217–220°C. and 114–118°C.) gave, in addition to some elaidic acid, both $\Delta^{8,9}$- and $\Delta^{10,11}$-oleic acids; methyl palmitoleic acid gave $\Delta^{8,9}$- and $\Delta^{10,11}$-octadecenoic acids; and methyl erucate gave $\Delta^{12,13}$- and $\Delta^{14,15}$-docosenoic acids. These isomeric acids appeared to be formed in apparently equal amounts in each case.

These observations are explained by Hilditch and Vidyarthi[28] as follows:

> “If, in the association of an ethylenic linkage with nickel



$$\begin{array}{c}—CH_2—CH_2—CH{=}CH—CH_2—CH_2— \\ \vdots \qquad \vdots \\ —Ni—Ni—\end{array}$$

> followed by union with hydrogen and formation of the corresponding saturated compound, the possibility of reversal of the process (dehydrogenation) before the saturated compound leaves the catalyst surface is considered, it appears most likely that such dehydrogenation will occur in the same position as that occupied by the original double bond, and lead to the formation of the original ethylenic compound or its geometrical isomeric form. Alternately, dehydrogenation may ensue on either side of either of the carbon atoms which, as components of the original ethylenic linkage, were brought into association with the catalyst.
>
> “We are thus led to ascribe the formation of both geometrical and structural

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[25] G. Ponzio and C. Gastaldi, *Gazz. chim. ital.*, **42**, II, 92–95 (1912).

[26] H. A. Levey, U. S. Pat. 1,374,589 (April 12, 1921).

[27] T. Suzuki and T. Kurita, *Sci. Papers Inst. Phys. Chem. Research Tokyo*, Suppl., **9**, 5–6 (1928).

[28] T. P. Hilditch and N. L. Vidyarthi, *Proc. Roy. Soc. London*, **A122**, 552–563, 563–570 (1929).

isomeric forms of oleic acids during hydrogenation (dehydrogenation) prior to the dis-association (or *desorption*) of the freshly-formed saturated compound from the catalyst surface."

Mazume[29] investigated the hydrogenation of the methyl esters of oleic and linoleic acids and concluded that in the hydrogenation of methyl oleate a large amount of iso-oleic acid was formed at the initial stage of hydrogenation and the iso-oleic acid thus formed was gradually transformed into oleic acid by further hydrogenation. Here again it may be assumed that hydrogenation–dehydrogenation occurred during the course of which equilibrium mixtures of positionally and geometrically isomeric oleic acids were formed.

Gutmann[30] found that at low temperatures dehydrogenation of ethyl oleate did not occur, but that it did occur at high temperatures (300°C.). He also confirmed the selective or progressive hydrogenation of linoleic and linolenic acids and the formation of solid iso acids.

Tzonev and Yavnel[31] appear to have been the first to demonstrate that dehydrogenation of a fat actually occurs under conditions similar to hydrogenation but in the absence of hydrogen. When sunflowerseed oil (iodine value, 131.4) was subjected to dehydrogenation for four hours at temperatures of 270°, 300°, and 320°C. in the presence of nickel–mercury catalyst in an atmosphere of carbon dioxide, the iodine values increased to 142, 145, and 144.4, respectively.

Tyutyunnikov and Kholodovskaya,[32] on the basis of hydrogenation of sunflowerseed oil, concluded that unsaturated solid acids were not formed by desaturation of stearic acid but this type of dehydrogenation would probably not occur in the same manner as in the case of an unsaturated compound, *i. e.*, immediately following the hydrogenation of the catalyst–unsaturated acid complex. These authors concluded that two-thirds of the linoleic acid in sunflowerseed oil was reduced in 90 minutes to solid $\Delta^{12,13}$-oleic acid. To explain these reactions it is necessary to assume that the 9,10-double bond is preferentially reduced and that simultaneously the 12,13-double bond is isomerized to give a solid *trans*-oleic acid. In order to explain the high proportion of liquid oleic acid in the latter stages of hydrogenation, the authors concluded that the solid $\Delta^{12,13}$-oleic acid is converted to liquid $\Delta^{9,10}$-oleic acid, thus necessitating a shift of the double bond and simultaneous isomerization back to a *cis*-configuration.

Zinov'ev and Kurochkina[33] observed that the maximum content of iso-

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[29] T. Mazume, *J. Soc. Chem. Ind. Japan*, **31,** 470–472 (1928); Suppl. binding, 112–113B.

[30] R. Gutmann, *Masloboĭno Zhirovoe Delo*, **1931,** No. 8–9, 32–36.

[31] N. Tzonev and N. Yavnel, *Masloboĭno Zhirovoe Delo*, **1930,** No. 62–63, 19.

[32] B. Tyutyunnikov and R. Kholodovskaya, *Masloboĭno Zhirovoe Delo*, **1929,** No. 5, 53–61.

[33] A. Zinov'ev and N. Kurochkina, *Masloboĭno Zhirovoe Delo*, **11,** 308–312 (1935).

oleic acid formed on hydrogenation of sunflowerseed oil occurred when one-half the linoleic acid had been reduced and concluded, therefore, that at this point for each molecule of linoleic acid which had been reduced to $\Delta^{9,10}$-oleic acid another molecule of linoleic acid had also been reduced to iso-$\Delta^{12,13}$-oleic acid.

Forbes and Neville[34] investigated the liquid phase dehydrogenation of oleic acid using different concentrations of Raney nickel and freshly precipitated chromic oxide. The use of the latter catalyst produced a product having about 3% greater unsaturation than the original acid. Vapor phase experiments with copper gauze as catalyst and temperatures up to 360°C. were unsuccessful, but when freshly precipitated chromic oxide on coke was used, the unsaturation was increased 9%. When the oleic acid was first heated with 1 to 2% of sulfur and the heating continued at 200–250°C. in the presence of sodium acid sulfate, hydrogen sulfide was evolved. When oleic acid was heated for 1 to 1.5 hours with 1% of sulfur, the unsaturation increased 10.5%; with 2% sulfur under the same conditions unsaturation increased 12.5%.

Although the evidence for the dehydrogenation of unsaturated acids is not indisputable, it does point to the possibility that hydrogenation-dehydrogenation to form positional isomers may occur at any double bond involved in the hydrogenation of mono- and polyunsaturated acids and esters. The importance of the dehydrogenation reaction varies with the degree of hydrogenation which is desired, *i. e.*, with the iodine value of the final product. If the hydrogenation is carried to complete saturation all of the newly formed, as well as the original, double bonds will be saturated. However, if the hydrogenation is stopped when the unsaturated acids have all been converted to oleic acids there will be present in addition to normal oleic acid some positional iso-oleic acids, or if hydrogenation is stopped while linoleic acid is present there will also be present variable quantities of positional iso-linoleic acids. Some of these positional isomers are probably formed as a result of dehydrogenation and some as a result of random addition of hydrogen at the double bonds of polyunsaturated acids.

Formation of Geometric Isomers.—It has been unequivocally established that partial hydrogenation of mono- as well as polyunsaturated acids is accompanied by the formation of solid unsaturated isomers. Moore,[35] as early as 1919, hydrogenated ethyl oleate with palladium and nickel catalysts at various temperatures and found that both liquid and solid oleic acids were produced. He concluded that solid iso-oleic acid was a mixture of $\Delta^{9,10}$-, $\Delta^{10,11}$-, and $\Delta^{11,12}$-iso-oleic acids and it is more than probable that they were in each case *trans*-isomers. On the basis of the observation that elaidic

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[34] W. C. Forbes and H. A. Neville, *Ind. Eng. Chem.*, **32**, 555–558 (1940).

[35] C. W. Moore, *J. Soc. Chem. Ind.*, **38**, 320–325T (1919).

acid on hydrogenation produced liquid oleic acid, Moore concluded that hydrogenation caused a reversion from the *trans*- to the *cis*-form and it is probable that positional isomers were also produced at the same time.

The formation of solid iso-oleic acid during partial hydrogenation of ordinary oleic acid can scarcely be explained on any assumption other than that of dehydrogenation, probably by some such mechanism as has been suggested by Hilditch and Vidyarthi.[28] On theoretical grounds the formation of solid iso-oleic acid by hydrogenation of ordinary linoleic acid appears to be the result of the same mechanism. Since ordinary linoleic acid possesses a *cis*-*cis*-configuration, hydrogenation of either double bond would produce oleic acids also possessing a *cis*-configuration and they should be liquids instead of solids. The liquid acids could then be converted to solid *trans*-acids by subsequent hydrogenation-dehydrogenation.

Kaufmann and Hansen-Schmidt[36] attempted to determine the nature of the addition of hydrogen in peanut and sunflowerseed oils during hardening by determining at intervals during hydrogenation the iodine and thiocyanogen values of the oils and of the separated acids. They concluded that hardening resulted primarily from the formation of glycerides of higher melting isomeric oleic acids rather than from the formation of saturated acids which remained practically constant throughout the process. The percentage of oleic acid glycerides and its isomers increased from 61.2 to 83.8 while the percentage of glycerides of linoleic acid were reduced from 19.2 to 0. The oleic acid glycerides amounted to 51%, or 10% less than the original oil. Glycerides of solid isomeric oleic acids amounted to 32.8% and saturated acid glycerides to 16.5%. These results seem to constitute ample evidence of the inversion of normal oleic acid to solid iso-oleic acid. The reduction of normal oleic acid glycerides to a value 10% less than in the original oil without an increase in the saturated acids can only be explained by their isomerization to solid oleic acid glycerides.

Similar results were reported by Ubbelohde and Savanoe[21] using less accurate methods than those employed by Kaufmann. Waterman and Bertram[37] applied the same analytical methods used by Kaufmann to an investigation of hydrogenated soybean oil (iodine value 133.7, saturated acids 14%) and found a constant increase in the saturated fatty acids as the iodine value decreased from 103.4 (17% saturated acids) to 61.9 (33.5% saturated acids).

The catalytic hydrogenation of cottonseed and peanut oils was investigated by Bailey and co-workers[38] with respect to the factors influencing the formation of solid iso-oleic acid. The factors included temperature, pressure of hydrogen, degree of agitation, and the concentration and nature

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[36] H. P. Kaufmann and E. Hansen-Schmidt, *Ber.*, B60, 50–57 (1927).
[37] H. I. Waterman and S. H. Bertram, *J. Soc. Chem. Ind.*, 48, 79–80T (1929).
[38] A. E. Bailey, R. O. Feuge, and B. A. Smith, *Oil & Soap*, 19, 169–176 (1942).

of the nickel catalyst. The following conclusions were drawn by the authors from forty-one separate hydrogenation experiments.

> "The formation of stearic acid was found to be repressed and the formation of *iso-oleic* acid simultaneously favored by increasing the temperature, increasing the catalyst concentration, decreasing the pressure, and decreasing the agitation.
>
> "The nature of the nickel catalyst, as influenced by its method of preparation, may have a large effect on the composition of the hydrogenated product. One of the nickel catalysts investigated formed excessive amounts of iso-oleic acid without being correspondingly selective.
>
> "In the hydrogenation of cottonseed oil, within a comparatively wide range of conditions, the production of total solid acids with a given catalyst is relatively constant, since the conditions leading to the formation of stearic and iso-oleic acids are mutually exclusive. Extremes in either direction, however, lead to the production of excessive amounts of total solid acids."

The amounts of both normal and iso-oleic acids produced on hydrogenation of cottonseed oil varied over a wide range but in no case was the normal oleic acid found to be less than in the original oil as was observed by Kaufmann and Hansen-Schmidt. However, Bailey and co-workers did not carry their hydrogenation to the complete disappearance of linoleic acid although in some cases only 2% to 3% of this acid remained.

In a considerable number of experiments it was observed that linoleic acid was converted to normal and solid iso-oleic acids in a ratio of 1:1, but other ratios such as 2:1 and 3:1 were also observed.

(*c*) *Hydrogenation of Glycerides*

A complicating factor in the *selective* principle of hydrogenation which is fairly well established in the case of monoesters is the point of attachment of the unsaturated acid to the glycerol molecule in the case of a natural oil. In general the fatty acid attached at the β-position of the glycerol molecule is less reactive than that attached at the α- or α′-position. Whether this lesser activity has any marked influence on the hydrogenation of the unsaturated acid attached at the β-position is not known with certainty.

It is possible that in the case of a triglyceride containing oleic, linoleic, and linolenic acids, the selectivity with respect to hydrogenation of the most highly unsaturated acid, followed by the next most highly unsaturated acid, etc., might be appreciably altered as compared to the corresponding monoesters both as to the particular acid which is first attacked and the position of the first double bond to be saturated. For example, linolenic acid attached at the β-position may be less readily hydrogenated than linoleic acid in the α-position, or linoleic acid in the β-position may be less readily hydrogenated than oleic acid in the α-position.

Hilditch and Paul[39] summarize the problem as follows:

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[39] T. P. Hilditch and H. Paul, *J. Soc. Chem. Ind.*, **54**, 336–338T (1935).

> "... the alterations in component glycerides during hydrogenation of a fat are the resultant of a number of factors, and the changes in question are not so simple in character as may appear at first sight. The glyceride structure of a hydrogenated fat depends, in fact, on (*a*) the glyceride structure of the original fat, (*b*) the manner in which the fatty acid radicals *per se* are affected during hydrogenation (*i. e.*, preferential hydrogenation of linoleic to oleic, etc.), and (*c*) the manner in which mixed glycerides of different configuration behave towards catalytic hydrogenation (*i. e.*, the apparent reluctance with which an unsaturated β-acyl group is hydrogenated in comparison with an unsaturated α-acyl group in the glyceride molecule)."

Experimental evidence adduced by Hilditch and co-workers,[40–45] while throwing some light on the problem does not provide a quantitative answer to the problem if indeed such is at all possible.

(*d*) *Conjugated Hydrogenation*

The term conjugated hydrogenation has been used to refer to a form of catalytic hydrogenation-dehydrogenation involving the use of a hydrogen donor and an unsaturated substance to be reduced. The reaction, which is probably molecular in nature, results from the direct transfer of hydrogen from an alcohol such as ethanol or propanol to the unsaturated compound with the formation of the corresponding aldehyde. Methanol is not reactive but any higher alcohol may be used. The reaction may be represented as occurring in accordance with the following equation:

$$CH_3(CH_2)_2OH + CH_3(CH_2)_nCH{:}CH(CH_2)_nR \longrightarrow CH_3CH_2CHO + CH_3(CH_2)_nCH_2CH_2(CH_2)_nR$$

The process appears to have received little attention outside of Russia where it has been systematically investigated principally by Lyubarskiĭ and co-workers.[46,47] As in the case of hydrogenation with molecular hydrogen, a nickel catalyst is employed at elevated temperature. The reaction with an alcohol as a source of hydrogen is apparently much more rapid than when molecular hydrogen is used. Under specified conditions, the same degree of hydrogenation is attained in one hour at 220°C. as in three hours at 200°. At 250° the same degree of hydrogenation is obtained in 15 minutes as at 200° in six hours. With alcohol as a source of hydrogen, the iodine number of cottonseed oil could not be reduced below 64 to 67, ir-

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[40] T. P. Hilditch and E. C. Jones, *J. Chem. Soc.*, **1932,** 805–820.
[41] T. P. Hilditch and W. J. Stainsby, *Biochem. J.*, **29,** 90–99 (1935).
[42] A. Banks, H. K. Dean, and T. P. Hilditch, *J. Soc. Chem. Ind.*, **54,** 77–82T (1935).
[43] T. P. Hilditch and H. Paul, *J. Soc. Chem. Ind.*, **54,** 331–336T, (1935).
[44] W. J. Bushell and T. P. Hilditch, *J. Chem. Soc.*, **1937,** 1767–1774.
[45] T. P. Hilditch, M. B. Ichaporia, and H. Jasperson, *J. Soc. Chem. Ind.*, **57,** 363–368T (1938).
[46] E. I. Lyubarskiĭ, *J. Applied Chem. U.S.S.R.*, **5,** 1025–1045 (1932).
[47] V. A. Rush, I. L. Dvinyaninkova, and E. I. Lyubarskiĭ, *J. Applied Chem. U.S.S.R.*, **10,** 702–708 (1937).

respective of the excess of ethanol over that required by theory or of catalyst above 0.9%.

The nature of the catalyst has a marked effect on the degree of destruction of the aldehyde which is formed on dehydrogenation of the alcohol as indicated in Table 116. In the case of conjugated hydrogenation, there can be no doubt of the hydrogenation-dehydrogenation nature of the reaction and Lyubarskiĭ has shown that the two reactions are balanced at the critical hydrogenation temperature. It may also be noted from Table 116 that the process is highly selective with respect to the formation of iso-oleic acid which seems to be further evidence that iso-oleic acid originates primarily as a result of a dehydrogenation reaction.

TABLE 116

CONJUGATED HYDROGENATION OF SUNFLOWERSEED OIL WITH PROPANOL AT 260°C. FOR FIFTEEN MINUTES

Composition of product	Type of catalyst	
	Unsupported nickel	Nickel on kieselguhr
Saturated acids, %	12.5–12.8	12.8–14.8
Oleic acid, %	50.8–54.5	53.2–56.3
Iso-oleic acid, %	33.1–27.4	22.0–26.8
Linoleic acid, %	3.6–5.3	4.7–10.3
Aldehyde destroyed, %	35.7	16.8

3. Reduction of Carbonyl Groups

(a) *Reduction of Fatty Esters to Alcohols*

Prior to 1903, four methods were available for the production of primary aliphatic alcohols by means other than distillation of wood and fermentation, both of which furnish only the lower members of the series, *e. g.*, methyl, ethyl, propyl, isobutyl, and isoamyl alcohols. Two of the four methods are those of Wurtz and of Friedel, both of which involve the use of the acid corresponding to the desired alcohol. The other two methods employ a lower homolog of the alcohol desired.

The Wurtz method involves reduction with sodium amalgam of the corresponding aldehyde obtained by the calcination of calcium formate and the calcium salt of another acid. The second method involves reduction by sodium amalgam or zinc–copper couple of the chloride or anhydride of the corresponding acid. These methods are tedious and give poor yields of the desired alcohols. The third method, which is due to Guerbet,[48]

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[48] M. Guerbet, *Compt. rend.*, **128**, 511–513, 1002–1004 (1899); **133**, 1220–1222 (1901); **134**, 467–469 (1902); *Bull. soc. chim.* **21**, 487–489, 489–491 (1899); **25**, 300–302 (1901); **27**, 578–581, 581–584, 1034–1036, 1036–1038 (1902).

consists in condensing, at high temperature and in the presence of sodium, two molecules of the same or different alcohols to produce the desired higher alcohol. The fourth method, namely, that of Grignard and Tissier,[49] consists in the condensation of trioxymethylene (metaformaldehyde) with derivatives of organomagnesium.

In 1903, Bouveault and Blanc[50] described a method which made it possible to prepare moderately large quantities of higher aliphatic alcohols by the reduction of the corresponding aliphatic esters with sodium and ethanol. Ten years later, Chablay[51] showed that the esters of aliphatic acids could be reduced to the corresponding alcohols by treatment with metal ammoniums, NH_3K and NH_3Na.

In 1931, Adkins and co-workers,[52,53] Schrauth, Schenck, and Stickdorn,[54] Normann,[55] and others described processes for accomplishing the same result by the catalytic reduction of ethyl esters at moderately high temperatures (200° to 250°C.) and correspondingly high pressures in the presence of copper-chromium oxide. These two methods have made it possible to obtain on a laboratory and industrial scale practically any desired aliphatic alcohol from the corresponding fatty acid ester.

(*b*) *Reduction with Sodium and Alcohol*

According to Bouveault and Blanc, ethyl esters of fatty acids are reduced with sodium and absolute ethanol to form primary alcohols according to the equations which they stated to be as follows:

$$RCOOC_2H_5 + 2\ H_2 \longrightarrow RCH_2OH + C_2H_5OH$$

$$RCOOC_2H_5 + 4\ Na + 3\ C_2H_5OH \longrightarrow RCH_2OH + 4\ C_2H_5ONa$$

Methanol or amyl alcohol can be substituted for ethanol. Yields up to 80% and higher were claimed under the best conditions in the case of normal alcohols. The method was found to be applicable to the preparation of secondary and tertiary alcohols from the corresponding acids, and even aromatic acids of the phenyl acetic series as well as normal aliphatic amides were observed to undergo reduction to form corresponding alcohols.

Two methods were originally described by the authors of which the preferred procedure comprises solution of the ester to be reduced in three to four times its weight of absolute ethanol and allowing the mixture to fall in small portions into a flask containing six atomic equivalents of sodium cut into large pieces. The flask was fitted with an efficient condenser and

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[49] V. Grignard and L. Tissier, *Compt. rend.*, **134**, 107–108 (1902).

[50] L. Bouveault and G. Blanc, *Compt. rend.*, **136**, 1676–1678 (1903); *Bull. soc. chim.*, **29**, 787–788 (1903); **31**, 666–672, 672–675 (1904).

[51] E. Chablay, *Compt. rend.*, **154**, 364–366 (1912); **156**, 1020–1022 (1913).

[52] H. Adkins and R. Connor, *J. Am. Chem. Soc.*, **53**, 1091–1095 (1931).

[53] H. Adkins and K. Folkers, *J. Am. Chem. Soc.*, **53**, 1095–1097 (1931).

[54] W. Schrauth, O. Schenck, and K. Stickdorn, *Ber.*, **64**, 1314–1318 (1931).

[55] W. Normann, *Z. angew. Chem.*, **44**, 714–717 (1931).

the rate of introduction of the ester solution was limited to the capacity of the condenser. The reaction was found to be very rapid and the sodium generally melted rapidly. Once the reaction subsided, boiling was maintained by application of heat for about six hours. If any sodium remained undissolved at the end of this time, additional absolute ethanol was added to dissolve it, and enough water to produce a homogeneous mixture. Steam distillation was employed to remove the ethanol and then the newly formed alcohol if it was volatile under these conditions.

The method of Bouveault and Blanc has many advantages because of the specificity of the reduction process. For example, esters of hydroxy acids can be reduced to glycols because the hydroxy group of the ester is unattacked during the reduction of the carbonyl group. Thus, Chuit and coworkers[56] were able to reduce the methyl ester of 10-hydroxyundecanoic acid to 2,11-undecanediol:

$$CH_3CHOH(CH_2)_8COOR \longrightarrow CH_3CHOH(CH_2)_8CH_2OH$$

It also has the advantage of effecting little change in the unsaturation of the hydrocarbon chain and can, therefore, be applied in the preparation of unsaturated alcohols from esters of unsaturated fatty acids.

Although possessing many advantages, the method of Bouveault and Blanc also has some disadvantages, the most serious of which is the fact that the strong alkaline reaction medium results in considerable saponification of the ester and consequent reduction in yield of the desired alcohol. To overcome this objection, the use of phenyl and other difficultly saponified esters has been proposed together with a large excess of sodium and absolute ethanol. However, even under these conditions, Jantzen and Tiedcke[57] obtained only 60% of octadecanol on reduction of phenyl stearate. To obtain this yield it was necessary to use a ratio of 1 part of phenyl ester to 200 parts of absolute ethanol.

Levene and Taylor[58] and Levene and Allen[59] prepared all of the normal aliphatic alcohols from C_{18} to C_{25} by reduction of the corresponding ethyl esters with sodium dust and ethanol in toluene solution. On the basis of the ester consumed the yields were stated to be 60% to 65%, but when allowance was made for the acid recovered, the yields were 90% to 95%. Marvel and Tanenbaum,[60] employing the same method, prepared lauryl and myristyl alcohols in 65 to 70% and 63 to 75% yields, respectively, from the corresponding ethyl esters.

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[56] P. Chuit, F. Boelsing, J. Hausser, and G. Malet, *Helv. Chim. Acta*, **9**, 1074–1093 (1926).

[57] E. Jantzen and C. Tiedcke, *J. prakt. Chem.*, **127**, 277–291 (1930).

[58] P. A. Levene and F. A. Taylor, *J. Biol. Chem.*, **59**, 905–921 (1924).

[59] P. A. Levene and C. H. Allen, *J. Biol. Chem.*, **27**, 433–462 (1916).

[60] C. S. Marvel and A. I. Tanenbaum, *J. Am. Chem. Soc.*, **44**, 2645–2650 (1922).

Prins[61] devised a method for circumventing excessive saponification by stratifying the ester to be reduced in an ether solution above a concentrated solution of sodium acetate. According to this procedure the solutions are cooled to −5°C. and the ether layer vigorously stirred while small pieces of sodium are added, followed by the dropwise addition of 30% acetic acid to keep the ether layer neutral or weakly acid to litmus. According to Prins, yields of alcohols up to 97% can be obtained by this method, but the reduction requires three to five days.

Bleyberg and Ulrich[62] claimed they were unable to duplicate the yields obtained by Levene and Taylor and devised a method for carrying out the reduction in petroleum naphtha solution. They dissolved the ester in low boiling petroleum naphtha in which sodium ethylate is practically insoluble, added 300% to 400% of the theoretical amount of sodium wire, warmed the solution, and slowly added over a period of an hour only as much absolute ethanol as was required to react with the sodium. All of the ethanol is consumed in the formation of sodium ethylate which is insoluble in the petroleum naphtha, hence saponification is reduced to a minimum. After heating for several hours, during which time most of the sodium is consumed, an excess of 95% ethanol is added to destroy the unreacted sodium and dissolve the reaction products. The mixture is then boiled an additional hour to saponify any unreduced ester. According to the authors, the use of this method makes possible the preparation of 100-g. quantities of the higher aliphatic alcohols in 80% yields starting with any ester melting below ethyl behenate. With ethyl behenate (m.p. 49°C.), the method requires modification because the sodium behenate formed on saponification of ethyl behenate is difficultly soluble in both water and dilute ethanol and the yield is therefore lowered to 60%. Substitution of butanol for ethanol leads to yields of 95% of docosanol from ethyl behenate.

Ford and Marvel[63] have described a modification of the method of Levene and Allen[59] for the preparation of lauryl alcohol by the reduction of ethyl laurate with sodium and ethanol which gives 65% to 75% yields of the desired product. The method has also been applied to the preparation of undecanyl, myristyl, and cetyl alcohols from the corresponding ethyl esters in yields of 70%, 70 to 80%, and 70 to 78%, respectively. Although the yields are slightly less than those claimed by Bleyberg and Ulrich,[62] the method is simple and rapid. The reaction is carried out in dry toluene (200 ml.) in which the sodium (70 g.) is dispersed by heating in an oil bath until it has melted, after which it is finely divided by rapid stirring. After the sodium is dispersed, the mixture is cooled and the ethyl ester (0.5 mole)

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[61] H. J Prins, *Rec. trav. chim.*, **42**, 1050–1052 (1923).

[62] W. Bleyberg and H. Ulrich, *Ber.*, **64**, 2504–2513 (1931).

[63] S. G. Ford and C. S. Marvel, in *Organic Syntheses*, Vol. 10. Wiley, New York, 1930, pp. 62–64.

dissolved in absolute ethanol (150 ml.) is added, followed by the rapid addition of more alcohol (500 ml.). The time required for the addition of the ethyl ester and ethanol should not exceed five minutes and preferably not more than two or three minutes. After the reaction has subsided the mixture is heated on a steam bath until the sodium has completely dissolved, after which it is steam-distilled to remove the toluene and ethanol. The residue is shaken in a separatory funnel with water and ether to separate the aliphatic alcohol and sodium soaps, and the alcohol is then recovered by the usual procedure.

According to a British patent,[64] a considerable improvement can be effected in the yield of alcohol by reducing the ester under a hydrogen pressure of the order of 15 to 20 atmospheres. A variation of this process employs finely divided sodium dispersed in toluene and the introduction of carbon dioxide into the reacting system which is under hydrogen pressure. Under these conditions the sodium alcoholate formed during the reaction is decomposed and its saponifying action on the still unattacked ester is prevented. On the other hand, no excess of acid can arise in the solution.

Mechanism of the Sodium–Alcohol Reduction Process.—The mechanism of the sodium–alcohol reduction was investigated by Bouveault and his associates who concluded that the reaction was one of simple reduction by nascent hydrogen produced by the action of sodium on ethanol or other alcohol. In one experiment, Bouveault and Blanc[50] dissolved methyl caprylate in ethyl ether and floated the solution on water. When sodium was added to the aqueous layer a considerable portion of the ester was reduced and only traces of sodium caprylate were found in the aqueous layer. The ester was maintained out of contact with the sodium and only in contact with the hydrogen, consequently, they concluded the reaction occurred according to the equation:

$$\mathrm{RCOOC_2H_5 + 4\,H \longrightarrow RCH_2OH + C_2H_5OH}$$

It was observed that small amounts of by-products accompanied the formation of the alcohol. These products consisted of glycols, RCHOH-CHOHR, and acyloins, RCOCHOHR.[65] The glycols were shown not to be intermediates in the production of the alcohols as they were resistant to reduction by sodium and absolute ethanol. They assumed that the hydroxy ketones were formed as a result of the action of sodium on the aliphatic ester and not as a result of hydrogenation. The mechanism of the reaction was assumed to be as follows:

$$\mathrm{2\,RCOOR' + 4\,Na \longrightarrow 2\,NaOR' + RC(ONa){=}C(ONa)R}$$

$$\mathrm{RC(ONa){=}C(ONa)R + 2\,H_2O \longrightarrow RC(OH){=}C(OH)R + 2\,NaOH}$$

$$\mathrm{RC(OH){=}C(OH)R \longrightarrow RCHOHCOR}$$

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[64] H. Th. Böhme A.-G., British Pat. 346,237 (April 30, 1931).

[65] L. Bouveault and R. Locquin, *Bull. soc. chim.*, 35, 629–633, 633–636 (1906).

Other mechanisms have been suggested by Scheibler and co-workers,[66,67] Egorova,[68] and others.

By modifying the reaction conditions used for the reduction of esters to alcohols, Bouveault and Locquin obtained yields up to 80% of acyloins. The reaction was carried out at 0°C. in acetic acid for several days. Corson, Benson, and Goodwin[69] improved the method by materially reducing the reaction time whereby 50% yields were obtained with the ethyl esters of the normal and iso acids from propionic to caproic. Snell and McElvain[70] also investigated the reaction of sodium on aliphatic esters with respect to the formation of acyloins and diketones and showed that the diketones were the intermediate products in these reactions. They concluded that the reaction occurred in two steps, in the first of which two molecules of the ester reacted with two atoms of sodium to form a diketone-sodium ethoxide addition product. The diketone-sodium ethoxide addition product then reacts with two more atoms of sodium to form sodium ethoxide and the sodium salt of the acyloin.

Most of the ethyl esters of the higher fatty acids have been subjected to

TABLE 117

PROPERTIES OF ALIPHATIC ALCOHOLS PREPARED BY REDUCTION OF ETHYL ESTERS WITH SODIUM AND ETHANOL

Ethyl	Alcohol		B.p., °C.	M.p., °C.	Specific gravity
	Name	Formula			
Caproate	Hexyl	$C_5H_{11}CH_2OH$	157	−52(−90)	0.833
Heptanoate	Heptyl	$C_6H_{13}CH_2OH$	176	−35.5	0.836
Octanoate	Octyl	$C_7H_{15}CH_2OH$	194.5	−14	0.839
Nonanoate	Nonyl	$C_8H_{17}CH_2OH$	213	−5	0.842
Decanoate	Decyl	$C_9H_{19}CH_2OH$	231	7	0.839
Undecanoate	Undecyl	$C_{10}H_{21}CH_2OH$	$131^{15\text{ mm.}}$ $124^{6\text{ mm.}}$	19	0.833^{23}_{4}
Laurate	Dodecyl (lauryl)	$C_{11}H_{23}CH_2OH$	$143^{15\text{ mm.}}$	24	0.831^{24}_{4}
Myristate	Tetradecyl (myristyl)	$C_{13}H_{27}CH_2OH$	$171^{20\text{ mm.}}$	39–39.5	0.824
Palmitate	Hexadecyl (cetyl)	$C_{15}H_{31}CH_2OH$	$180^{13\text{ mm.}}$	48.5–49.5	0.798
Stearate[a]	Octadecyl (stearyl)	$C_{17}H_{35}CH_2OH$	$210.5^{15\text{ mm.}}$	58.5	0.812
Behenate	Docosyl (behenyl)	$C_{21}H_{43}CH_2OH$	...	70.0–70.5	..
Tetracosanoate	Tetracosyl	$C_{23}H_{47}CH_2OH$	...	75.2–75.5	...
Hexacosanoate	Hexacosyl	$C_{25}H_{51}CH_2OH$	...	79.3–79.6	...
Octacosanoate	Octacosyl	$C_{27}H_{55}CH_2OH$	...	82.9–83.1	...

[a] Alcohol not prepared by sodium–ethanol reduction process.

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[66] H. Scheibler and J. Voss, *Ber.*, **53**, 388–409 (1920).

[67] H. Scheibler and F. Emden, *Ann.*, **434**, 265–284 (1923).

[68] V. I. Egorova, *J. Russ. Phys.-Chem. Soc.*, **60**, 1199–1210 (1928).

[69] B. B. Corson, W. L. Benson, and T. T. Goodwin, *J. Am. Chem. Soc.*, **52**, 3988–3995 (1930).

[70] J. M. Snell and S. M. McElvain, *J. Am. Chem. Soc.*, **53**, 750–760 (1931).

sodium–ethanol reduction for the preparation of the corresponding alcohols as indicated by the compilation in Table 117.

(*c*) *Reduction with Sodium–Ammonia*

Chablay[71] showed that the ethyl esters of fatty acids could be reduced to the corresponding alcohols by treatment with sodium–ammonia prepared by dissolving metallic sodium in liquid ammonia. The over-all reaction was assumed to occur according to the following equation:

$$3\ RCOOC_2H_5 + 2\ (NH_3Na)_2 \longrightarrow 2\ RCONH_2 + RCH_2ONa + 3\ NaOC_2H_5 + 2\ NH_3$$

Since the yield of alcohol is theoretically only one-third of the original ester, owing to the simultaneous formation of the amide, Chablay sought to increase the yield by reducing the amide as rapidly as it was formed by carrying out the reaction in absolute ethanol.

The method as finally developed is as follows: A solution of sodium–ammonia is prepared by placing a quantity of sodium wire in a one-liter flask and adding 200 to 300 ml. of liquid ammonia. The ester to be reduced is dissolved in absolute ethanol and added through a dropping funnel into the solution of sodium–ammonia previously cooled to −80°C. The blue color of the sodium–ammonia solution is rapidly decolorized as the reduction proceeds. The ammonia is allowed to evaporate and the residue treated with water after which the alcohol is recovered by distillation or other means.

Although the conversion of ester to alcohol proceeds in part according to the equation shown above, this is followed by a further reaction involving the reduction of the amide by nascent hydrogen as follows:

$$2\ C_2H_5OH + (NH_3Na)_2 \longrightarrow 2\ C_2H_5ONa + 2\ NH_3 + H_2$$

$$RCONH_2 + 2\ H_2 \longrightarrow RCH_2OH + NH_3$$

The over-all reaction may therefore be written:

$$RCOOC_2H_5 + 2\ C_2H_5OH + 2\ (NH_3Na)_2 \longrightarrow RCH_2ONa + 3\ C_2H_5ONa + 4\ NH_3$$

When considered from the viewpoint of the over-all reaction, the reduction may be assumed as being brought about entirely by nascent hydrogen produced by the action of sodium on ethanol and, therefore, it is essentially similar to the method of Bouveault and Blanc.

Chablay applied his method to the preparation of most of the normal aliphatic alcohols from butanol to hexadecanol by reduction of the methyl or ethyl esters of the corresponding acids. The method is applicable to the reduction of dibasic acids to produce the corresponding glycols. Phenylacetic ester gives phenylethanol and methyl cinnamate is reduced to phenyl

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[71] E. Chablay, *Compt. rend.*, **156**, 1020–1022 (1913).

propyl alcohol as the double bond of the side chain and the carbonyl group are reduced simultaneously.

(*d*) *Reduction with Copper Chromite*

From the industrial viewpoint the use of sodium and alcohol as a reducing agent for carbonyl groups possesses a number of disadvantages, especially high cost, poor yields, undesirable side reaction products, and operational difficulties, consequently considerable efforts have been devoted to the development of catalytic hydrogenation methods to accomplish this reduction. These efforts resulted in the almost simultaneous development by a number of workers of several processes for the production of alcohols by the catalytic hydrogenation or hydrogenolysis of aliphatic esters and acids. Several processes employing copper,[72] copper in the presence of a promoter,[73] and especially copper chromite,[74-78] were developed and described in the patent and scientific literature within a period of less than a year. This almost simultaneous description of these processes has resulted in considerable confusion concerning the priority and independence of these discoveries which has never been completely clarified.

When finely divided copper or copper on kieselguhr is used as catalyst, temperatures of 300° to 400°C. and pressures of 100 to 200 atmospheres are required for the reduction of ethyl laurate or the mixed ethyl esters of coconut oil to the corresponding alcohols. Copper in the presence of a promoter, and especially copper chromite, appears to be a considerably more effective catalyst for the reduction of carbonyl groups in general, and particularly for the carbonyl groups of the fatty acid esters and natural oils, consequently copper chromite is preferred for this operation both on an industrial and laboratory scale.

Although the high-pressure catalytic reduction method possesses many advantages over the use of sodium and alcohol from the industrial point of view, it possesses certain disadvantages when applied in the laboratory. The principal disadvantages result from the fact that it employs special high-pressure equipment which is expensive and requires skill and care to operate. Furthermore, a single reaction vessel is not adaptable to all types of work which necessitates having available several high-pressure vessels of different sizes. If, however, such equipment is available and the types of compounds to be reduced are relatively similar as in the case of

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[72] H. T. Böhme A.-G., British Pats. 356,606 (Sept. 10, 1931); 358,869 (Oct. 15, 1931). See French Pat. 708,206 (July 22, 1921).

[73] I. G. Farbe industrie A.-G., British Pat. 356,731 (Sept. 8, 1931).

[74] W. Normann, *Z. angew. Chem.*, **44**, 714–717 (1931).

[75] O. Schmidt, *Ber.*, **64**, 2051–2053 (1931).

[76] W. Schrauth, O. Schenck, and K. Stickdorn, *Ber.*, **64**, 1314–1318 (1931).

[77] H. Adkins and K. Folkers, *J. Am. Chem. Soc.*, **53**, 1095–1097 (1931).

[78] W. A. Lazier (to E. I. du Pont de Nemours), U. S. Pats. 1,839,974 (Jan. 5, 1932); 2,079,414 (May 4, 1937); 2,109,844 (March 1, 1938).

fatty esters and natural oils, the method is of considerable utility. Complete catalytic hydrogenation equipment suitable for laboratory hydrogenation may be constructed according to the directions of Adkins[79] or it may be purchased from several manufacturers who specialize in this type of equipment.

Details concerning the preparation of the copper chromite catalyst, design of the apparatus, and method of procedure are described by Adkins and are therefore but briefly mentioned here. Several forms of copper chromium oxide or copper chromite catalyst have been described.[80-82] They differ somewhat in physical properties and activity toward different organic compounds. Adkins[79] describes the preparation of a catalyst suitable for reducing fatty esters or acids to alcohols as follows:

> "Nine hundred ml. of a solution (at 80°C.) containing 260 g. of trihydrated copper nitrate and 31 g. of barium nitrate was added to 900 ml. of a solution (at 25°C.) containing 151 g. of ammonium dichromate and 225 ml. of 28 per cent ammonium hydroxide. The precipitate was filtered, the cake pressed with a spatula, and sucked as dry as possible. The product was dried in an oven at 75° to 80°C. for twelve hours and then pulverized. It was decomposed in three portions in a casserole over a free flame. In carrying out the decomposition, the powder was continuously stirred with a spatula and the heating so regulated that the evolution of gases did not become violent. This was accomplished by heating only one side of the casserole and stirring the powder more rapidly when the decomposition started to spread throughout the mass. During this process the color of the powder changed from orange to brown and finally to black. When the entire mass had become black, the evolution of gases ceased, and the powder was removed from the casserole and allowed to cool. The combined product was then leached for thirty minutes with 600 ml. of 10 per cent acetic acid solution, filtered, and washed with 600 ml. of water in six portions, dried for twelve hours at 125°, and pulverized. The yield of catalyst was 170 g."

The actual catalyst in this preparation is believed to be copper oxide which is stabilized toward reduction by the presence of chromium oxide.

As in other hydrogenations, time, temperature, pressure of hydrogen, weight of catalyst, and speed of agitation are interdependent variables in the rate of hydrogenation of esters to alcohols, consequently Adkins recommends the use of relatively high ratios of catalyst, for example, 3% to 5% of copper chromite with 50 to 100 g. of ester. Since a solvent is not generally used in hydrogenating the higher aliphatic esters, acids, amines, aldehydes, ketones, and cyanides, the maximum pressure attained is primarily

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[79] H. Adkins, *Reactions of Hydrogen with Organic Compounds over Copper-Chromium Oxide and Nickel Catalysts.* Univ. of Wisconsin Press, Madison, 1937.

[80] W. A. Lazier, British Pat. 301,806 (Jan. 30, 1928); U. S. Pat. 1,746,783 (Feb. 11, 1930).

[81] R. Connor, K. Folkers, and H. Adkins, *J. Am. Chem. Soc.*, **54**, 1138–1145 (1932).

[82] G. Calingaert and G. Edgar, *Ind. Eng. Chem.*, **26**, 878–880 (1934).

dependent on the pressure produced by the hydrogen at the temperature of the hydrogenation reaction. Generally, hydrogen is admitted to the reaction vessel from commercial cylinders of gas compressed to 125 atmospheres. Hydrogen, for example, admitted to the reaction vessel at a pressure of 100 atmospheres at room temperature will, on heating to 200°C., attain a maximum pressure of approximately 175 atmospheres. The effect of variations in the conditions of hydrogenation are illustrated by the data in Table 118 for the reduction of ethyl laurate to lauryl alcohol.[83]

TABLE 118

HYDROGENATION OF ETHYL LAURATE[a]

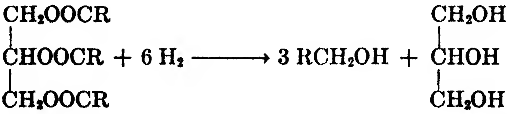
Ester 0.13 mole, copper chromite 3.0 g., temp. 250°C.		Ester 0.13 mole, copper chromite 1.0 g., acetone 1.7 moles		
Pressure, atm.	Time, hrs.	Pressure, atm.	Ester hydrogenated in 30 and 60 min., %	
106	7	35	17	22
214	1	148	60	92
333	0.25	212	95	100

[a] K. Folkers and H. Adkins, *J. Am. Chem. Soc.*, **54**, 1145–1154 (1932).

According to Adkins,[79] most of the saturated aliphatic esters react with hydrogen over copper–chromium oxide at 200° to 250°C. in a manner similar to ethyl laurate to produce almost quantitative yields of alcohols or glycols. The glycerides and free acids likewise react in a similar manner according to one of the following equations:

$$(1)\quad RCOOH + 2\,H_2 \longrightarrow RCH_2OH + H_2O$$

$$(2)\quad RCOOR' + 2\,H_2 \longrightarrow RCH_2OH + R'OH$$

(3) 

$$(3)\quad \begin{array}{l} CH_2OOCR \\ | \\ CHOOCR \\ | \\ CH_2OOCR \end{array} + 6\,H_2 \longrightarrow 3\,RCH_2OH + \begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array}$$

In the case of monoesters, the alcohol esterified with the fatty acid may be of either low or high molecular weight, *e. g.*, ethanol, butanol, or cetyl alcohol. The acyl portion of the ester may comprise either a normal or branched chain. Optically active alcohols are generally produced from optically active esters.

It should be noted that the temperature (250°C.) mentioned by Adkins for optimum reduction of aliphatic esters to alcohols on a batch scale in the laboratory is considerably below those cited by Lazier for continuous or semicontinuous, industrial scale operation. Lazier[78] cites examples indi-

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[83] K. Folkers and H. Adkins, *J. Am. Chem. Soc.*, **54**, 1145–1154 (1932).

cating a yield of 53% of hexamethylene glycol by continuous hydrogenation of diethyl adipate at a temperature of 380°C. and a pressure of 3000 lbs. per sq. in., compared with a yield of 85% to 90% when operating on a batch scale (autoclave) at a temperature of 255° and 3000 lbs. per sq. in. pressure. In the case of the glyceride esters and natural oils, Lazier[78] generally indicates temperatures in the vicinity of 360° to 380° for semi-continuous method and 260° to 300° for batch operation (autoclave).

In actual practice it has been found that hydrogenation temperatures in the vicinity of 285°C. give good yields of the desired alcohols from coconut and similar oils. A peculiarity of the high-pressure hydrogenation of glycerides or natural oils for the production of fatty alcohols is the fact that at the higher temperatures the reaction appears to occur in true vapor phase, whereas at the lower temperatures it appears to occur as a liquid-phase reaction.

The unsaturated and saturated acids behave somewhat differently on reduction in the presence of copper chromite because the reaction is not entirely specific with respect to the reduction of carbonyl groups. Other types of chromite catalysts have been found by Sauer and Adkins[84] to be more selective than copper chromite. For example, zinc–chromium oxide was found to reduce butyl oleate to oleyl alcohol (octadecenol), and butyl erucate to erucyl alcohol (docosenol), in about 68% yields, provided a high ratio of catalyst to ester was used together with a high temperature (300° C.).

(*e*) *Clemmensen Reduction*

Several satisfactory syntheses of long chain fatty acids have been developed which proceed by way of the keto acids to normal acids. These methods which involve the reduction of carbonyl groups to methylene groups are due to the efforts of Clemmensen and Wolff-Kishner.

Clemmensen[85] originally developed his method for the preparation of pure hydrocarbons by the reduction of the corresponding ketones. Ordinary reducing agents such as zinc and acids, sodium amalgam, sodium and absolute ethanol react with aliphatic ketones to give either pinacones or secondary alcohols instead of hydrocarbons. However, Clemmensen found that if the zinc was amalgamated superficially by immersion for a short time in a dilute solution of mercuric chloride, the reduction of the ketones to the corresponding hydrocarbons took place with great ease on heating with hydrochloric acid. The hydrocarbons were obtained in good yield and in very pure form. Clemmensen found that aliphatic ketones, whether short or long chain, symmetrical or unsymmetrical, could be re-

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[84] J. Sauer and H. Adkins, *J. Am. Chem. Soc.*, **59,** 1–3 (1937).

[85] E. Clemmensen, *Orig. Com. 8th Intern. Congr. Applied Chem.*, **6,** 68–76 (1912); *Ber.*, **46,** 1837–1843 (1913); **47,** 51–63, 681–687 (1914).

duced practically quantitatively to the corresponding hydrocarbons. For example, stearone, $(C_{17}H_{35})_2CO$, was quantitatively reduced to *n*-pentatriacontane, $C_{35}H_{72}$.

Le Sueur and Withers[86] found that the Clemmensen method of reducing ketones was applicable to the reduction of long chain aliphatic keto acids. 9-Ketomargaric acid[87] and 12-ketoheneicosanoic acid were quantitatively reduced by these authors to the corresponding margaric and heneicosanoic acids by boiling the substituted acids with amalgamated zinc and hydrochloric acid.

Others have used this method with minor variations for the reduction of various long chain aliphatic keto acids. For example, Robinson[88] reduced 13-keto-*n*-triacontanoic acid to *n*-triacontanoic acid by this method. A mixture of 13-ketotriacontanoic acid (5 g.), amalgamated zinc (100 g.), concentrated hydrochloric acid (100 ml.), and acetic acid (20 ml.) was heated so as to maintain gentle boiling for four days. Every six hours the mixture was cooled, the zinc and solid acid collected, fresh hydrochloric and acetic acids and zinc (10 g.) added, and the heating resumed. The reduced acid was finally extracted from the reaction mixture with boiling acetic acid and recovered by dilution with water.

Hills and Robinson[89] also applied the Clemmensen method to the reduction of 13-keto-15-phenylpentadecanoic acid and 13-keto-22-phenylbehenic acid to give the corresponding 15-phenylpentadecanoic and 22-phenylbehenic acids.

In general it is essential that the keto group be located at some distance from the carboxyl group in order to obtain complete reduction by the Clemmensen method; α-, β-, and γ-keto acids are not readily or completely reduced but δ-keto acids and other aliphatic acids react normally.

(*f*) *Wolff-Kishner Reduction*

In 1912, Wolff[90] described a method for reducing aldehydes and ketones to hydrocarbons by heating their hydrazones, phenylhydrazones or semicarbazones with sodium ethylate at a temperature of 150° to 180°C. for 8 to 18 hours. Later, Kishner found that the same result could be achieved by heating the carbonyl compound with hydrazine sulfate and excess sodium ethylate. Presumably the hydrazone is formed *in situ* and then re-

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[86] H. R. Le Sueur and J. C. Withers, *J. Chem. Soc.*, **107**, 736–739 (1915).

[87] H. R. Le Sueur and J. C. Withers, *J. Chem. Soc.*, **105**, 2800–2819 (1914).

[88] G. M. Robinson, *J. Chem. Soc.*, **1934**, 1543–1545.

[89] G. M. Hills and R. Robinson, *J. Chem Soc.*, **1936**, 281–283.

[90] L. Wolff, *Ann.*, **394**, 68–85, 86–108 (1912). See N. Kishner, *J. Russ. Phys.-Chem. Soc.*, **43**, 582–595, 1398–1401 (1911); **45**, 1779–1787 (1913); E. Thielepape, *Ber.*, **55**, 136–138 (1922); E. Thielepape and O. Spreckelsen, *Ber.*, **55**, 2929–2939 (1922); M. D. Soffer, M. B. Soffer, and K. W. Sherk, *J. Am. Chem. Soc.*, **67**, 1435–1436 (1945); F. C. Whitmore, C. H. Herr, D. G. Clarke, C. S. Rowland, and R. W. Schiessler, *ibid.*, **67**, 2059–2061 (1945); C. H. Herr, F. C. Whitmore, and R. W. Schiessler, *ibid.*, **67**, 2061–2063 (1945); Huang-Minlon, *ibid.*, **68**, 2487–2488 (1946).

duced by the action of the sodium ethylate. The method has been extended by various workers to the reduction of keto acids. Because the double bond is unaffected by this reduction, it is useful in reducing unsaturated keto acids. It has been applied, for example, to the reduction of ketochaulmoogric acid to chaulmoogric acid and various ketooctadecenoic acids to *n*-octadecenoic acids.[91] In the latter instance the unsaturated keto acids were heated with sodium ethoxide and hydrazine hydrochloride in a bomb at a temperature of about 185° for 60 hours. The Wolff-Kishner method has recently been modified and improved by the use of glycols or other high boiling alcohols as solvents which permit the reduction to be carried out at atmospheric pressure.

(*g*) *Reduction of Keto Acids to Hydroxy Acids*

Long chain aliphatic keto acids can be reduced with sodium to the corresponding hydroxy acids by treatment of the sodium salt in absolute ethanol. Thus, sodium ketostearate can be reduced to 10-hydroxystearic acid by treatment with metallic sodium in absolute ethanol.[92]

4. Reduction of Triple Bonds to Double Bonds

An important reduction process which is useful in the synthesis of monoethenoid aliphatic acids is that applied by Robinson and Robinson[92] in the reduction of stearolic acid, $CH_3(CH_2)_7C{:}C(CH_2)_7COOH$, to oleic acid, $CH_3(CH_2)_7CH{:}CH(CH_2)_7COOH$. Reduction of the triple bond to a double bond is accomplished by the action of zinc and hydrochloric acid in the presence of acetic acid and titanous chloride. Hydrochloric acid (15 ml., 40% solution) is slowly added to a gently boiling mixture of acetic acid (30 g.), aqueous titanous chloride (10 g., 15% solution), stearolic acid (3 g.), and zinc dust (10 g.), which are contained in a flask closed by a tube with a Bunsen valve. After two hours, zinc dust (5 g.) and acetic acid (20 ml.) are added and the heating continued for an additional two hours. The oleic acid, which is unaccompanied by either elaidic or stearic acid, is recovered by extraction with ether.

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[91] R. Kapp and A. Knoll, *J. Am. Chem. Soc.*, **65**, 2062–2064 (1943).

[92] G. M. Robinson and R. Robinson, *J. Chem. Soc.*, **127**, 175–180 (1925).

CHAPTER XV

OXIDATION AND HYDROXYLATION

1. Introduction

Reactions involving the oxidation of fatty acids, and especially unsaturated fatty acids, are perhaps the most frequently occurring reactions of fat chemistry. They are of fundamental importance in such processes as the utilization of fats in the animal body; in the drying of oil films and the manufacture of various products of the drying oil industry; in the spoilage of fats; and in the investigation of the structure of fatty acids and their derivatives.

The reagents which are capable of effecting oxidation in fats and oils are both numerous and diverse, consequently the end products of their reaction are likewise numerous and diversified. Three distinct classes of oxidizing reagents and reactions may be differentiated: (*1*) chemical oxidation by reagents other than atmospheric oxygen, (*2*) oxidation by atmospheric oxygen, and (*3*) biological or enzymic oxidation. Although it cannot be rigidly maintained, it is possible that oxidation with most oxidizing agents other than air results from reaction of atomic oxygen, whereas oxidation with air is molecular in nature. Because of the distinctive nature of the oxidation mechanisms involved in these three classes of oxidations they are best considered under separate heads.

The list of oxidation agents, other than atmospheric oxygen, which have been applied in fat chemistry includes nearly all of those used in organic chemistry generally. Many of these reagents have not been found to possess any special merit in the investigation of fats and fatty acids and consequently they have not come into general use. Some, like nitric and sulfuric acids, for example, while of value in certain industrial processes are now of only historical interest as reagents in investigations of the constitution of fatty acids. Others, like chromic acid, are still used to a limited extent for special purposes but for the most part they have been superseded by reagents, *e. g.*, potassium permanganate, which react in an analogous manner while, at the same time, permitting more ready control of the action.

Certain of the oxidation reagents are highly specific in their activity while others are quite general in both reactivity and application. For example, potassium permanganate and perbenzoic acid are widely applicable in investigating the structure of unsaturated fatty acids, whereas the use of lead tetraacetate and periodic acid is restricted to the fission of polyhydroxylated or other partially oxidized fats or fatty acids.

In general, the products of oxidation of unsaturated fatty acids vary with the oxidation reagent and the conditions of oxidation, *i. e.*, temperature, concentration of reagent and sample, solvent, catalyst, etc. Oxidation may proceed slowly through a series of intermediates, or rapidly and directly to a specific end product. In the former case, at any given instant, an appreciable number of oxidation products may coexist and the investigation of the oxidation mechanism is therefore fraught with difficulties. Some investigators have attempted to study the effect of a given oxidation process using a single pure fatty acid or ester and a specific oxidizing agent in an effort to determine the mechanism of the oxidation process and the nature of the intermediate and end products of the reaction. Even such restricted conditions have not always resulted in a successful elucidation of the process of oxidation.

Notwithstanding the exceedingly large amount of work which has been done, no single generalization concerning the mechanism of oxidation of unsaturated fatty acids has been proposed or found acceptance by the majority of workers in this field. The extant literature comprises many scattered investigations, numerous hypotheses, and some efforts toward generalization of the existing mass of experimental data. In the following pages the more significant experimental work and observations have been brought together, but as yet without any entirely satisfactory generalization concerning the over-all mechanism of fatty acid oxidation.

2. Oxidation with Nitric Acid

Nitric acid, although a powerful oxidizing agent, has been used but little in recent years for the oxidation of fatty acids. Prior to the introduction of potassium permanganate as an oxidizing agent for fatty acids, many investigations were carried out in which nitric acid was employed for this purpose. This work is now merely of historical interest and is therefore mentioned but briefly.

Arppe[1] investigated the action of nitric acid on the lower members of the saturated fatty acid series. Dieterle[2] oxidized stearic acid with three times its weight of concentrated nitric acid (sp.gr. 1.3) and obtained a number of short-chain monobasic acids, considerable amounts of sebacic and suberic acids, and small amounts of adipic and succinic acids. Carette[3] oxidized stearic acid, and a mixture of stearic and palmitic acids, by re-

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[1] A. E. Arppe, *Ann.*, **95**, 242–252 (1855); **120**, 288–295 (1861); **124**, 98–101 (1862).

[2] W. I. Dieterle, *Über die Oxydations-produkte reiner Stearinsäure durch Salpetersäure. II. Beitrag zur Kenntnis der Adipinsäure.* [Bern] G. F. Rapp, Cannstatt, 1883, 66 pp.

[3] H. Carette, *Compt. rend.*, **102**, 692–693 (1886).

fluxing them for nine days with twelve times their weight of strong nitric acid (sp.gr. 1.36). Succinic and glutaric acids were isolated from the reaction mixture, but these were assumed to arise from oxidation of sebacic acid which was considered as the primary product of oxidation. Oleic acid gave propylene dicarboxylic acid, $HOOC \cdot CH_2CH:CHCOOH$, when similarly oxidized. Noerdlinger[4] oxidized myristic acid with nitric acid (sp.gr. 1.3) and obtained, in addition to carbon dioxide, principally succinic and adipic acids, some glutaric acid, and small amounts of pimelic, suberic, and oxalic acids.

Recently Price and Griffith[5] were granted a patent covering the oxidation of hydroxylated and unsaturated fatty acids or oils with nitric acid in the presence of manganese or its salts or oxides. Oleic acid (56 parts), manganese dioxide (0.6 part), and nitric acid (190 parts of 70%) when heated to 80°C. for four hours gave a mixture of monobasic and dibasic (azelaic and suberic) acids. Similar products were obtained on oxidation of hydroxystearic, dihydroxystearic, and ricinoleic acids.

3. Oxidation with Chromic Acid

Simon[6] investigated the relation between the structure of various organic compounds and the extent to which they undergo oxidation when treated with chromic–sulfuric acid and with silver bichromate. He included in these investigations various normal and substituted fatty acids of the saturated and unsaturated series. According to Simon, reaction of fatty acids and related compounds with silver bichromate yields *oxidation values* (carbon dioxide) in relatively close agreement with their theoretical carbon content, whereas the values found with chromic anhydride depend on the molecular structures of the compounds which are subjected to oxidization. As a measure of oxidation he proposed the term *oxidation deficiency* which he defined as:

$$\Delta = \frac{C_2 - C_1}{C_2} n$$

where C_2 is the percentage of carbon found by oxidation with chromic acid, C_1 the percentage found by oxidation with silver bichromate, and n the number of carbon atoms in the compound. Actually the numerical value of Δ was considered to represent the number of carbon atoms per molecule which escaped oxidation with chromic–sulfuric acid.

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[4] H. Noerdlinger, *Ber.*, **19**, 1893–1899 (1886).

[5] D. Price and R. Griffith (to National Oil Products Co.) U .S. Pat. 2,365,290, (Dec. 19, 1944).

[6] L. J. Simon, *Compt. rend.*, **174**, 1706–1708 (1922); **175**, 1070–1072 (1922); **179**,. 975–977 (1924); **180**, 673–675, 833–836, 1405–1407 (1925).

The deficiency in the carbon completely oxidized to carbon dioxide by chromic–sulfuric acid was found to amount to two atoms per molecule in the case of straight chain acids of which stearic, oleic, elaidic, tariric, ketotariric, and others were investigated. In derivatives such as the ethyl esters and glycerides, a deficiency was found which corresponded to nearly two carbon atoms for each carbon chain in the molecule.

In the case of the unsaturated fatty acids, Simon concluded that complete oxidation of carbon to carbon dioxide with chromic–sulfuric acid occurs only if the unsaturated linkage occupies a terminal position in both the monobasic and dibasic acid series. However, allylacetic, $CH_2{:}CH(CH_2)_2COOH$, and $\Delta^{10,11}$-undecenoic, $CH_2{:}CH(CH_2)_8COOH$, acids were found to be exceptions to this generalization since the oxidation deficiency was found to be one in the case of allylacetic acid, and two in the case of undecenoic acid. The former discrepancy was explained by the assumption that the presence of sulfuric acid in the oxidation mixture converted allylacetic acid to the γ-lactone and the oxidation deficiency corresponded to that obtained with saturated hydroxy acids. The discrepancy in the case of the undecenoic acid was considered to be evidence of the incorrectness of the accepted structure of this acid. Simon therefore proposed that the acid be assigned a $\Delta^{9,10}$-structure, namely, $CH_3CH{:}CH(CH_2)_7COOH$. However, the isolation by Noller and Adams[7] of methyl aldehydononanoate, $CHO(CH_2)_8COOCH_3$, in 65% to 70% yield after ozonation of methyl undecenoate appears to be ample proof that this acid is $\Delta^{10,11}$-undecenoic acid.

In addition to its use as a reagent for wet combustion, chromic acid has been applied to the disruptive oxidation of unsaturated acids and to the further oxidation of partially oxidized products such as hydroxy and keto acids. Under the mildest conditions, chromic acid oxidation produces hydroxy acids, but compared with potassium permanganate it is infrequently applied for this purpose. Unless the conditions of oxidation are carefully controlled, oxidation with chromic acid produces with oleic acid a variety of monobasic acids ranging from nonanoic (pelargonic) to acetic, and dibasic acids ranging from azelaic to oxalic.[8] Edmed[8] oxidized oleic acid with aqueous chromic acid (2% potassium dichromate plus an equivalent amount of sulfuric acid) by heating under reflux. No reaction occurred at first, but after four days reduction of chromate occurred slowly and after ten days nonanoic and azelaic acids were obtained. No other product except unchanged oleic acid was isolated from the reaction mixture. An experiment described by Armstrong and Hilditch[9] in which ethyl oleate was oxidized at room temperature with aqueous chromic acid would seem to

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[7] C. R. Noller with R. Adams, *J. Am. Chem. Soc.*, **48**, 1074–1080 (1926).
[8] F. G. Edmed, *J. Chem. Soc.*, **73**, 627–634 (1898).
[9] E. F. Armstrong and T. P. Hilditch, *J. Soc. Chem. Ind.*, **44**, 43–47T (1925).

indicate that under these conditions oxygen is absorbed to form an oxido or peroxido compound which is probably further oxidized to a hydroxy acid. That hydroxy acids are readily split by chromic acid has been demonstrated by subsequent workers.

Asahina and Ishida[10] observed that chromic acid oxidation of dihydroxy acids resulted in fission of the carbon chain between the adjacent hydroxyl groups. When dihydroxystearic acid, prepared by permanganate oxidation of oleic acid obtained from olive oil, was further oxidized by chromic acid, nonanoic and azelaic acids were formed. Trihydroxystearic acid, obtained by permanganate oxidation of ricinoleic acid from castor oil, gave heptanoic ($C_6H_{13}COOH$) and azelaic acids. The method consisted of heating in a bath at 110° to 118°C., one part of dihydroxystearic acid with five parts of sulfuric acid, twenty parts of water, and two parts of sodium dichromate. When the temperature of the reaction reached 80° to 90°, steam was passed through the mixture until the distillate no longer contained nonanoic acid (b.p. 150°C. at 22 mm.). The azelaic acid (m.p. 106° to 107°C.) was recovered from the residue.

Grün and Wittka[11] applied Asahina and Ishida's method to the oxidation of stearolic acid. Ten grams of stearolic acid was treated with 250 ml. of 25% sulfuric acid and 20 g. of sodium dichromate. The reaction mixture was heated to 120°C. and steam at the same temperature was passed into the solution. After five hours, 4.5 g. of a volatile acid had distilled which on analysis proved to be pure nonanoic acid. The undistilled residue gave 6.0 g. of azelaic acid which indicated that the reaction had been almost quantitative. In order to be sure that small quantities of other oxidation products had not been overlooked, the reaction was repeated using 150 g. of stearolic acid. This time there were obtained 78.5 g. of azelaic acid (m.p. 106.5°C.) and 9.6 g. of suberic acid (m.p. 139.5°C.) from the nonvolatile portion, and 55.0 g. of nonanoic acid from the steam distillate.

King[12] observed that 9-hydroxy-10-ketostearic and 9-keto-10-hydroxystearic acids were converted by chromic acid oxidation to stearoxylic acid (m.p. 85.5°C.). The reaction was carried out at room temperature for 24 hours in glacial acetic acid to which chromic acid was added in the ratio of 25 ml. of glacial acetic to 0.25 g. of chromic acid.

Long chain alcohols are readily converted by chromic acid oxidation to the corresponding acids. For example, Chibnall *et al.*[13] converted cocceryl alcohol (15-keto-*n*-tetratriacontanol) into the corresponding 15-keto-*n*-tetratriacontanoic acid in 50% yield by oxidation with chromium trioxide in glacial acetic acid at 65° to 70°C. for 20 minutes.

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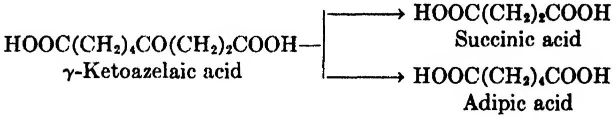
[10] Y. Asahida and Y. Ishida, *J. Pharm. Soc. Japan*, **481**, 171–179 (1922).

[11] A. Grün and F. Wittka, *Chem. Umschau Fette Öle Wachse Harze*, **32**, 257–259 (1925).

[12] G. King, *J. Chem. Soc.*, **1936**, 1788–1792.

[13] A. C. Chibnall, A. L. Latner, E. F. Williams, and C. A. Ayre, *Biochem. J.*, **28**, 313–325 (1934).

Beckmann[14] described a chromic acid oxidation reagent which has been successfully applied to many types of organic oxidations.[15] It is prepared by dissolving 120 g. (0.4 mole) of crystalline sodium dichromate in a solution of 100 g. (0.97 mole) of concentrated sulfuric acid and 600 ml. of water. Brown and Farmer[16] applied this reagent to the determination of the structure of γ-ketoazelaic acid obtained by permanganate oxidation of licanic acid from oiticica oil. γ-Ketoazelaic acid (3.5 g.) was boiled with 45 ml. of Beckmann's chromic acid mixture until the latter was completely reduced. Oxidative fission occurred at the points of attachment of the keto group to produce a mixture of succinic and adipic acids according to the following equations:



$$\underset{\gamma\text{-Ketoazelaic acid}}{\mathrm{HOOC(CH_2)_4CO(CH_2)_2COOH}} - \left|\begin{array}{l} \longrightarrow \underset{\text{Succinic acid}}{\mathrm{HOOC(CH_2)_2COOH}} \\ \longrightarrow \underset{\text{Adipic acid}}{\mathrm{HOOC(CH_2)_4COOH}} \end{array}\right.$$

Myers and Sprang[17] obtained a patent on the selective oxidation of mixed unsaturated acids and oils containing these acids. According to the claims of the patentees, di- and triethenoid acids can be preferentially oxidized with chromic acid without action on any oleic acid which may be present in the mixture. Mixed fatty acids, *e. g.*, from corn, soybean, cottonseed, and similar oils, are oxidized at a temperature of 80° to 100°C. with 6% to 7% chromic acid. From 100 parts of mixed soybean oil fatty acids, 27 parts of oleic can be recovered after oxidation at 80° to 90°C. with 156.6 parts of chromic acid dissolved in 1033 parts of water containing 300 parts of sulfuric acid. It is claimed that the di- and triethenoid acids are oxidized to mono- and dibasic acids under these conditions while the oleic acid remains unattacked.

4. Oxidation with Potassium Permanganate

The oxidizing agent most extensively employed in investigating the structures of unsaturated fatty acids is potassium permanganate. Long chain saturated fatty acids are generally unaffected by potassium permanganate except at elevated temperatures and long, continued action. Gröger,[18] for example, treated palmitic acid with potassium permanganate under various conditions of time, temperature, and concentration of reagent, and found that after 18 hours at the temperature of the water bath 40% of the original acid was unaffected by a concentrated solution of

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[14] E. Beckmann, *Ann.*, **250**, 322–375 (1889); see especially pp. 325–327.

[15] H. Gilman, ed., *Organic Syntheses.* Collective Vol. I, 2nd ed., Wiley, New York, 1941, pp. 340–341.

[16] W. B. Brown and E. H. Farmer, *Biochem. J.*, **29**, 631–639 (1935).

[17] L. D. Myers and C. A. Sprang (to Emery Industries, Inc.), U. S. Pat. 2,369,108 (Feb. 6, 1945).

[18] M. Gröger, *Monatsh.*, **8**, 484–497 (1887).

alkaline permanganate. The products of oxidation of palmitic acid included the dibasic acids, oxalic, succinic, and adipic; short chain monobasic acids, acetic, butyric, and caproic; and the hydroxy acids, hydroxyvaleric and hydroxypalmitic.

In contrast to the behavior of the higher saturated acids, mono- and polyethenoid acids react rapidly and at relatively low temperatures. Two types of permanganate oxidation are now clearly recognized: (*a*) oxidation in aqueous alkaline medium at low temperatures, 0° to 30°C., and (*b*) oxidation in nonaqueous (acetone) or acidic media at elevated temperatures. The first type of oxidation produces predominantly polyhydroxy acids which are geometric isomerides of the original acid. The second type of oxidation produces predominantly fission products through rupture of the molecule at the double bonds. In the earliest investigations these two types of oxidation were not clearly distinguished. Conditions may be varied with respect to *p*H, concentration, and temperature, consequently various types of reactions may proceed concurrently. For example, when the oxidation is carried out at low temperature in a neutral, instead of an alkaline medium, the products of oxidation are generally hydroxyketo acids rather than polyhydroxy acids. However, fission generally results when highly unsaturated acids are oxidized at 0°C., in fairly concentrated aqueous sodium carbonate-potassium permanganate solutions. Oxido or peroxido acids do not appear to be formed during permanganate oxidation or, if so, they are too rapidly transformed to other products to permit their isolation.

(*a*) *Oxidation of Monoethenoid Acids with Aqueous Alkaline Potassium Permanganate*

Saytzeff[19] appears to have been the first to employ potassium permanganate in alkaline solution for the oxidation of oleic and elaidic acids, and therefore was the first to observe that the primary products of this reaction were dihydroxy acids. This discovery of the action of alkaline permanganate on unsaturated acids was followed by the systematic and classical oxidation studies of Hazura and co-workers.[20-27] These workers employed in their investigations a wide variety of fatty acids including the mixed liquid fatty acids of hempseed, walnut, poppyseed, linseed, and cottonseed oils, as well as isolated mono- and polyethenoic acids, including oleic,

[19] A. Saytzeff, *J. prakt. Chem.*, **33**, 300–318 (1886).
[20] A. Bauer and K. Hazura, *Monatsh.*, **7**, 216–229 (1886).
[21] K. Hazura, *Monatsh.*, **8**, 147–155 (1887).
[22] K. Hazura and A. Friedreich, *Monatsh.*, **8**, 156–164 (1887).
[23] K. Hazura, *Monatsh.*, **8**, 260–270 (1887).
[24] K. Hazura, *Monatsh.*, **9**, 180–197 (1888).
[25] K. Hazura and A. Grüssner, *Monatsh.*, **9**, 198–207 (1888).
[26] K. Hazura, *Monatsh.*, **9**, 469–474 (1888).
[27] K. Hazura and A. Grüssner, *Monatsh.*, **9**, 475–484, 944–946, 947–955 (1888).

elaidic, ricinoleic, erucic, brassidic, undecenoic, linoleic, and linolenic acids. Hazura was the first to isolate and name the tetrahydroxy acids (sativic acids) obtained on oxidation of linoleic acid and the hexahydroxy acids (linusic acids) obtained from linolenic acid. The results of the oxidations of these acids were summarized by Hazura[23] in part as shown in Table 119. In these early experiments there was obtained, in addition to hydroxy acids, azelaic acid to the extent of 20% of the original unsaturated acid, and small amounts of low molecular weight acids including butyric. With improvement of the method of oxidation, the yields of hydroxy acids were increased and lesser amounts of fission products were obtained.

TABLE 119

PRODUCTS OF ALKALINE PERMANGANATE OXIDATION OBTAINED BY HAZURA[a]

Acid	Formula	Principal oxidation product	
		Hydroxy acid	Formula
Oleic	$C_{18}H_{34}O_2$	Dihydroxystearic	$C_{18}H_{34}O_2(OH)_2$
Elaidic	$C_{18}H_{34}O_2$	Isodihydroxystearic	$C_{18}H_{34}O_2(OH)_2$
Ricinoleic	$C_{18}H_{33}O_2(OH)$	Trihydroxystearic	$C_{18}H_{33}O_2(OH)_3$
Linoleic	$C_{18}H_{32}O_2$	Sativic	$C_{18}H_{32}O_2(OH)_4$
Linolenic	$C_{18}H_{30}O_2$	Linusic	$C_{18}H_{30}O_2(OH)_6$
Erucic	$C_{22}H_{42}O_2$	Dihydroxybehenic	$C_{22}H_{42}O_2(OH)_2$
Brassidic	$C_{22}H_{42}O_2$	Isodihydroxybehenic	$C_{22}H_{42}O_2(OH)_2$
Undecenoic	$C_{11}H_{20}O_2$	Dihydroxyundecanoic	$C_{11}H_{20}O_2(OH)_2$

[a] K. Hazura, *Monatsh.*, 8, 260–270 (1887).

Stearolic acid was found to resist oxidation under the conditions which gave hydroxy acids from acids containing only double bonds. Hazura recognized that different hydroxy acids were produced when *cis*- and *trans*-forms of the same acid were oxidized. He failed, however, to differentiate the various polyhydroxy acids obtained on oxidation of linoleic and linolenic acids.

Somewhat later, Edmed,[28] Albitzki,[29] and Le Sueur[30] investigated the reactions of oleic, elaidic, erucic, brassidic, and other acids with potassium permanganate under various conditions. In one series of experiments, Edmed refluxed oleic and elaidic acids with a dilute solution of acid permanganate to determine whether the double bond underwent rupture in a manner analogous to chromic acid oxidation. In contrast to the latter oxidation which produced only fission products, potassium permanganate gave dihydroxystearic acids, fission products, and secondary oxidation products of the latter. For example, oleic acid gave 60% of dihydroxystearic acid (m.p. 134°C.), a small amount of nonanoic (pelargonic) acid,

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[28] F. G. Edmed, *J. Chem. Soc.*, **73**, 627–634 (1898).

[29] A. Albitzki, *J. Russ. Phys.-Chem. Soc.*, **31**, 76–100 (1899); **34**, 788–810, 810–828 (1902).

[30] H. R. Le Sueur, *J. Chem. Soc.*, **79**, 1313–1324 (1901).

and 16% each of azelaic and oxalic acids. Elaidic acid, under the same conditions, gave 33% of dihydroxystearic acid (m.p. 96°C.), 13% to 14% of nonanoic acid, 26% of azelaic acid, and 15% to 20% of oxalic acid. The respective yields of oxidation products were considered evidence of the relative ease of oxidation of elaidic as compared with oleic acid.

Still later, Rollett,[31] Nicolet and Jurist,[32] Robinson and Robinson,[33] Lapworth and Mottram,[34] Hilditch and co-workers,[35,36] as well as others, investigated the action of alkaline permanganate with a view to improving the yield of hydroxy acids, determining the optimum reaction conditions, and for other reasons.

Robinson and Robinson found that dihydroxystearic acid (m.p. 132°C.) was obtained in excellent yield when oleic acid was oxidized in dilute alkaline solution at 0°C. Lapworth and Mottram investigated the various factors which affected the oxidation reaction with the result that they were able to formulate specifications for obtaining the maximum yield of dihydroxystearic acids from monoethenoid acids. These conditions are: (*1*) Low temperature (0° to 10°C.) during oxidation; (*2*) concentration of oleic acid or other monoethenoid acid in the form of its sodium or potassium salt not in excess of 0.1%; (*3*) concentration of the added aqueous permanganate solution not in excess of 1.0%; (*4*) a very short reaction time, about 5 minutes; and (*5*) slight excess of alkali at the outset to avoid the production of ketohydroxy acids.

With comparatively pure oleic acid, dihydroxystearic acid equivalent to 96% of the original acid can be obtained under the conditions mentioned. Comparatively impure oleic acid containing stearic, palmitic, linoleic, or linolenic acids can be analyzed by this method since the oxidation products of the more highly unsaturated acids are insoluble in petroleum naphtha or are volatile with steam.

According to Lapworth and Mottram, their method, although giving 96% yields of dihydroxystearic acid with relatively pure oleic acid, gave considerably lower yields in the presence of as much as 12% to 13% of linoleic acid. Nunn and Smedley-Maclean[37] found that Rollett's method gave remarkably constant yields (about 96%) of dihydroxystearic acid, even in the presence of considerable quantities of higher unsaturated acids (linoleic and linolenic). The method, employing the mixed acids from linseed oil, is described as follows: 15 g. of the mixed acids was dissolved in 18 ml. of 33% potassium hydroxide solution, and three liters of water was

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[31] A. Rollett, *Z. physiol. Chem.*, 62, 422–431 (1909).
[32] B. H. Nicolet and A. E. Jurist, *J. Am. Chem. Soc.*, 44, 1136–1141 (1922).
[33] G. M. Robinson and R. Robinson, *J. Chem. Soc.*, 127, 175–180 (1925).
[34] A. Lapworth and E. N. Mottram, *J. Chem. Soc.*, 127, 1628–1631 (1925).
[35] T. P. Hilditch, *J. Chem. Soc.*, 1926, 1828–1836.
[36] T. P. Hilditch and E. E. Jones, *J. Soc. Chem. Ind.*, 46, 174–177T (1927).
[37] L. C. A. Nunn and I. Smedley-Maclean, *Biochem. J.*, 32, 1974–1981 (1938).

added. The solution was cooled to 0°C. and two liters of 1.0% solution of potassium permanganate previously cooled to 0°C. was added during a period of thirty minutes. The mixture was constantly stirred and cooled with ice so that the temperature never rose above 5°C. Sulfur dioxide was then passed into the solution until the manganese dioxide was dissolved, after which it was acidified with dilute sulfuric acid. The precipitate, which separated at once, was filtered off, dried, and extracted for 24 hours with boiling light petroleum (b.p. 60° to 80°C.) The residue was then thoroughly extracted with boiling water to remove tetra- and hexahydroxystearic acids, dried, and weighed.

Under the conditions of oxidation set forth by Robinson and Robinson and by Lapworth and Mottram, oleic acid produces, in practically quantitative yield, the high melting dihydroxystearic acid (m.p. 132°C.), whereas, per acid oxidation yields only the low melting dihydroxystearic acid (m.p. 95°C.). On the other hand, alkaline permanganate oxidation of elaidic acid produces the low melting dihydroxy acid (m.p. 95°C.) as has been shown by nearly all of the previously mentioned workers.

One or another of the various modifications of the alkaline permanganate method of oxidation described by Hazura, Lapworth and Mottram, and Rollett has been applied to the oxidation of practically all of the known monoethenoid acids from C_{10} to C_{24} and the corresponding dihydroxy acids have been isolated and characterized.

(b) *Oxidation of Monoethenoid Acids with Neutral Aqueous Potassium Permanganate*

In the case of the previously discussed oxidation of oleic and elaidic acids, the reaction is carried out in alkaline solution. When, however, an excess of alkali is avoided the principal product of oxidation is not dihydroxystearic acid but hydroxyketostearic acid as was observed by Holde and Marcusson.[38] King[39] observed that permanganate oxidation of oleic and elaidic acids, under conditions analogous to those employed by Lapworth and Mottram except that the oxidation was conducted close to neutrality (about *p*H 8.5), led to the formation of mixtures of 9-hydroxy-10-ketostearic and 10-hydroxy-9-ketostearic acids together with varying amounts of dihydroxystearic acid. According to King, the conditions under which good yields of hydroxyketo acids are formed are: (*1*) the acid and potassium hydroxide should be in equivalent proportion and the amount of potassium permanganate subsequently added should be approximately two moles per mole of oleic acid; (*2*) the concentration of the acid should not exceed one gram per liter of the reaction mixture; and (*3*)

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[38] D. Holde and J. Marcusson, *Ber.*, **36**, 2657–2662 (1903).
[39] G. King, *J. Chem. Soc.*, **1936**, 1788–1792.

the duration of the oxidation should be eight to ten minutes at 8° to 10°C. for oleic acid, and 25° for elaidic acid.

Under these conditions, commercial samples of oleic acid gave 30% to 40% yields of the two hydroxyketostearic acids and 20% to 35% of dihydroxystearic acid (m.p. 132°C.). Elaidic acid, under the same conditions, gave 55% to 60% of the mixed hydroxyketostearic acids and 10% to 20% of dihydroxystearic acid (m.p. 95°C.). The two hydroxyketostearic acids are formed in approximately equal quantities but the mixture (m.p. 64.5° to 65.5°C.) can be resolved by means of the semicarbazones. The 9-hydroxy-10-ketostearic acid melts at 74°C. and is characterized by a semicarbazone melting at 152°. It is oxidized smoothly by periodic acid at room temperature to nonanoic acid and azelaic semialdehyde. Its isomeride melts at 75.5°C., gives a semicarbazone melting at 138.5°C., and undergoes oxidation with periodic acid to yield nonaldehyde and azelaic acid. As by-products of the reaction, dihydroxystearic acids melting at 132° and 95°C. were formed exclusively from oleic acid and elaidic acid, respectively, and thus correspond to the principal products obtained on alkaline permanganate oxidation of these acids.

Dorée and Pepper[40] subjected erucic (*cis*) and brassidic (*trans*) acids to both alkaline and neutral permanganate oxidation and found that the principal products of oxidation were dihydroxybehenic acids under alkaline conditions and hydroxyketobehenic acids under neutral conditions. Erucic acid, when oxidized with alkaline permanganate at 27°C. for 30 minutes, gave 13,14-dihydroxybehenic acid melting at 132°, in 85% yield. Brassidic acid, under the same conditions, gave 13,14-dihydroxybehenic acid melting at 100.5°, in 80% yield. Erucic acid, when oxidized with potassium permanganate in neutral solution at 40° for 15 minutes, gave a mixture of hydroxyketobehenic acids and, as a by-product, 13,14-dihydroxybehenic acid melting at 132°. This by-product dihydroxybehenic acid was the same high melting form obtained on oxidation in alkaline solution.

(c) *Oxidation of Polyethenoid Acids with Alkaline Potassium Permanganate*

Discussion of the alkaline and neutral permanganate oxidation reactions up to this point has been concerned with monoethenoid acids. Polyethenoid acids and esters have also been investigated with these reagents but not with the precise results obtained with monoethenoid acids. Part of the lack of precision in the former case was a result of the inability of the various investigators to prepare polyunsaturated acids and esters in pure form. Until the techniques of low temperature crystallization and precise distillation were developed, polyethenoid acids had to be prepared by debromination of derivatives obtained from brominated natural acids. Since

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[40] C. Dorée and A. C. Pepper, *J. Chem. Soc.*, **1942**, 477–483.

bromination of these acids produces mixtures of isomeric bromides comprising both solid and liquid forms, only the solid isomer could be obtained in pure form. Regeneration of the acid from the solid bromo acid is generally presumed to yield the same unsaturated acid which is present in natural fats, and the oxidation products have therefore been presumed to be identical with those which would have been obtained by oxidation of the natural acid. Present evidence indicates that this is not always the case.

Hazura[21] oxidized the liquid fraction of mixed fatty acids obtained from sunflowerseed oil with dilute aqueous permanganate and isolated two tetrahydroxy acids, melting at 160° to 162° and 173° to 175°C., respectively, in amounts corresponding to approximately 24% and 7% of theory. In the same manner, Rollett[31] oxidized linoleic acid obtained on debromination of solid tetrabromostearic acid, and isolated crude tetrahydroxystearic acids melting at 173°C. in a yield of approximately 33% of theory. Nicolet and Cox[41] oxidized linoleic acid from a similar source and obtained a yield of 43% of tetrahydroxystearic acid, melting at 162° to 168°C. This product was resolved by repeated crystallizations into two acids melting at 153° and 170°C.

Green and Hilditch[42] oxidized a linoleic acid obtained by debromination of tetrabromostearic acid (m.p. 114°C.), using a modification of Hazura's method and the method of Lapworth and Mottram. In both cases they isolated two tetrahydroxystearic acids, melting at 173° and 155°C., respectively, and several incompletely identified oily or solid by-products. These authors also subjected to similar oxidation the liquid acid fraction obtained from safflowerseed oil, isomerized linoleic acid (linolelaidic acid), and linoleic acid obtained by debromination of liquid or β-tetrabromostearic acid. As indicated in Table 120 the type and yield of tetrahydroxystearic or sativic acids which were recovered depend on the nature of the original linoleic acid.

Under the best conditions of oxidation, linoleic acid, obtained by debromination of the solid or α-tetrabromostearic acid, gave tetrahydroxystearic acids equivalent to 65% of the original acid. On the other hand, only very small amounts of tetrahydroxystearic acids were isolated after oxidation of linoleic acid obtained by debromination of the liquid or β-tetrabromostearic acid. Even these amounts were attributed to the presence of α-linoleic acid in the β-linoleic acid. The main product of oxidation of the latter acid consisted of an oily substance which appeared to consist only of short chain compounds presumably produced as a result of fission at the double bonds.

Nunn and Smedley-Maclean[87] oxidized the mixed acids from linseed oil

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[41] B. H. Nicolet and H. L. Cox, *J. Am. Chem. Soc.*, **44**, 144–152 (1922).
[42] T. G. Green and T. P. Hilditch, *Biochem. J.*, **29**, 1552–1563 (1935).

TABLE 120

TETRAHYDROXYSTEARIC OR SATIVIC ACIDS OBTAINED BY GREEN AND HILDITCH ON ALKALINE PERMANGANATE OXIDATION OF VARIOUS LINOLEIC ACIDS[a]

Acid oxidised	Yield of sativic acids, %			Method
	m.p. 155°C.	m.p. 173°C.	Total	
Liquid acids from safflowerseed oil	20	18	38	Hazura
α-Linoleic	43	22	65	Hazura
α-Linoleic	23	15	38	Lapworth and Mottram
Linolelaidic	10	6	16	Lapworth and Mottram
β-Linoleic	2	3	5	Hazura

[a] T. G. Green and T. P. Hilditch, *Biochem. J.*, 29, 1552–1563 (1935).

and linoleic acid obtained by debromination of crystalline tetrabromostearic acid, using the same method which they applied to oleic acid. They obtained yields varying from 52% to 54% of tetrahydroxystearic acid from linoleic acid, compared to 28% to 32% of the same acid from the mixed acids of linseed oil. An oily product, similar to that obtained by Green and Hilditch, was recovered by Nunn and Smedley-Maclean. This product consisted of a small amount of azelaic acid (1.2%) and a considerable amount of the γ-lactone of 3,4-dihydroxydecanedicarboxylic acid, $C_{12}H_{18}O_4$. The latter acid was formed by fission of the linoleic acid between the twelfth and thirteenth carbon atoms which were presumed to be oxidized first to the hydroxy state. Fission by alkaline permanganate oxidation is additional and independent evidence of the susceptibility of this bond to attack in preference to that between the ninth and tenth carbon atoms.

Permanganate oxidation of linolenic acid has also been investigated, especially by Hazura,[22,24,25] Rollett,[31] Green and Hilditch,[42] and Nunn and Smedley-Maclean.[37] Hazura[22,24,25] obtained a high melting hexahydroxystearic (linusic) acid upon oxidation of linolenic acid and the liquid acids derived from different oils of which linolenic acid was a component. Rollett[31] oxidized linolenic acid, regenerated from its hexabromide, and obtained, in addition to the high melting hexahydroxystearic acid (m.p. 201° to 203°C.), a second hexahydroxystearic acid melting at 171° to 173°C., which Hazura had designated isolinusic acid. Hazura had previously isolated isolinusic acid from various oils but failed to note its presence in the oxidation products of linolenic acid itself, probably because of its appreciable solubility in water.

Green and Hilditch,[42] employing the method of Hazura, oxidized α-linolenic acid, obtained by debromination of crystalline hexabromostearic acid, with alkaline permanganate and isolated in 15% to 18% yield two hexahydroxystearic acids melting at 203° and 169°C., respectively. All attempts to increase these yields were unsuccessful.

Nunn and Smedley-Maclean,[37] using Rollett's conditions of oxidation, obtained 10.7% of linusic and 14.7% of isolinusic acids, a total of 25.4% of hexahydroxystearic acids, from linolenic acid prepared from linseed oil. Oxidation of the mixed acids of linseed oil yielded 40% to 52% of hexahydroxystearic acids which led these workers to conclude that the presence of linoleic acid in the mixed acids exercises a protective action on the oxidation of linolenic acid and retards its further oxidation to short chain acids.

(*d*) *Permanganate Oxidation of Acetylenic Acids*

The naturally occurring acetylenic acid, tariric or 6,7-stearolic acid, was found by Steger and van Loon[43] to yield 6,7-diketostearic acid (m.p. 98°C.) on oxidation with alkaline permanganate. No other products of oxidation were isolated. However, complete disruptive oxidation of the ethyl ester occurred when the oxidation was carried out in boiling acetone by a modification of the Bertram oxidation method in which the condensed acetone was passed through a layer of potassium permanganate before returning to the reflux flask.

(*e*) *Quantitative Methods of Oxidation with Potassium Permanganate*

Two quantitative methods of oxidation with aqueous potassium permanganate have been applied in the analysis of fats or fatty acids. One, that of Lapworth and Mottram, is used for estimating oleic acid in crude oleic acid, and the other, that of Bertram, is used for the determination of the saturated fatty acids in the mixed fatty acids obtained from natural fats.

Lapworth-Mottram Method.—The procedure of Lapworth and Mottram[34] for the determination of oleic acid in crude oleic acid is as follows: The clear solution of the sodium salts, obtained by warming about 5 g. of ordinary oleic acid on the water bath with an equal weight of caustic soda, is dissolved in 500 ml. of water and cooled. Four liters of ice-cold water is added, and the solution is shaken at 10°C. while 400 ml. of a 1% solution of potassium permanganate is quickly added. After five minutes, the solution is decolorized with sulfur dioxide, and 150 ml. of concentrated hydrochloric acid is added. The white, flocculent precipitate, *A*, of crude solid dihydroxystearic acid which separates is filtered off, drained for a short time, and washed with about 50 ml. of petroleum naphtha to facilitate drying, and then dried in a vacuum desiccator to constant weight.

The solubility of dihydroxystearic acid in petroleum naphtha (b.p. 80° to 100°C.) is not more than 0.002 g. in 100 ml. at 15°C., and therefore the loss due to washing is negligible. The aqueous filtrate contains no appreciable quantities of higher fatty acids, but does contain about 0.15 g. of products

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[43] A. Steger and J. van Loon, *Rec. trav. chim.*, **52**, 593–600 (1933).

of lower molecular weight, such as nonanoic, octanoic, azelaic, and suberic acids, formed by the breaking down of a small amount of the dihydroxystearic acid.

The dried crude acid is extracted with 100 to 150 ml. of warm petroleum naphtha (b.p. about 70° to 80° C.), the extract cooled, filtered, and the residue, *B*, of nearly pure dihydroxystearic acid washed with several successive quantities of cold solvent. The petroleum naphtha extracts and washings are united and evaporated.

In order to effect, if desired, a complete conversion of the small quantity of oleic acid which escaped oxidation, the residue left on evaporation of the petroleum naphtha is reoxidized as described above using 50 ml. of cold 0.1 *N* sodium hydroxide, 100 ml. of ice water, 15 ml. of 1% potassium permanganate solution, and 10 ml. of concentrated hydrochloric acid. The precipitate, *C*, is washed with water, dried at room temperature, and extracted with cold light petroleum naphtha.

The residue left on evaporation of the collected petroleum naphtha extracts is distilled with steam to remove traces of volatile fatty acids, and treated with low boiling petroleum naphtha. This treatment extracts the nonvolatile acids, which, after evaporation of the solvent, are heated on the water bath to constant weight. The residue, *D*, which sets to a waxy solid on cooling comprises the higher saturated fatty acids which were present in the crude oleic acid.

The unsaponifiable constituents in the original sample are not, in general, found in the residue, *D*, at least not in appreciable quantity. If desirable, however, the quantity of such constituents can easily be determined by the usual method of determining unsaponifiable matter, or more simply by dissolving the residue, *D*, in a little methanol, adding an excess of methanolic barium hydroxide, evaporating the solution to complete dryness, and extracting the residue with dry acetone, in which barium hydroxide and barium salts of saturated fatty acids are insoluble.

Bertram Oxidation.—Bertram[44-46] was the first to apply oxidation with potassium permanganate to the quantitative determination of saturated acids in mixtures of saturated and unsaturated acids. The original method has been modified by various workers, notably by Hilditch and Priestman,[47] Jamieson,[48] Lyutenberg and Dudkina,[49] and Pelikan and von Mikusch.[50] The method consists essentially of the oxidation of a mixture of fatty acids, obtained by saponification of a fat or oil, to convert the un-

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[44] S. H. Bertram, *Z. deut. Öl- u. Fett-Ind.*, **45**, 733–736 (1925).
[45] S. H. Bertram, *Chem. Weekblad*, **24**, 226–229, 320 (1927).
[46] S. H. Bertram, *Z. Untersuch. Lebensm.*, **55**, 179–187 (1928).
[47] T. P. Hilditch and J. Priestman, *Analyst*, **56**, 354–367 (1931).
[48] G. S. Jamieson, *Vegetable Fats and Oils.* 2nd ed., Reinhold, New York, 1943.
[49] A. Lyutenberg and T. Dudkina, *Trudy* VNIIZh, **2**, 60–62 (1934).
[50] K. A. Pelikan and J. D. von Mikusch, *Oil & Soap*, **15**, 149–150 (1938).

saturated acids into lower molecular weight normal acids and polyhydroxy acids which can be separated from the unattacked saturated acids.

As generally applied, the alkali soaps from a 5-g. sample of saponified fat are oxidized in an aqueous alkaline solution of potassium permanganate. The procedure as described by Jamieson[48] is as follows: The soap solution contained in a casserole is heated on a steam bath until most of the alcohol is removed. It is then heated carefully over a flame until the remainder of the alcohol is volatilized. After cooling, about 300 ml. of water is added and the mixture heated until the soaps have dissolved, after which it is transferred to a two-liter flask, the casserole is rinsed several times with hot water, and the rinsings are added to the flask. After cooling the solution to room temperature (not above 25°C.) there is added 35 g. of potassium permanganate dissolved in 750 ml. of water. After the mixture has stood 12 to 18 hours with occasional shaking, it must still contain excess permanganate. If it is not violet colored, further permanganate solution must be added, in which case it is necessary to allow the oxidation reaction to proceed for another 12 hours. Otherwise, the reaction mixture is acidified with sulfuric acid (1:2) and sufficient powdered sodium bisulfite added to decolorize it and dissolve the precipitated manganese oxides with the aid of heat.

Heating on a steam bath is continued until the fatty acids have entirely separated from the aqueous solution, after which the mixture is cooled and transferred to a separatory funnel of suitable size. It is then extracted three or four times using 200- to 250-ml. portions of petroleum naphtha. The petroleum naphtha extracts are combined in a separatory funnel and washed with three 100-ml. portions of water. The extract is transferred to a flask and the solvent distilled off as completely as possible and the residue dried by heating in an oven at 110°C. for an hour. This residue is treated with 200 ml. of hot water and an excess of ammonium hydroxide and heated until it is completely dissolved. Thereafter, 30 ml. of a 10% ammonium chloride solution and an excess of a 15% solution of magnesium sulfate are added. The solution is cooled and the precipitate is filtered off and washed thoroughly with water. The precipitate is transferred to the original flask with water and the magnesium soaps decomposed by heating with a slight excess of dilute sulfuric acid, after which the precipitation of the magnesium soaps is repeated. The precipitate is filtered, washed, and returned to the original flask and completely decomposed as before by heating with dilute sulfuric acid. The solution is cooled, transferred to a separatory funnel, and the saturated fatty acids extracted with three 200-ml. portions of petroleum naphtha. The petroleum naphtha extracts are combined and washed with two 50-ml. portions of water. The extract is then transferred to a flask and distilled until the volume of the solvent is reduced to about 50 ml., after which it is transferred to a weighed flask and the remaining solvent distilled off and the residue of saturated fatty acids dried to constant weight in an oven at 110°C.

Gay[51] concluded that the temperature used by Bertram (max. 25°C.) was insufficient to insure complete oxidation of the unsaturated acids of linseed oil and recommended two successive oxidations at 50° to 60° and 70° to 80°C., respectively. Hilditch and Priestman[47] employed a single oxidation at 35° to 50° and omitted the extraction of the unsaponifiable matter. Pelikan and von Mikusch[50] determined the proportion of saturated fatty acids in cottonseed oil by all three methods and found that Gay's method gave results approximately 50% lower than either the original Bertram method or the Hilditch and Priestman modified method. The latter two methods gave nearly identical results and Bertram's method gave almost theoretical recovery of saturated acids in a synthetic mixture of pure oleic and palmitic acids.

Since the recovery of saturated acids was practically identical by either the original Bertram method or the Hilditch-Priestman modification, Pelikan and von Mikusch recommended that heating or cooling be dispensed with and the oxidation be carried out at room temperature. They also recommended that where the unsaponifiable matter was less than 2% it need not be removed, but above this amount it is essential to do so if accurate results are to be obtained.

As a result of their investigation of the Bertram method, Pelikan and von Mikusch introduced a number of minor improvements which facilitate the quantitative determination of saturated fatty acids, and experience in the author's laboratory with their modification indicates that it is preferable to either the original method or any other modification thereof. The directions as given by the authors, are as follows:

Weigh out 5 grams of dry sample in a 250-ml. Erlenmeyer flask. Add 75 ml. of approximately 0.5 *N* alcoholic potassium hydroxide and reflux under an open air or water condenser for 0.5 hour. Wash into a 300-ml. porcelain dish with 50 ml. of water. Evaporate the soap solution until it begins to solidify. Add 100 ml. of water and boil again until the odor of alcohol has entirely disappeared. Then wash into a two-liter Florence flask with 100 ml. of water and add 5 ml. of potassium hydroxide (50%). Warm while swirling until the solution is clear. Cool thoroughly with cold water and slowly with swirling add a solution of 35 g. of potassium permanganate in about 0.75 liter of water, then allow to stand overnight.

After twelve hours or more add dilute sulfuric acid (50%) and concentrated potassium bisulfite solution until all manganese is reduced and dissolved. Heat to just below the boiling point. Cool and extract three times with 50 ml. of petroleum naphtha. Collect the extractions in a 250-ml.

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[51] P. J. Gay, *J. Soc. Chem. Ind.*, 51, 126–129T (1932).

separatory funnel and wash 3 times by running 50 ml. of water down along the inside of the funnel and swirling gently. Filter the solution into a 500-ml. extraction flask, following it with enough fresh petroleum naphtha to insure quantitative transference.

Distill off the petroleum ether and warm the remaining fatty acids with a few milliliters of ammonia. Add 200 ml. of hot distilled water and when all fatty acids have gone into solution add 30 ml. of a 10% ammonium chloride solution. Heat to boiling and add 20 ml. of a 15% magnesium sulfate solution. Heat again to boiling, cool and filter with suction through a layer of absorbent cotton, which is placed inside a Buchner funnel so as to cover the perforated plate as well as the walls. Wash flask and filter, neglecting any precipitate adhering to the inside of the flask. Transfer the cotton with the precipitate into the flask and add a few milliliters of sulfuric acid (50%). Heat, avoiding boiling, and swirl until the cotton wad is disintegrated and the fatty acids form a clear layer. Cool, add an excess of ammonia and warm until all the fatty acids are dissolved. Repeat the precipitation and filtration as above. Transfer back to flask and decompose as before with sulfuric acid. After cooling transfer to a separatory funnel with outlet wide enough to allow the cotton fibres to pass, using petroleum naphtha to wash the flask. Extract twice with petroleum naphtha and wash the petroleum naphtha solution three times with water by rinsing and swirling as above. Filter into a weighed 250-ml. extraction flask washing funnel and filter with petroleum naphtha. Take care that all water droplets are retained by the filter paper as their presence in the filtrate is undesirable. Distill off the solvent on a steam bath and dry the flask containing the saturated fatty acids in the oven at 105°C. for 10 minutes. Cool, weigh and repeat the drying in the oven until constant weights are obtained or the loss of weight does not exceed 2 mg.

The isolated fatty acids will in many cases contain several tenths of a per cent of unsaturated fatty acid. These may be assumed to consist mostly of oleic acid because the ease of oxidation increases with the degree of unsaturation. To obtain the actual saturated content it is advisable to determine the approximate iodine value of the product. This is done directly in the flask after dissolving in 10 ml. of chloroform. Add 10 ml. of Hanůs or Wijs solution from the burette or pipette, swirl 2 minutes, then add 10 ml. of potassium iodide solution and proceed to titrate as usual. A blank run in similar fashion is required to calculate the iodine value.

The "corrected" higher saturated fatty acid content is then calculated from the following equation:

$$G = \frac{100}{S}\left(W - \frac{IW}{90}\right)$$

where G = higher saturated fatty acids content in per cent, W = weight of isolated fatty acids, I = iodine value of the isolated f. a., S = weight of sample used.

Several years prior to the work of Pelikan and von Mikusch, Lyutenberg and Dudkina[49] investigated the Bertram oxidation method and recommended that the reaction be carried out at room temperature. These authors claim that the aqueous filtrate need not be extracted with petroleum naphtha and that the saturated acids can be filtered easily after cooling. They further claim, in contrast to the original Bertram method and modifications thereof, that their modification gives saturated acids with practically zero iodine values.

The Bertram method of oxidation is not applicable to fats containing lauric or lower fatty acids, to fats which contain unsaturated acids such as petroselinic acid ($\Delta^{6,7}$-oleic acid), to Picramnia oils which contain $\Delta^{6,7}$-tariric acid, or to any oil or fatty acid which yields lauric or similar acids on disruptive oxidation. When applied to coconut, palm kernel, or myristica oils, low results are obtained owing to loss of part of the lauric and other acids of low molecular weight. As pointed out by Hilditch and Priestman,[47] the successful application of the method depends on the following conditions: (*1*) The oxidation of unsaturated acids must be complete; (*2*) dihydroxy and polyhydroxy acids produced by oxidation must be completely insoluble in petroleum naphtha and the higher fatty acids must be completely soluble in the same solvent; and (*3*) the lower fatty acids produced by oxidation and the dibasic acids insoluble in petroleum naphtha must form water-soluble magnesium salts.

Since a great many fats do not conform to these conditions, the method is not universally applicable. With some fats low results are obtained and with others the reverse occurs. According to Hilditch and Priestman, myristic acid lies on the border line with respect to these solubility relations and its presence may lead to low results in some cases. However, in the case of fats to which the method is generally applied, results tend to be high, at least higher than those obtained by the lead salt–alcohol method, owing either to incomplete oxidation of the unsaturated acids, or to the incomplete removal of oxidation products from the saturated fatty acids, or to both. In the presence of large amounts of stearic acid as in beef tallow, complete separation of stearic and dihydroxystearic acid is difficult.

In many cases it is found that the recovered saturated acids have an iodine value thereby indicating the oxidation was not complete. Generally, a correction is applied to the yield of saturated acids on the basis of the observed iodine value. As previously mentioned, Hilditch and Priestman proposed that the oxidation temperature be increased to 35° to 50°C. to insure complete oxidation, or that the oxidation be carried out on the fat in acetone solution followed by saponification. In most cases where the Bertram oxidation and lead salt–alcohol methods are equally applicable (absence of myristic or lower acids), the results of the former method are 0.5% to 1.0% or more higher than in the latter method. This difference has been attributed to the incomplete separation of the oxidation products from stearic and palmitic acids or to the incomplete oxidation of the unsaturated acids.

(*f*) *Nonaqueous (Acetone) or Acidic Oxidation with Potassium Permanganate*

As has been previously mentioned, when unsaturated fatty acids are oxidized with potassium permanganate in acidic or nonaqueous (acetone) solutions, fission occurs at the double bonds instead of formation of hydroxy acids as in the case of oxidation in an alkaline medium. Theoretically, disruptive oxidation of monoethenoid acids should produce two short-chain acids, one dibasic and the other monobasic, or in the case of oxidation of the ester, a monobasic acid and the half-ester of a dibasic acid. For example, disruptive oxidation of oleic acid should produce only azelaic acid and nonanoic (pelargonic) acid in equimolar quantities in accordance with the following equation:

$$\underset{\text{Oleic acid}}{CH_3(CH_2)_7CH{:}CH(CH_2)_7COOH} \longrightarrow \underset{\text{Nonanoic acid}}{CH_3(CH_2)_7COOH} + \underset{\text{Azelaic acid}}{HOOC(CH_2)_7COOH}$$

Although these two acids are generally observed in the products of disruptive oxidation, various other products have also been detected, and the two acids are generally not produced in the same proportions. The explanation of this divergence from theory resides in the fact that intermediate products of oxidation, such as hydroxy acids, are formed prior to fission and the fission products are themselves subject to further oxidation. The two fission products from oleic acid mentioned above do not undergo additional oxidation at the same rates, the monobasic acid oxidizing much more rapidly than the dibasic acid, which often results in appreciably lower yields of the former as compared with the latter acid.

Even in the case of alkaline permanganate oxidation which produces predominantly hydroxy acids, Lapworth and Mottram[34] and Green and Hilditch[42] have shown that further oxidation leads to the production of suberic, oxalic, and *n*-octanoic acids. Hilditch[52] pointed out the fact that alkaline permanganate oxidation of various monoethenoid acids produces not only dihydroxy acids, but also a series of acids containing one less carbon atom than that corresponding to the theoretical fission product.

The nature of the fission products obtained on disruptive oxidation with potassium permanganate depends therefore on the reaction conditions. For example, Spiridonoff[53] oxidized oleic acid under conditions somewhat

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[52] T. P. Hilditch, *Chemical Constitution of Natural Fats.* Wiley, New York, 1941, p. 322.

[53] N. Spiridonoff, *J. Russ. Chem. Soc.*, **19**, 646–654 (1887).

similar to those used by Saytzeff; but, instead of obtaining dihydroxystearic acid as the principal product of reaction, he obtained instead nonanoic, azelaic, and oxalic acids. Edmed[54] employed aqueous permanganate at 60°C. for the oxidation of oleic acid and obtained 60% of dihydroxystearic acid (m.p. 132°C.), 16% each of azelaic and oxalic acids and a small amount of nonanal. Other workers have shown that still other and shorter chain acids are produced under more drastic conditions of permanganate oxidation.

Armstrong and Hilditch[55] described a method for the disruptive oxidation of methyl oleate in acetone solution which they claim yields 80% to 90% of the theoretical amount of nonanoic acid. The method consists essentially of refluxing an acetone solution of the ester in the ratio of 10:1 and adding an excess of finely powdered potassium permanganate (4 parts of permanganate to 1 of ester) in small portions over a period of about 1.5 hours. These authors also described a similar method which involves the use of glacial acetic acid as the solvent at the temperature attainable on the steam bath. Ethyl oleate under these conditions gave yields of azelaic and nonanoic acids equivalent to 95% and 59%, respectively, of theory. These yields, however, are calculated on the basis of the weight of ester converted into fission products and not on the weight of ester subjected to oxidation. Generally, about 25% of the ester was converted to neutral oily products of very low iodine value.

Grün and Wittka[56] proposed a modification of the permanganate and chromic acid methods of oxidation whereby quantitative yields of the fission products can be obtained with monoethenoid acids. The method consists in forming the dibromo- acid and from it the corresponding acetylenic acid by debromination with alcoholic potash. The acetylenic acid is then oxidized with potassium permanganate or chromic acid to give the corresponding monobasic and dibasic acids in quantitative yields. The reaction is illustrated with oleic acid by:

$$CH_3(CH_2)_7CH{:}CH(CH_2)_7COOH \longrightarrow CH_3(CH_2)_7CHBrCHBr(CH_2)_7COOH \longrightarrow$$
$$CH_3(CH_2)_7C{:}C(CH_2)_7COOH \longrightarrow CH_3(CH_2)_7COOH + HOOC(CH_2)_7COOH$$

The actual oxidation was carried out as follows: 10 g. of stearolic acid was dissolved in 100 ml. of water containing 3.5 g. caustic potash, and 500 ml. of a 2% solution of potassium permanganate was slowly added. With the first additions of permanganate, reaction occurred only slowly but became quite rapid with further addition of the reagent. At the end of the oxidation the reaction mixture was acidified with sulfuric acid and the excess permanganate destroyed with oxalic acid; the precipitated manganese

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[54] F. G. Edmed, *J. Chem. Soc.*, **73**, 627–634 (1898).
[55] E. F. Armstrong and T. P. Hilditch, *J. Soc. Chem. Ind.*, **44**, 43–47T (1925).
[56] A. Grün and F. Wittka, *Chem. Umschau Fette Öle Wachse Harze*, **32**, 257–259 (1925).

dioxide and insoluble fatty acid (unchanged stearolic acid and by-products) were separated by filtration, and the aqueous filtrate extracted with ether. Pure azelaic acid (4.2 g. or 60% of theory) crystallized from the ether solution and an equivalent quantity of nonanoic acid remained in the mother liquor. The insoluble residue from the first oxidation was reoxidized in the same manner as before, whereupon 2.5 g. of azelaic acid was obtained, or a total of 6.7 g., which corresponds to a theoretical yield. No suberic acid could be detected.

Steger and van Loon[57] have described an improved method of adding the permanganate to the reaction mixture which employs a percolator containing powdered permanganate situated immediately below the reflux condenser. This arrangement automatically adds the permanganate to the reaction mixture and is especially advantageous where gaseous products of oxidation are evolved and quantitatively estimated.

Where monoethenoid acids are subjected to oxidation, simple distillation as described above serves to separate the two reaction products (mono- and dibasic acids), or they may be partially separated by extraction with ether and then reextracted with petroleum naphtha. However, with the more complex reaction mixtures resulting from the oxidation of polyethenoid acids or esters, the procedure described by Farmer and van den Heuvel[58] is preferable. Toyama and co-workers have found it advantageous to oxidize monoethenoid acids to dihydroxy acids by means of Hazura's alkaline permanganate method and then oxidize the separated hydroxy acids with potassium permanganate in acetone solution to split the acid between the adjacent hydroxyl groups.

Most of the known monoethenoid fatty acids have been subjected to disruptive oxidation with potassium permanganate by one or another of the previously mentioned methods. Toyama and Tsuchiya,[59] for example, obtained formic and azelaic acids through oxidation of the decenoic acid, $C_{10}H_{18}O_2$, obtained from sperm oil, thus establishing its structure as $CH_2{:}CH(CH_2)_7COOH$. Dodecenoic acid, $C_{12}H_{22}O_2$, and tetradecenoic acid, $C_{14}H_{26}O_2$, isolated from sperm blubber oil and sperm head oil by Toyama and Tsuchiya,[60] were found to produce *n*-heptanoic and glutaric acids, and *n*-nonanoic and glutaric acids, respectively, on permanganate oxidation which established their structures as $CH_3(CH_2)_5CH{:}CH(CH_2)_3COOH$ and $CH_3(CH_2)_7CH{:}CH(CH_3)_3COOH$. The tetradecenoic acid (physeteric) was also isolated from sardine oil and sperm blubber oil by Toyama and Tsuchiya[61] and likewise shown by permanganate oxidation to have the $\Delta^{5,6}$-structure given above.

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[57] A. Steger and J. van Loon, *Rec. trav. chim.*, **52**, 593–600 (1933); **54**, 284–288 (1935).
[58] E. H. Farmer and F. A. van den Heuvel, *J. Chem. Soc.*, **1938**, 427–430.
[59] Y. Toyama and T. Tsuchiya, *Bull. Chem. Soc. Japan*, **11**, 26–29 (1936).
[60] Y. Toyama and T. Tsuchiya, *Bull. Chem. Soc. Japan*, **10**, 563–569, 570–573 (1935).
[61] Y. Toyama and T. Tsuchiya, *J. Soc. Chem. Ind. Japan*, **38**, 1484–1487 (1935).

Hexadecenoic acid, $C_{16}H_{30}O_2$, was oxidized by Armstrong and Hilditch[62] with powdered potassium permanganate in acetone solution with the production of good yields of *n*-heptanoic and azelaic acids, thus establishing its structure as $CH_3(CH_2)_5CH{:}CH(CH_2)_7COOH$. The oxidation of oleic acid, $C_{18}H_{34}O_2$, has already been discussed. The three positional isomers of oleic acid, namely, the $\Delta^{6,7}$-isomer, petroselinic acid; the $\Delta^{11,12}$-isomer, vaccenic acid; and the $\Delta^{12,13}$-isomer have also been subjected to permanganate oxidation.

The acetone permanganate method of oxidation has been applied with more success to polyethenoid fatty acids than has been the case with the aqueous alkaline permanganate method. Linoleic acid, when oxidized in acetone solution in the presence of sodium bicarbonate, has been shown to result in fission at both double bonds to give azelaic, caproic, and oxalic acids. Toyama and Tsuchiya[63] obtained succinic acid, acetic acid, and monomethyl adipate on permanganate oxidation of the methyl ester of hiragonic acid, $C_{18}H_{26}O_2$, thus establishing the constitution of the acid as $\Delta^{6,7,10,11,14,15}$-hexadecatrienoic acid. Dolby, Nunn, and Smedley-Maclean[64] and Mowry, Brode, and Brown[65] applied disruptive permanganate oxidation to an investigation of the constitution of arachidonic acid, $C_{20}H_{32}O_2$. With aqueous alkaline permanganate, Dolby *et al.* definitely identified oxalic acid and obtained evidence of the presence of glutaric, succinic, caproic, valeric, and formic acids in the reaction mixture. Mowry *et al.* refluxed methyl arachidonate for 18 hours in acetone in the presence of a large excess of potassium permanganate obtaining good yields of four reaction products, namely, oxalic acid (39%), glutaric acid (49%), succinic acid (38%), and caproic acid (28%). These results led the latter authors to conclude that arachidonic acid is $\Delta^{5,6,8,9,11,12,14,15}$-eicosatetraenoic acid.

Toyama and Tsuchiya[66] subjected methyl and potassium clupanodonates to permanganate oxidation in acetone and aqueous solutions, respectively. In the first case, propionic, acetic, and succinic acids, and monomethyl succinate were obtained. The acetic acid was presumed to arise from the secondary decomposition of malonic acid. Butyric, adipic, and pimelic acids could not be identified. The same results were obtained with the potassium salts in aqueous solution. The structure of clupanodonic acid determined by permanganate oxidation agrees, therefore, with that obtained by ozonation.

Permanganate oxidation of the disruptive type has been successfully applied in investigating the structures of polyethenoid acids containing

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[62] E. F. Armstrong and T. P. Hilditch, *J. Soc. Chem. Ind.*, **44**, 180–189T (1925).

[63] Y. Toyama and T. Tsuchiya, *Bull. Chem. Soc. Japan*, **10**, 192–199 (1935).

[64] D. E. Dolby, L. C. A. Nunn, and I. Smedley-Maclean, *Biochem. J.*, **34**, 1422–1426 (1940).

[65] D. T. Mowry, W. R. Brode, and J. B. Brown, *J. Biol. Chem.*, **142**, 679–691 (1942).

[66] Y. Toyama and T. Tsuchiya, *Bull. Chem. Soc. Japan*, **11**, 745–750, 751–753 (1936); see **10**, 441–453 (1935).

conjugated double bonds. Oxidation at room temperature of α-elaeostearic acid, $CH_3(CH_2)_3(CH{:}CH)_3(CH_2)_7COOH$ by Brown and Farmer[67] with 4.8% permanganate solution containing a small amount of sodium carbonate gave valeric, azelaic, and oxalic acids in good yields. Morrell and Samuels[68] prepared the maleic anhydride adducts of α- and β-elaeostearic acids and subjected them to permanganate oxidation in boiling neutral acetone solution. The α-acid gave azelaic acid, and the β-acid gave valeric acid, as the principal products of fission. These fission products were considered to establish the structure of elaeostearic acid as $\Delta^{9,10,11,12,13,14}$-octadecatrienoic acid.

A geometrically isomeric elaeostearic acid, punicic acid, obtained from pomegranate seed oil was oxidized at 0°C. by Farmer and van den Heuvel[69] by means of a 10% aqueous acetone solution containing 3% potassium permanganate and 2% sodium carbonate. Good yields of valeric and azelaic acids and some oxalic acid were obtained as products of oxidation. The constitution of this acid was previously established by Toyama and Tsuchiya[70] by means of ozonation which also gave valeric and azelaic acids as the principal degradation products together with some oxalic acid and glyoxal.

Disruptive oxidation with 3% permanganate solution at 0°C. of the tetraene conjugated acid, parinaric acid, obtained from *Parinarium laurinum*, gave azelaic, propionic, and oxalic acids which would be expected if structure of the original acid corresponded to $\Delta^{9,10,11,12,13,14,15,16}$-octadecatetraenoic acid.[71]

Brown and Farmer[67] oxidized licanic acid, $C_{18}H_{30}O_3$ obtained from oiticica oil with neutral 3% potassium permanganate solution at 0°C. and observed that it absorbed 7.3 atoms of oxygen at which stage there were obtained valeric acid, γ-ketoazelaic acid, and some oxalic acid. On oxidation with permanganate in sodium carbonate solution at 0°C., 37.5 g. of licanic acid gave 12.6 g. ketoazelaic acid, 5.9 g. valeric acid, and 3.6 g. calcium oxalate. Morrell and Davis[72] subjected the maleic anhydride adducts of α- and β-licanic acid to permanganate oxidation in the presence of sodium carbonate and obtained 34% of γ-ketoazelaic from the former, and 87% of azelaic acid from the latter. These products established the constitution of licanic acid as 4-keto-$\Delta^{9,10,11,12,13,14}$-octadecatrienoic acid.

5. Oxidation with Hydrogen Peroxide and Per Acids

Hydrogen peroxide and the per acids which can be formed by the reaction of hydrogen peroxide with various acids and acid anhydrides have been

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[67] W. B. Brown and E. H. Farmer, *J. Chem. Soc.*, **1935**, 761–763.
[68] R. S. Morrell and H. Samuels, *J. Chem. Soc.*, **1932**, 2251–2254.
[69] E. H. Farmer and F. A. van den Heuvel, *J. Chem. Soc.*, **1936**, 1809–1811.
[70] Y. Toyama and T. Tsuchiya, *J. Soc. Chem. Ind. Japan*, **38**, 182–185B (1938).
[71] E. H. Farmer and E. Sunderland, *J. Chem. Soc.*, **1935**, 759–761.
[72] R. S. Morrell and W. R. Davis, *J. Chem. Soc.*, **1936**, 1481–1484.

used as oxidizing agents for fatty acids. The literature relative to the reaction of hydrogen peroxide with saturated and monoethenoid acids is conflicting with respect to the extent of the oxidation, the reaction mechanism, and the nature of the reaction products which are formed.

(a) *Action of Hydrogen Peroxide on Saturated Acids*

Dakin[73] oxidized ammonium butyrate (one mole) with a 3% solution of hydrogen peroxide (two moles) at the boiling point of the reaction mixture. The reaction was allowed to proceed during the continuous distillation of water and volatile reaction products after which the volatile and nonvolatile fractions were examined. There were detected among the reaction products acetoacetic acid, acetone, propionaldehyde, acetaldehyde, acetic acid, formic acid, and carbon dioxide. The amount of acetone and acetaldehyde combined was approximately 40%, and the carbon dioxide approximately 26% of the oxidized portion of the original acid. Similar, but less extensive, reaction occurred at 37°C.

Subsequently, Dakin[74] determined the extent to which carbon dioxide was produced when the ammonium salts of the saturated fatty acids from formic to stearic were oxidized by a boiling 3% aqueous solution of hydrogen peroxide. The lower molecular weight acids produced 20% to 47% of carbon dioxide compared to 8% to 16% for the higher acids. Somewhat later, Dakin[75] repeated the oxidation experiments with a view to determining the nature of the ketonic oxidation products which were formed. Each acid from butyric to stearic was found to yield a methyl-β-ketone ($R \cdot CO \cdot CH_3$) having one less carbon atom than the original acid. It was presumed, therefore, that the first step in the oxidation was the formation of a ketonic acid which underwent decarboxylation to form a ketone according to the following scheme:

$$RCH_2CH_2COOH \longrightarrow RCOCH_2COOH \longrightarrow RCOCH_3 + CO_2$$

Since β-hydroxybutyric acid was not detected as an oxidation product of butyric acid, Dakin concluded that the keto acid represented the first product of oxidation.

Clutterbuck and Raper[76] subjected the ammonium salts of stearic, palmitic, myristic, caproic, *n*-heptanoic, and caprylic acids to oxidation with hydrogen peroxide. The general method of oxidation employed was as follows: Stearic acid (10 g.), water (250 ml.), and ammonia (4 ml., 23% solution) were heated under reflux in a three-liter flask to 60°C. Hydrogen peroxide (21 ml., 30% solution) was then added and the temperature gradu-

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[73] H. D. Dakin, *J. Biol. Chem.*, **4**, 77–89 (1908).
[74] H. D. Dakin, *J. Biol. Chem.*, **4**, 227–233 (1908).
[75] H. D. Dakin, *Am. Chem. J.*, **44**, 41–48 (1910).
[76] P. W. Clutterbuck and H. S. Raper, *Biochem. J.*, **19**, 385–396 (1925).

ally raised to 90°C. and maintained at this temperature for four hours. At the end of the reaction period the solution was acidified with phosphoric acid and cooled, and the precipitated acids and ketone were separated by filtration. The various reaction products were then separated and identified by recognized methods. It was found that in addition to the β-keto acids obtained by Dakin, γ-keto acids were obtained from myristic, palmitic, and stearic acids, and both γ- and δ-keto acids were obtained from caproic, n-heptanoic, and caprylic acids. No evidence of the presence of hydroxy acids was obtained and it was, therefore, concluded as maintained by Dakin that the first step in the oxidation of a saturated acid with hydrogen peroxide is the production of series of keto rather than hydroxy acids. Small amounts of succinic acid were also observed among the reaction products which were presumed to arise from further oxidation of the keto acids.[77] Some evidence was obtained that unsaturated acids were formed but they could not be identified. In all cases the proportion of the original saturated acid which underwent oxidation was small, generally less than 10%.

Smedley-Maclean and Pearce[78] observed that palmitic acid was readily oxidized by hydrogen peroxide in the presence of cupric sulfate. Three to four hours' boiling with a large excess of hydrogen peroxide containing a few drops of cupric sulfate resulted in conversion of 70% of the palmitic acid to carbon dioxide and volatile fatty acids. The main product of oxidation appeared to consist of a mixture of isomeric substances in which unsaturated dihydroxy acids and hydroxy lactones predominated. Keto hydroxy acids could not be detected. The unsaturation was assumed to occur in the 2,3(α,β)- and 3,4(β,γ)-positions. The isolation of lactones in considerable amount indicated that oxidation had occurred in the γ- and δ-positions. Succinic acid was identified at every stage of the oxidation except the earliest. Volatile acids of low molecular weight were also formed. According to the observations of these authors, desaturation and hydroxylation appeared to take place simultaneously at several points along the palmitic acid chain which was gradually broken down to give unsaturated hydroxy acids containing 13, 10, and 7 carbon atoms as the main intermediate products of oxidation.

Allen and Witzemann[79] found that certain buffered oxidation systems such as disodium acid phosphate–hydrogen peroxide, Na_2HPO_4–H_2O_2, ammonia–hydrogen peroxide, and diammonium acid phosphate–hydrogen peroxide, $(NH_4)_2HPO_4$–H_2O_2, were conducive to oxidation of saturated fatty acids. When the fatty acids or their salts, in the case of the less soluble acids, were heated on a water bath with hydrogen peroxide in the presence of the above-mentioned buffers, all of the acids from acetic to

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[77] P. W. Clutterbuck, *Biochem. J.*, **21**, 512–521 (1927).
[78] I. Smedley-Maclean and M. S. B. Pearce, *Biochem. J.*, **28**, 486–494 (1934).
[79] R. H. Allen and E. J. Witzemann, *J. Am. Chem. Soc.*, **63**, 1922–1927 (1941).

capric were oxidized primarily to carbon dioxide (50% to 80%). Acetic acid and acetone were found among the end products of oxidation in the case of the acids above acetic. The authors interpreted the catalytic effect of the buffered reaction as a promotion of the reduction of hydrogen peroxide by supplying hydrogen from another source (the organic acid) to reduce it to water, and that the final oxidation of the substrate to carbon dioxide is a secondary reaction depending on the addition of water and is not primarily due to the peroxide itself. They assumed further that when oxidation of saturated fatty acids by hydrogen peroxide occurs in the presence of glycine, ammonium glycolate, or the ammonium salt of a fatty acid, it does so by virtue of the catalytic effect of the amino or ammonio compound.

(b) *Action of Hydrogen Peroxide on Unsaturated Acids*

The literature with respect to the oxidation of monoethenoid acids by hydrogen peroxide is similarly confusing. Hazura[80] investigated the oxidation of oleic acid with hydrogen peroxide at ordinary temperature in the absence of alkali, but failed to obtain any evidence of oxidation. Hilditch[81] reported the isolation in unspecified yield of dihydroxystearic acid melting at 92–93°C. which was produced on boiling, under reflux for eight hours, 5 g. of methyl oleate, 10 g. of concentrated hydrogen peroxide, and 50 ml. of acetone. Hilditch[82] states that pure hydrogen peroxide (Perhydrol) alone, or in the presence of a neutral solvent such as acetone, acts on oleic acid or its esters only very slowly to produce dihydroxystearic acid (m.p. 95°C.) in small amounts.

Smedley-Maclean and Pearce[83] oxidized oleic acid by heating it to 95°C. for 3 to 3.5 hours with a slightly alkaline solution of hydrogen peroxide. About 40% of the original oleic acid was recovered. Carbonic, acetic, and formic acids corresponding to 5–10% of the original acid were found among the reaction products, together with diketostearic, dihydroxystearic, and α-ketodecanoic acids. When the experiment was carried out under otherwise similar conditions except that a small amount of copper sulfate was added to the reaction mixture, more than 70% of the original acid was converted to carbonic, formic, and acetic acids. Small amounts of succinic and 4-keto-7-hydroxycaprylic acids were also identified. When the reaction was carried out at 60°C. in the presence of the cupric salt, about 20% of the original acid was converted to carbonic, formic, and acetic acids and the proportion of succinic acid was greatly increased, but 4-keto-7-hydroxycaprylic acid was found to be the principal product of the reaction. In some

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[80] K. Hazura, *Monatsh.*, 9, 469–474 (1888).

[81] T. P. Hilditch, *J. Chem. Soc.*, 1926, 1828–1836.

[82] T. P. Hilditch, in *Chemie und Technologie der Fette und Fettproduckte*, edited by G. Hefter and H. Schönfeld. Vol. I, Springer, Vienna, 1936, pp. 328–331.

[83] I. Smedley-Maclean and M. S. B. Pearce, *Biochem. J.*, 25, 1252–1266 (1931).

experiments the yield of the latter acid corresponded to approximately half of the original oleic acid.

Harris and Smith[84] found that hydrogen peroxide was relatively unreactive even with partially oxidized acids since they observed that when 10,11-epoxyundecanoic acid was allowed to remain in contact with hydrogen peroxide in ligroin solution no reaction occurred. Also, Dorée and Pepper[85] found that when erucic acid (2 g.) was refluxed for eight hours with 100 ml. of acetone containing 20 ml. of hydrogen peroxide, 1.9 g. of the acid was recovered unchanged. Refluxing oleic acid for fifty hours under otherwise similar conditions gave the same result, and no reaction was observed to occur with brassidic acid under these conditions.

(c) *Action of Benzoyl Peroxide on Fatty Acids*

Benzoyl peroxide, $(C_6H_5CO)_2O_2$, a solid substance melting at 108°C., is an oxidation reagent which may be considered as being structurally related to hydrogen peroxide, H_2O_2. Benzoyl peroxide readily reacts with saturated and aromatic hydrocarbons, with alcohols, organic acids, etc., at temperatures above 100°C. The peroxide decomposes thermally in the vapor phase to give the free radicals C_6H_5— and C_6H_5COO—,[86,87] and these are presumed to attack an organic substance, *RH*, with formation of new compounds and new free radicals. As an oxidizing agent for unsaturated acids it is generally used in solution at atmospheric temperature under which conditions it is probably less reactive than hydrogen peroxide, and it probably reacts to liberate free oxygen rather than to produce free radicals. It has not been generally used as an oxidation reagent in structural investigations of unsaturated fatty acids but it is used industrially for bleaching certain fatty products such as lecithin.

Piguleviskii and Petrov[88] oxidized oleic acid (38.4 g.) dissolved in dry ether at 2–3°C. for two days with an ethereal solution of benzoyl peroxide (18.92 g.). At the end of the reaction period a solid product, which was soluble in organic solvents and corresponded to the formula $C_{18}H_{36}O_3$, was hydrolyzed by boiling for one hour with water containing a few drops of sulfuric acid. A dihydroxystearic acid (m.p. 137°C.) was recovered from the hydrolyzate. Since the high melting hydroxy acid would be expected to result from the oxidation of elaidic rather than oleic acid, it was assumed that an inversion occurred during the reaction which was attributed by the authors to the hydrolytic reaction rather than to the original oxidation.

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[84] P. L. Harris and J. C. Smith, *J. Chem. Soc.*, **1935**, 1572–1576.

[85] C. Dorée and A. C. Pepper, *J. Chem. Soc.*, **1942**, 477–483.

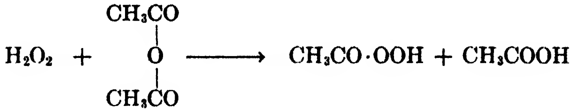
[86] D. H. Hey and W. A. Waters, *Chem. Revs*, **21**, 169–208 (1937).

[87] E. H. Farmer, *Trans. Faraday Soc.*, **38**, 340–348 (1942).

[88] G. V. Pigulevskii and M. A. Petrov, *J. Russ. Phys.-Chem. Soc.*, **58**, 1062–1066 (1926), see **48**, 1763 (1916).

(*d*) *Oxidation of Monoethenoid Acids with Per Acids*

The per acids, which may be considered as being derived by interaction of hydrogen peroxide and an acid anhydride, are energetic oxidizing agents. The per acids which have been chiefly used in the investigation of fatty acids are peracetic, perbenzoic, monopersulfuric (Caro's acid), and periodic. Peracetic acid is formed by the action of hydrogen peroxide on acetic anhydride as indicated in the following equation:



$$H_2O_2 + \begin{matrix} CH_3CO \\ | \\ O \\ | \\ CH_3CO \end{matrix} \longrightarrow CH_3CO{\cdot}OOH + CH_3COOH$$

It may be preferable to form the per acid by other means. Perbenzoic acid, for example, may be prepared *in situ* by the action of hydrogen peroxide on benzoic acid, but if it is desired to isolate the acid in the solid state it is preferable to prepare it by the action of sodium methylate on benzoic peroxide in chloroform solution.[89] The reactions involved are as follows:

$$(C_6H_5CO)_2O_2 + CH_3ONa \longrightarrow C_6H_5COO_2Na + C_6H_5COOCH_3$$

$$C_6H_5COO_2Na + H_2SO_4 \longrightarrow C_6H_5COO_2H + NaHSO_4$$

Oxidation of an unsaturated fatty acid with a per acid produces a variety of reaction products depending on the nature of the reagent, the conditions of oxidation, and the structure of the unsaturated acid. The known reaction products resulting from the oxidation of monoethenoid acids include oxido acids, peroxido acids, ketohydroxy acids, and dihydroxy acids. Complete fission appears to occur with monethenoid acids only as a result of severe hydrolysis of the intermediate oxidation products.

Caro's acid, monopersulfuric acid, was discovered in 1898 and shortly thereafter was applied by Albitzki[90] as an oxidizing agent for oleic and elaidic acids. He obtained a low melting dihydroxystearic acid by oxidation of oleic acid and a high melting dihydroxystearic acid by oxidation of elaidic acid, which products were identical with the acids previously obtained by the action of hydrogen peroxide and acetic acid on these unsaturated fatty acids. Albitzki also oxidized erucic and brassidic acids with monopersulfuric acid prepared by the action of concentrated sulfuric acid on ammonium persulfate $(NH_4)_2S_2O_8$. Erucic acid was found to give dihydroxybehenic acid (m.p. 98–100°C.) whereas brassidic acid gave dihydroxybehenic acid (m.p. 131–33°C.). Albitzki assumed that the reaction occurred first by addition of the elements of monopersulfuric acid to the double bond, followed by hydrolysis in acid solution as follows:

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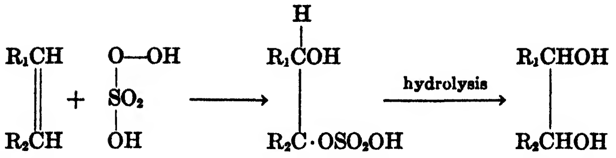
[89] H. Gilman, *Organic Syntheses*. Collective Vol. I, 2nd ed., Wiley, New York, **1941**, pp. 431–434.

[90] A. Albitzki, *Ber.*, **33**, 2909–2910 (1900); *J. Russ. Phys.-Chem. Soc.*, **34**, 788–810, 810–828 (1902); *J. prakt. Chem.*, **67**, 289–315, 357–376 (1903).



$$\begin{matrix} R_1CH \\ \| \\ R_2CH \end{matrix} + \begin{matrix} O\text{—}OH \\ | \\ SO_2 \\ | \\ OH \end{matrix} \longrightarrow \begin{matrix} H \\ | \\ R_1COH \\ | \\ R_2C\cdot OSO_2OH \end{matrix} \xrightarrow{\text{hydrolysis}} \begin{matrix} R_1CHOH \\ | \\ R_2CHOH \end{matrix}$$

Afanasievski[91] oxidized petroselinic acid with monopersulfuric acid and obtained 6,7-dihydroxystearic acid.

Little subsequent interest was shown in per acid oxidation until about 1926 when Böeseken and Belinfante, Hilditch and co-workers, Bauer and co-workers, Smit, and others investigated the reaction of unsaturated acids with peracetic and perbenzoic acids. Böeseken and Belinfante[92] and Smit[93] oxidized oleic and elaidic acids with peracetic and perbenzoic acids and concluded that the two per acids did not react in the same manner. According to the first-mentioned authors, peracetic acid was presumed, like monopersulfuric acid, to add at the double bond as follows:

$$\begin{matrix} R_1\text{—}CH \\ \| \\ R_2\text{—}CH \end{matrix} + CH_3C\begin{matrix} \diagup O\cdot OH \\ \diagdown O \end{matrix} \longrightarrow \begin{matrix} R_1\text{—}CHOH \\ | \\ R_2\text{—}CH(O\cdot COCH_3) \end{matrix}$$

Obviously, alternate addition would also occur and an isomeric pair of addition products would be formed. If, however, subsequent hydrolysis of the hydroxyacetoxy addition products occurred, the resulting dihydroxy acids would be identical. Perbenzoic acid, on the other hand, was presumed to form an oxido compound, $R_1\text{—}\underset{\diagdown O \diagup}{CH\cdot CH}\text{—}R_2$, which in the presence of dilute sulfuric acid was converted to a dihydroxy acid. Smit observed that oleic and elaidic acids could be quantitatively titrated with peracetic acid, exactly as with Wijs iodine solution but they could not be titrated quantitatively with perbenzoic acid. Various natural fats and oils were also observed to add oxygen quantitatively when titrated with peracetic acid.

Hilditch and Lea[94] investigated the reaction of oleic and elaidic acid esters with hydrogen peroxide in acetic acid solution. They observed that reaction occurred only slowly at low temperatures but rapidly at 70–90°C., and that the reaction products consisted of about 15% of 9,10-dihydroxystearic acid (m.p. 95°C.), about 55% of acetylated dihydroxystearic acid, and about 30% of a peroxidic oily product. It was concluded, therefore, that hydrogen peroxide reacted with acetic acid to produce peracetic acid

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[91] I. Afanasievski, *J. Russ. Phys.-Chem. Soc.*, **47**, 2124–2127 (1915).

[92] J. Böeseken, *Rec. trav. chim.*, **45**, 838–844 (1926). See J. Böeseken and A. H. Belinfante, *ibid.*, **45**, 914–918 (1926); J. Böeseken and G. Elsen, *ibid.*, **48**, 363–369 (1929); J. Böeseken, W. C. Smit, and Gaster, *Proc. Acad. Sci. Amsterdam*, **32**, 377–383 (1929).

[93] W. C. Smit, *Rec. trav. chim.*, **49**, 539–551, 675–685, 686–690, 691–696 (1930).

[94] T. P. Hilditch and C. H. Lea, *J. Chem. Soc.*, **1928**, 1576–1583. See T. P. Hilditch, *ibid.*, **1926**, 1828–1836.

which added to the double bond. The ester of elaidic acid under the same conditions gave the ester of 9,10-dihydroxystearic acid melting at 132°C.

Bauer and Bähr[95] carried out an extensive investigation of the reaction of perbenzoic acid with mono- and polyethenoid acids. The monoethenoid acids used in this investigation included oleic, elaidic, erucic, ricinoleic, and ricinelaidic. In all cases the principal product of oxidation was found to be an oxido acid which when heated with aqueous potash was converted to the corresponding hydroxy acid. In general, the method consisted of dissolving the acid in chloroform and adding an excess of perbenzoic acid. The absorption of oxygen was determined daily by titration and at the end of the reaction period the chloroform was evaporated and the excess perbenzoic acid destroyed by boiling with water. The oxido acid was converted to polyhydroxy acid by heating with aqueous potash in a sealed tube at 130–150°C.

Under these conditions of oxidation, oleic acid gave oxido-oleic acid (m.p. 52°C.) from which dihydroxystearic acid (m.p. 96°C.) was obtained by the action of alkali. Elaidic acid gave oxidoelaidic acid (m.p. 57.5–58.5°C.) which on hydrolysis gave dihydroxystearic acid (m.p. 132°C.). In both cases only one atom of oxygen was absorbed. Methyl elaidate when oxidized with perbenzoic acid gave methyl oxidoelaidate (m.p. 32–33.5°C.), which product was also produced from oxidoelaidic acid by methylation with diazomethane.

Erucic acid gave oxidoerucic acid (m.p. 67.5°C.) which on heating for six hours at 170°C. with alkali gave dihydroxybehenic acid (m.p. 133°C.). In the light of later work by Dorée and Pepper,[85] it is apparent that the drastic hydrolytic action employed by Bauer and Bähr resulted in an inversion of the *cis*-oxido acid to the *trans*-dihydroxy acid. Dorée and Pepper observed that hydrolysis of oxido acids in alkaline medium occurred with difficulty, whereas acid hydrolysis occurs readily and proceeds without inversion.

Ricinoleic acid treated in the same manner gave an oily product containing one additional oxygen atom. This product when heated with alkali gave trihydroxystearic acid (m.p. 110°C.). The high melting form of trihydroxystearic acid (m.p. 142°C.) was not detected. Ricinelaidic acid gave a solid reaction product insoluble in chloroform which on further reaction with alkali gave the same trihydroxystearic acid (m.p. 110–11°C.) as was obtained with ricinoleic acid.

Dorée and Pepper[85] obtained the same dihydroxystearic acids as were obtained by Hilditch when oleic and elaidic acids were oxidized with hydrogen peroxide in acetic acid solution in the absence of a catalyst. However, when osmium tetroxide was added to the reacting system and the reaction carried out at 60°C., the converse products of oxidation were obtained in 60%

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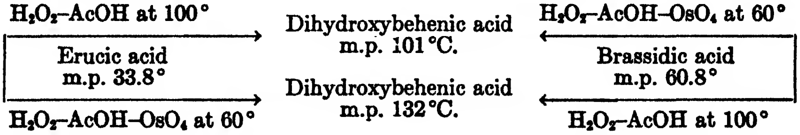
[95] K. H. Bauer and O. Bähr, *J. prakt. Chem.*, 122, 201–213 (1929)

yields. These authors concluded, therefore, that an inversion occurred during the oxidation owing to the action of the catalyst. This conclusion was confirmed and extended by their investigations of the oxidative action of peracetic and perbenzoic acids on erucic (*cis*) and brassidic (*trans*) acids, $CH_3(CH_2)_7CH:CH(CH_2)_{11}COOH$.

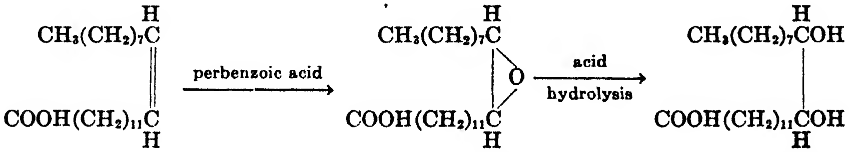
Erucic and brassidic acids were found to be unaffected after heating for eight or fifty hours with acetone–hydrogen peroxide solution (5:1 by volume). Neither acid was found to react with acetic acid–hydrogen peroxide (2.5:1 by volume), in the presence of vanadium pentoxide as a catalyst, either at room temperature for ten days or at 70°C. for forty hours. Glacial acetic acid and hydrogen peroxide (2.5:1 by volume) when heated with erucic acid (50 g.) at 100°C. for four hours in the absence of a catalyst gave a good yield (32 g.) of dihydroxybehenic acid (m.p. 101°C.). The mother liquor contained an oily product corresponding to 22.2% of erucic acid peroxide. On distillation of the erucic acid peroxide there was obtained a yield of approximately one-third of the product in the form of oxidobrassidic acid (m.p. 69.5°C.) which presumably was derived from the erucic acid peroxide by thermal action during distillation. Brassidic acid under similar conditions of oxidation gave the corresponding dihydroxybehenic acid melting at 132°C.

When the same reactions were carried out with the addition of osmium tetroxide as catalyst either at room temperature for fifty days or at 60°C. for one hour, erucic acid was found to yield dihydroxybehenic acid melting at 132°, whereas brassidic acid gave dihydroxybehenic acid melting at 101°, or the converse of that which occurred without a catalyst. Oxidation and saponification of the corresponding methyl esters gave the same final products as were obtained with the unesterified acids. In the case of the acids these reactions are illustrated in the accompanying scheme.

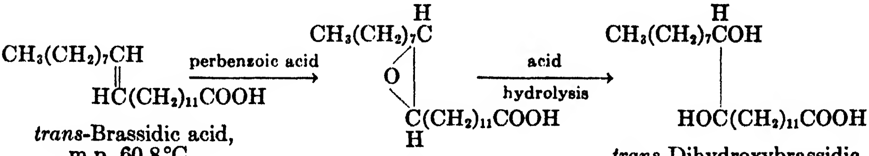


It is thus evident that oxidation with hydrogen peroxide in acetic acid, in the absence of a catalyst, occurs without inversion to give the *cis*-hydroxy acid from the *cis*-unsaturated acid and the *trans*-hydroxy acid from the *trans*-unsaturated acid. However, in the presence of the catalyst inversion occurs and the forms of the hydroxy acids are the converse of those obtained in its absence. The authors infer that inversion was due to the presence of the catalyst. However, by one definition of a catalyst, it cannot initiate a reaction or change the course of the reaction except to increase its velocity. If this is indeed the case, then oxidation with hydrogen peroxide and acetic acid would appear to result in the production of both isomeric dihydroxy acids but at different rates, one of which might be very much more rapid than the other. The addition of a catalyst to the reacting system could result in a preferential acceleration of the relative rates of the two reactions so that the converse dihydroxy acid becomes the predominant end product of the reaction.

Dorée and Pepper observed further that oxidation of *cis*-erucic acid with perbenzoic acid gave *cis*-oxidoerucic acid (m.p. 63.5°C.) in 60–70% yields and on acid hydrolysis this product gave *cis*-dihydroxybehenic acid (m.p. 101°C.). The *trans*-brassidic acid under the same conditions gave *trans*-oxidobrassidic acid (m.p. 70.5°C.), which on hydrolysis give *trans*-dihydroxybehenic acid (m.p. 132°C.). The reactions occurred in each case without inversion and may be illustrated as in the accompanying scheme.

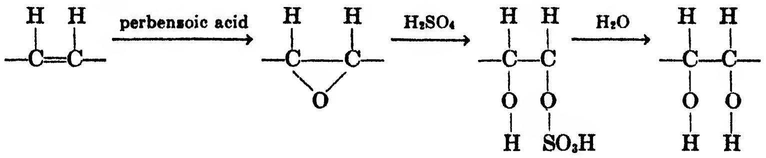


cis-Erucic acid, m.p. 33.8°C. *cis*-Oxidoerucic acid, m.p. 63.5°C. *cis*-Dihydroxybehenic acid, m.p. 101°C.



trans-Brassidic acid, m.p. 60.8°C. *trans*-Oxidobrassidic acid, m.p. 70.5°C. *trans*-Dihydroxybrassidic acid, m.p. 132°C.

Steger and van Loon[96] prepared petroselinic (*cis*-$\Delta^{6,7}$-octadecenoic) acid and petroselidinic or petroselinelaidic (*trans*-$\Delta^{6,7}$-octadecenoic) acid and subjected them to oxidation with perbenzoic acid and alkaline potassium permanganate. The corresponding 6,7-oxidostearic acids obtained by perbenzoic oxidation were subsequently sulfated and hydrolyzed to produce the corresponding 6,7-dihydroxystearic acids. The reactions occurring at the original double bond may be represented as follows:



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[96] A. Steger and J. van Loon, *Rec. trav. chim.*, **46**, 703–708 (1927).

The melting points of the derivatives of petroselinic and petroselidinic acids prepared by Steger and van Loon are recorded in Table 121. These melting points indicate that no inversion occurred in the course of any of the reactions—low melting derivatives have been obtained in each case from petroselinic acid, and high melting derivatives from petroselidinic acid. When, however, the *cis*- and *trans*-isomers were oxidized with alkaline potassium permanganate an inversion occurred and the high melting (122°C.) 6,7-dihydroxystearic acid was obtained from petroselinic acid and the low melting (117°C.) was obtained from petroselidinic acid.

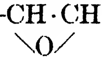
TABLE 121

MELTING POINTS IN DEGREES CENTIGRADE OF DERIVATIVES OF *cis*- AND *trans*-PETROSELINIC ACIDS

Acid	Triglyceride	Methyl ester	Oxido ester	Oxido acid	Dihydroxy acid
Petroselinic	26.2	liq.	26.4	59.2	117
Petroselidinic[a]	50.1	20.0	26.4	65.4	122

[a] Better known as petroselinelaidic acid. The present author has retained the nomenclature of Steger and van Loon, *Rec. trav. chim.*, **46**, 703–708 (1927).

Recently, Swern, Findley, and Scanlan[96a] reinvestigated the mechanism of peracetic and perbenzoic acid oxidations of unsaturated acids and concluded that in both cases the primary reaction product is an epoxy acid, but under the conditions generally employed with peracetic acid the oxirane ring, $\underset{\diagdown O \diagup}{\text{—CH}\cdot\text{CH—}}$, is opened to form hydroxyacetoxy derivatives. Either a short reaction time at high temperatures or a longer time at lower temperatures resulted in opening of the oxirane ring. These authors found that with a wide variety of unsaturated fatty acids or glyceride oils, oxidation to the epoxy stage was complete at room temperature in two to four hours when 1.1 to 1.2 moles of peracetic acid per mole of double bond was used. On dilution of the reaction mixture with water, the epoxy derivative was readily isolated by filtration or separation of the oil obtained. These products were primarily epoxy derivatives of the original acid or esters contaminated with a small amount of unreacted double bond and hydroxyacetoxy compounds.



In addition to the per acids previously mentioned, others have been prepared and used in oxidation reactions. Monoperphthalic acid has been proposed[97] as an oxidizing agent in the place of perbenzoic acid, but it appears to have found only limited application in investigations on unsaturated fatty acids despite a number of advantages. Solutions of monoperphthalic

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[96a] D. Swern, T. W. Findley, and J. T. Scanlan, *J. Am. Chem. Soc.*, **66**, 1925–1927 (1944), **67**, 412–414 (1945).

[97] H. Böhme, *Ber.*, **70**, 379–383 (1937).

acid are more stable than solutions of perbenzoic acid, are less sensitive to water and alkali, and are in many cases quantitative in their action.

Böhme and Steinke[98] proposed the so-called "per acid number" based on the number of milligrams of monoperphthalic acid required to oxidize a given fatty acid or oil under specified conditions of time, temperature, and concentration. Böhme and Steinke investigated these conditions for oleic and elaidic acids, triolein, and a conjugated octadecadienoic acid, as well as for a number of natural oils, including olive oil, cocoa butter,[99] sesame, poppyseed, and linseed oils. Oleic and elaidic acids and triolein were found to absorb oxygen quantitatively in a manner similar to that observed by Smit with peracetic acid. Polyethenoid acids and oils which contain these acids did not, however, react quantitatively with monoperphthalic acid although a number of them reacted to about 90% of theory.

(e) *Oxidation of Polyethenoid Acids with Per Acids*

Per acid oxidation of polyethenoid acids has not been attended with the same degree of success obtained with monoethenoid acids. Bauer and Kutscher[100] and Bauer and Bähr[95] investigated the action of perbenzoic acid on linoleic, linolenic, and elaeostearic acids. Linoleic acid, when treated with perbenzoic acid in chloroform solution for four days, was found to absorb oxygen corresponding to complete saturation of both double bonds. However, the resulting product was an oily liquid which could not be crystallized and on the basis of analysis and molecular weight determinations it appeared to have undergone polymerization. Alkaline hydrolysis did not produce tetrahydroxystearic (sativic) acid but gave instead a linoxylin-like product.

Linolenic acid similarly absorbed oxygen corresponding to complete saturation of all three double bonds. Two products, corresponding to $C_{18}H_{30}O_6$ and $C_{18}H_{30}O_5$, were obtained and on the basis of molecular weight determinations they were presumed to have undergone polymerization to form a dimer. The ethyl ester likewise absorbed three atoms of oxygen but the reaction product consisted of a monomer, $C_{20}H_{34}O_5$.

Elaeostearic acid, after reaction for seven days with perbenzoic acid in chloroform solution, produced an oily product having an iodine value of 18 to 19. No hexahydroxystearic acid could be isolated after alkaline hydrolysis of the reaction product but there was obtained instead an oily product of unknown constitution.

When methyl linoleate was oxidized with hydrogen peroxide in acetic acid solution, Green and Hilditch[101] obtained, in very small yields, two

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[98] H. Böhme and G. Steinke, *Ber.* **70**, 1709–1713 (1937).

[99] K. Bodendorf, *Pharm. Ztg.*, **74**, 384–385 (1929).

[100] K. H. Bauer and G. Kutscher, *Chem. Umschau*, **32**, 57–64 (1925).

[101] T. G. Green and T. P. Hilditch, *Biochem. J.*, **29**, 1552–1563 (1935).

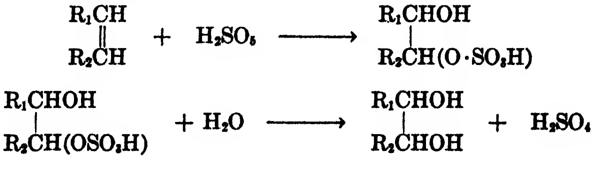
tetrahydroxystearic acids melting at 126° and 146°C. According to the authors, neither of these products bore any simple relationship to the hydroxy acids obtained by oxidation with potassium permanganate of either linoleic or linolelaidic acids. Oxidation of methyl linoleate with perbenzoic acid led to the formation of dioxidostearic acid but not to tetrahydroxystearic acid. Ethyl linolenate when oxidized with peracetic acid or perbenzoic acid gave neither crystalline hydroxy or oxido acids but only oily and gummy reaction products.

(*f*) *Oxidation of Fatty Oils with Per Acids*

Oda[102] attempted to produce a castor-oil-like product by the oxidation of soybean oil with hydrogen peroxide in acetic acid solution. When soybean oil was refluxed for one hour with acetic acid and hydrogen peroxide, both hydroxylation and acetylation occurred as was evident from the increased acetyl and saponification values of the reaction product compared with those of the original product.

Isii[103] extended the investigation of the behavior of soybean oil with various oxidation reagents and methods in a further effort to develop a castor-oil-like product from this oil. The oxidative reagents used by Isii included hydrogen peroxide in acetic acid and sulfuric acid solutions, and air in acetic acid solution. It was found that 30% hydrogen peroxide and 60% sulfuric acid in ratios from approximately 1:1 to 1:2 at 85° C., resulted in appreciable hydroxylation in three hours and produced a good substitute for castor oil. The reaction was represented as being similar to that occurring with monopersulfuric acid as originally proposed by Albitzki, namely:

$$H_2SO_4 + H_2O_2 \rightleftharpoons H_2SO_5 + H_2O$$



$$\begin{array}{c} R_1CH \\ \| \\ R_2CH \end{array} + H_2SO_5 \longrightarrow \begin{array}{c} R_1CHOH \\ | \\ R_2CH(O\cdot SO_3H) \end{array}$$

$$\begin{array}{c} R_1CHOH \\ | \\ R_2CH(OSO_3H) \end{array} + H_2O \longrightarrow \begin{array}{c} R_1CHOH \\ | \\ R_2CHOH \end{array} + H_2SO_4$$

Besides peracetic and persulfuric acids, Isii prepared performic, perpropionic, perbutyric, percaproic, perbenzoic, perphthalic, percamphoric, pernitric, perphosphoric, permolybdic, peruranic, perstannic, *et al.* acids by treatment of the appropriate acid or anhydride with hydrogen peroxide, and these in turn were used in the presence of 30% hydrogen peroxide to hydroxylate soybean oil. Hydrogen peroxide in the presence of hydro-

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[102] R. Oda, *J. Soc. Chem. Ind. Japan*, Suppl. binding, **41**, 195–196 (1938).

[103] Y. Isii, *J. Soc. Chem. Ind. Japan*, Suppl. binding, **43**, 255–256, 256–257, 315–317, 374–377, 377–379 (1940).

chloric, boric, and chromic acids did not produce measurable hydroxylation of soybean oil.

The effects of peracetic and persulfuric acids on soybean oil were compared under identical conditions with respect to time, temperature, concentration, etc., using solutions of 30% hydrogen peroxide in 98% acetic acid and in 60% sulfuric acid. The reactions of soybean oil and these two reagents were followed analytically at half hour intervals by determination of the acid number, iodine, thiocyanogen, hydroxyl, and acetyl values, viscosity, and solubility of the reaction product. Hydroxylation occurred with both reagents, but at different rates, of which the acetic acid reaction was the faster of the two. The combined acetic acid increased as the reaction time increased, whereas the percentage of combined SO_4 decreased. The content of active oxygen (peroxide) in neither case exceeded 0.025%.

In the course of an investigation on the absorption of oxygen by unsaturated oils in different solvents, Ueno and co-workers[104] observed that the presence of acetic acid led to accelerated absorption. Following this observation, Isii[103] investigated the action of oxygen and acetic acid as a hydroxylation agent with soybean oil using a temperature of 105–108°C., 98% acetic acid in concentrations from 10% to 200% of the oil, and an air velocity of 65 cc. per min. It was found that any increase in the concentration of acetic acid up to 20% of the mixture resulted in corresponding decreases in hydroxylation. Concentrations of acetic acid above 20% resulted in hydroxylation occurring and the maximum reaction was reached with 100% acetic acid to oil (1:1 ratio) but above this ratio a dilution effect was observed.

Hydroxylation was assumed to occur through intermediate formation of peroxides at the double bond of the unsaturated acids. The peroxide thus formed underwent acetylation to give a monohydroxymonoacetyl compound with the liberation of oxygen which in turn reacted with the acetic acid to form peracetic acid. The peracetic acid was presumed to react with other unattacked double bonds to form additional hydroxyacetyl products. Hydrolysis of the acetylated compound was not observed to occur.

When methyl oleate in acetic acid solution was also blown with air under conditions similar to those used with soybean oil, the reaction product was found to have the following characteristics: acid number 41.3, saponification number 271.1, acetyl saponification number 326.5, iodine value 40.2. After saponification and crystallization from ethyl acetate, dihydroxystearic acid (m.p. 130–31°C.) was obtained.

The reactions involved in the oxidations of soybean oil with per acids were represented to occur in the following manner:

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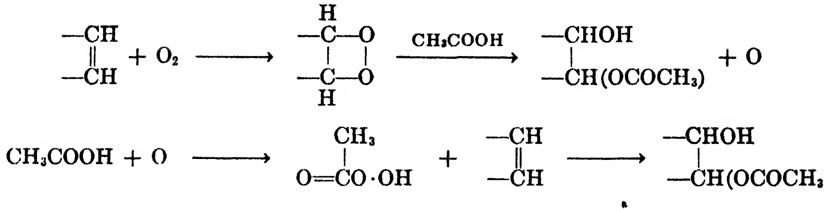
[104] S. Ueno, Z Okamura, and T. Saida, *J. Soc. Chem. Ind. Japan*, Suppl. binding, 34, 106–108 (1931).



$$\begin{matrix}\mathrm{-CH}\\ \| \\ \mathrm{-CH}\end{matrix} + O_2 \longrightarrow \begin{matrix}\mathrm{H}\\ \mathrm{-C-O}\\ |\quad |\\ \mathrm{-C-O}\\ \mathrm{H}\end{matrix} \xrightarrow{\mathrm{CH_3COOH}} \begin{matrix}\mathrm{-CHOH}\\ | \\ \mathrm{-CH(OCOCH_3)}\end{matrix} + \mathrm{O}$$

$$\mathrm{CH_3COOH} + \mathrm{O} \longrightarrow \begin{matrix}\mathrm{CH_3}\\ | \\ \mathrm{O{=}CO\cdot OH}\end{matrix} + \begin{matrix}\mathrm{-CH}\\ \| \\ \mathrm{-CH}\end{matrix} \longrightarrow \begin{matrix}\mathrm{-CHOH}\\ | \\ \mathrm{-CH(OCOCH_3)}\end{matrix}$$

6. Oxidation with Ozone

Ozone has been used since about 1900 as an oxidation reagent in determining the structures of unsaturated fatty acids. For such purpose it is applicable to both mono- and polyethenoid acids. As a general rule the method of oxidation with alkaline potassium permanganate is preferable for use with monoethenoid acids while ozonation yields more satisfactory results with polyethenoid acids. Readily identifiable dihydroxy acids are obtained in high yield under proper conditions of dilute alkaline permanganate oxidation of monoethenoid acids, whereas polyethenoid acids yield on oxidation with this reagent, a mixture of difficultly identifiable hydroxy acids. Ozonation of polyunsaturated acids occurs smoothly and with the formation of much less secondary oxidation than is the case with the more drastic permanganate oxidation.

The unsaturated acid or ester whose structure is being investigated is converted to an ozonide or polyozonide by dissolving it in chloroform or acetic acid and passing into the solution a stream of ozonized oxygen at ice temperature. The chloroform is then removed under vacuum (or about 30°C.) and the ozonide decomposed by heating with water (about 65°C.) in an atmosphere of hydrogen. The reaction comprises the addition of a molecule of ozone at the double bond and subsequent hydrolysis of the ozonide to produce molecular fragments by fission at the positions originally occupied by the unsaturated linkages. Volatile products of hydrolysis are collected in absorption towers containing appropriate reagents. The volatile and nonvolatile products of hydrolysis are usually identified in the form of characteristic derivatives.

Owing to the instability of ozone it is necessary to generate this reagent at or close to the site of the reacting product or system. Commercial generators for this purpose may be purchased, but it is often preferable to construct the generator and assemble the other equipment for conducting the ozonation in a special cabinet. Ozonizers and ozonation assemblies have been described by various workers.[105–107a] The ozonizer of Goss and Phillips is compact, safe, and easy to operate.

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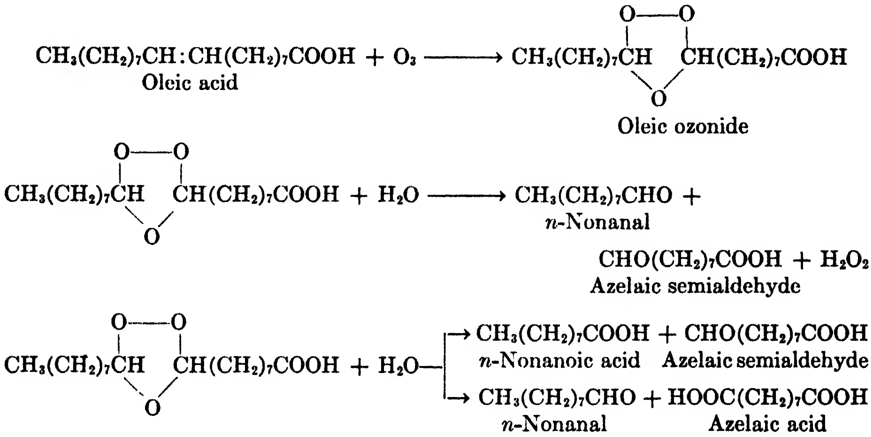
[105] E. Briner, R. Patry, and E. de Luserna, *Helv. Chim. Acta*, **7**, 62–74 (1924).
[106] L. I. Smith, *J. Am. Chem. Soc.*, **47**, 1844–1850 (1925).
[107] M. J. Goss and M. Phillips, *J. Assoc. Official Agr. Chem.*, **21**, 327–331 (1938).
[107a] A. L. Henne and W. L. Perikstein, *J. Am. Chem. Soc.*, **65**, 2183–2185 (1943).

Ozonation was used by Harries and co-workers[108–110] and by Molinari and co-workers[111–113] in establishing the position of the double bonds in oleic, elaidic, and other unsaturated acids. According to these authors, ozonation of oleic acid and subsequent hydrolysis in the presence of air occurs according to the following scheme:



From time to time various improvements have been made in the methods of hydrolysis of the ozonides especially to reduce the number of products formed and to increase the yields. The original method of hydrolysis used by Harries and co-workers consisted in boiling the ozonide with water (oxidizing hydrolysis) which, in the case of a monoethenoid acid, leads to the formation of four products as indicated by the previously mentioned equations. Because of the unfavorable conditions of oxidizing hydrolysis, the yields of hydrolytic products are low and at times the results are complicated by the presence of side reaction products.

Noller and Adams[114] improved the method of hydrolysis by conducting it under reducing conditions. In this method zinc dust and hydrochloric acid are added to the solution of the ozonide to prevent oxidation of the aldehydes; therefore, only two instead of four ozonation products are obtained for any given monoethenoid acid. This method was applied in the preparation of aldehyde esters from methyl oleate, undecylenate (9-hendecenoate), and erucate. The aldehyde esters were obtained in yields of about 55%. Methyl oleate and methyl erucate gave nonanal (pelargonic aldehyde) in yields of 60–70% by this method of hydrolysis.

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[108] C. Harries and C. Thieme, *Ann.*, **343**, 354–360 (1905); *Ber.*, **39**, 3728–3732 (1906).
[109] C. Harries and H. O. Türk, *Ber.*, **39**, 3732–3737 (1906).
[110] C. Harries and W. Franck, *Ann.*, **374**, 356–368 (1910).
[111] E. Molinari and E. Soncini, *Ber.*, **39**, 2735–2744 (1906).
[112] E. Molinari and P. Fenaroli, *Ber.*, **41**, 2789–2794 (1908).
[113] E. Molinari and C. Barosi, *Ber.*, **41**, 2794–2799 (1908).
[114] C. R. Noller with R. Adams, *J. Am. Chem. Soc.*, **48**, 1074–1080 (1926).

Riebsomer and Tallman[115] found that hydrolysis of the ozonide could be accomplished by adding hydrogen peroxide (30% aqueous solution) to the acetic acid solution and refluxing it on a steam bath. Under these conditions there are also obtained only two reaction products but both are acids instead of aldehydes as in the case of reducing hydrolysis. Hydrolysis of the ozonide of methyl erucate gives approximately 62% of nonanoic acid and methyl brassylate, $COOH(CH_2)_{11}COOCH_3$. Mowry, Brode, and Brown[116] likewise used hydrogen peroxide for the hydrolysis of the ozonide formed by treating methyl arachidonate with ozone at dry ice temperature and obtained caproic, glutaric, and succinic acids in yields comparable with those obtained by permanganate oxidation.

Toyama and co-workers carried out the hydrolysis of the ozonides of highly unsaturated acids or esters from fish oils in a current of hydrogen. The flask containing the ozonide was connected to two other flasks, the first of which contained ice water and the second barium hydroxide. The hydrogen carried over the volatile degradation products which were (*a*) dissolved in the ice water, (*b*) separated as an oil on the surface of the ice water, or (*c*) converted to a barium salt.

The method of ozonation has been particularly successful in the hands of Japanese workers and has been applied especially by Toyama and his associates in their numerous investigations of both monoethenoid and polyethenoid fatty acids from marine animal oils and oriental seed fats. Toyama and Tsuchiya[117] applied ozonation to the determination of the structure of punicic acid (m.p. 43.5–44°C.):

$$CH_3(CH_2)_3CH{:}CHCH{:}CHCH{:}CH(CH_2)_7COOH$$

isolated from pomegranate seed oil. The fission products consisted of *n*-valeric, azelaic, and oxalic acids and glyoxal which indicated that the acid was an isomer of elaeostearic acid.

These authors[118] also applied the method of ozonation to the establishment of the structure of gadoleic acid:

$$CH_3(CH_2)_9CH{:}CH(CH_2)_7COOH$$

obtained from cod liver, sardine, and herring oils. Ozonation and subsequent hydrolysis in this case produced undecanoic acid, undecanal, and azelaic acid. Ozonation and hydrolysis of the methyl ester of hiragonic acid:

$$CH_3CH{:}CH(CH_2)_2CH{:}CH(CH_2)_2CH{:}CH(CH_2)_4COOH$$

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[115] J. L. Riebsomer and R. C. Tallman, *Proc. Indiana Acad. Sci.*, **43**, 136–139 (1934).

[116] D. T. Mowry, W. R. Brode, and J. B. Brown, *J. Biol. Chem.*, **142**, 679–691 (1942).

[117] Y. Toyama and T. Tsuchiya, *J. Soc. Chem. Ind. Japan*, **38**, 454–457; Suppl. binding, 182–185 (1935).

[118] Y. Toyama and T. Tsuchiya, *J. Soc. Chem. Ind. Japan*, **37**, 31–34, 34–37; Suppl. binding, 14–16, 17–20 (1934).

prepared from Japanese sardine oil gave succinic acid, acetic acid, methyl hydrogen adipate, acetaldehyde, methyl adipate semialdehyde, succinic semialdehyde, and succinic aldehyde.[119]

The constitution of moroctic acid from Japanese sardine oil was established as:

$$CH_3CH_2CH{:}CHCH_2CH{:}CH(CH_2)_2CH{:}CH(CH_2)_2CH{:}CH(CH_2)_2COOH$$

by Toyama and Tsuchiya[120] through ozonation of the methyl ester which led to the isolation of propionic acid, propyl aldehyde, succinic acid, succinic semialdehyde, methyl hydrogen succinate, methyl succinic semialdehyde, carbon dioxide, acetic acid, and acetaldehyde. The three last products were considered to be secondary decomposition products of malonic acid and malonic aldehyde.

The constitutions of an eicosatetraenoic acid, $C_{20}H_{32}O_2$, and eicosapentaenoic acid, $C_{20}H_{30}O_2$, were likewise established by these authors by means of ozonation.[121] They also established the constitution of clupanodonic acid, $C_{22}H_{34}O_2$, by means of ozonation of the amyl ester and the dibromo-, tetrabromo-, and hexabromo- derivatives[122] of this acid. The constitution of a docosahexaenoic acid, $C_{22}H_{32}O_2$, and of nisinic acid, $C_{24}H_{36}O_2$, occurring with clupanodonic acid in sardine oil, was established by the same technique.[123]

Ozonolysis was also applied by Toyama and Tutiya[124] to the location of the unattacked double bonds remaining after partial bromination and partial thiocyanation of linoleic and linolenic acids.

Ozonation is applicable to the investigation of acids containing triple bonds as indicated by Steger and van Loon[125] in their work on Picramnia oils. The naturally occurring 6,7-stearolic acid was found to yield exclusively adipic and lauric acids on ozonation and hydrolysis. These authors[126] also identified licanic acid from Po-yoak oil by ozonation. The identity of the acid was established by isolation of azelaic, ketoazelaic, and valeric acids among the products of hydrolysis of the ozonide.

Other applications of ozonation include the determination of the structure of elaidic acid by Harries and Thieme,[127] of linoleic acid by Noorduyn[128] and Thieme,[129] linolenic acid and methyl and ethyl linolenate by Erdmann,

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[119] Y. Toyama and T. Tsuchiya, *Bull. Chem. Soc. Japan*, **10**, 192–199 (1935).

[120] Y. Toyama and T. Tsuchiya, *Bull. Chem. Soc. Japan*, **10**, 232–241 (1935).

[121] Y. Toyama and T. Tsuchiya, *Bull. Chem. Soc. Japan*, **10**, 296–300, 301–304 (1935).

[122] Y. Toyama and T. Tsuchiya, *Bull. Chem. Soc. Japan*, **10**, 441–453 (1935).

[123] Y. Toyama and T. Tsuchiya, *Bull. Chem. Soc. Japan*, **10**, 539–543, 547–551 (1935).

[124] Y. Toyama and T. Tutiya, *J. Soc. Chem. Ind. Japan*, **38**, 86–89, 89–94; Suppl. binding, **35**, 36–37 (1935).

[125] A. Steger and J. van Loon, *Rec. trav. chim.*, **52**, 593–600 (1933).

[126] A. Steger and J. van Loon, *Rec. trav. chim.*, **57**, 620–628 (1938).

[127] C. Harries and C. Thieme, *Ann.*, **343**, 354–360 (1905); *Ber.*, **39**, 2844–2846 (1906).

[128] A. C. Noorduyn, *Rec. trav. chim.*, **38**, 317–344 (1919).

[129] C. Thieme, *Ueber die Einwirkung des Ozons auf Säuren der Oelsäurereihe und auf Sterolsäure*, Inaugural Dissertation, Kiel, 1906, 29 pp. See M. Stoll and A. Rouvé, *Helv. Chim. Acta*, **27**, 950–961 (1944).

Bedford, and Raspe,[130] ricinoleic acid by Thieme,[129] erucic and brassidic acids by Thieme[129] and Holde and Zadek,[131] undecylenic acid by Noorduyn,[128] elaeostearic acid by Majima,[132] methyl and ethyl oleate by Helferich and Schäfer,[133] methyl ricinoleate by Haller and Brochet,[134] triolein by Molinari and Fenaroli,[112] triricinolein by Noorduyn,[128] and methyl undecylenate by Harding, Walsh, and Weizmann.[135]

7. Oxidation with Periodic Acid

Periodic acid, H_5IO_6, which is formed by the action of sulfuric acid on such periodate salts as potassium or barium periodate, has been extensively applied in the oxidation of polyhydric alcohols[136] and has proved to be a useful reagent for the further oxidation of partially oxidized fatty acids. King,[137] for example, applied periodic acid to the disruptive oxidation of the isomeric 9-hydroxy-10-ketostearic and 9-keto-10-hydroxystearic acids. The oxidation was carried out by adding to the hydroxyketo acids dissolved in alcohol solution, the calculated quantity of potassium periodate in an aqueous solution acidified with normal sulfuric acid. After standing 48 hours, the reaction mixture was neutralized and steam-distilled. Oxidation of 9-hydroxy-10-ketostearic acid gave nonanoic (pelargonic) acid and azelaic semialdehyde in high yields, whereas 9-keto-10-hydroxystearic acid under the same conditions gave nonanal and azelaic acid, likewise in high yield. The products of periodic oxidation thus substantiate the structure assigned these two hydroxyketo acids.

King[138] also applied periodic oxidation to the naturally occurring dihydroxystearic acid (m.p. 141°C.) obtained from the sludge deposited from technical ricinoleic acid. Fission occurred between the hydroxyl groups with the formation of nonanal and azelaic semialdehyde (m.p. 38°C.).

Dorée and Pepper[139] oxidized 13,14-dihydroxybehenic acid with periodic acid and obtained nonanal and brassylic semialdehyde. The oxidation was carried out by dissolving the dihydroxy acid in 95% alcohol and rapidly adding a solution of potassium periodate in normal sulfuric acid.

Ross, Gebhart, and Gerecht[139a] have recently developed a method whereby α,β-dihydroxy compounds may be quantitatively estimated by

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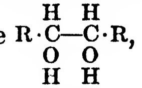
[130] E. Erdmann, F. Bedford, and F. Raspe, *Ber.*, **42,** 1334–1346 (1909).
[131] D. Holde and F. Zadek, *Ber.*, **56,** 2052–2058 (1923).
[132] R. Majima, *Ber.*, **42,** 674–680 (1909).
[133] B. Helferich and N. Schäfer, *Ber.*, **57,** 1911–1917 (1924).
[134] A. Haller and A. Brochet, *Compt. rend.*, **150,** 496–503 (1910).
[135] V. J. Harding, G. M. Walsh, and C. Weizmann, *J. Chem. Soc.*, **99,** 448–451 (1911).
[136] L. Malaprade, *Compt. rend.*, **186,** 382–384 (1928); *Bull. soc. chim.*, **43,** 683–696 (1928).
[137] G. King, *J. Chem. Soc.*, **1936,** 1788–1792.
[138] G. King, *J. Chem. Soc.*, **1942,** 387–391.
[139] C. Dorée and A. C. Pepper, *J. Chem. Soc.*, **1942,** 477–483.
[139a] J. Ross, A. I. Gebhart, and J. F. Gerecht, *J. Am. Chem. Soc.*, **67,** 1275–1278 (1945).

means of periodic acid. A known quantity of the dihydroxy compound is allowed to stand in an alcoholic solution of periodic acid for 15 to 45 minutes, after which the solution is diluted with water. Sodium bicarbonate and potassium iodide are added and the liberated iodine is titrated with 0.1 *N* potassium arsenite solution.

8. Oxidation with Lead Tetraacetate

In 1931, Criegee[140] introduced his lead tetraacetate method for cleaving glycols of the type  $R\cdot\underset{\underset{H}{O}}{\overset{H}{C}}-\underset{\underset{H}{O}}{\overset{H}{C}}\cdot R$, where R may be hydrogen or any radical. The oxidation which is highly specific results in cleavage between the two carbon atoms to which the hydroxyl groups are attached. The method, which has been extensively applied in the investigation of the constitution of sugars and related glycols, is of obvious value in determining the position of double bonds of unsaturated acids provided that the unsaturated compound is first oxidized to the corresponding hydroxy compound. For example, a monoethenoid acid can be oxidized with potassium permanganate to the corresponding dihydroxy acid, which in turn can be cleaved with lead tetraacetate to give an aldehyde and an aldehydo acid. These reactions may be illustrated with oleic acid by the following equations:

$$\underset{\text{Oleic acid}}{CH_3(CH_2)_7CH{:}CH(CH_2)_7COOH} \xrightarrow{KMnO_4} \underset{\text{Dihydroxystearic acid}}{CH_3(CH_2)_7CHOH\cdot CHOH(CH_2)_7COOH}$$

$$CH_3(CH_2)_7CHOH\cdot CHOH(CH_2)_7COOH \xrightarrow{Pb(OCOCH_3)_4}$$

$$\underset{n\text{-Nonanal}}{CH_3(CH_2)_7CHO} + \underset{\text{Azelaic semialdehyde}}{CHO\cdot(CH_2)_7COOH}$$

Identification of the fission products of the hydroxy acid thus establishes the position previously occupied by the double bond of the original unsaturated acid.

Despite the general applicability of this method for determining the position of double bonds in unsaturated fatty acids, it has been applied by only a few investigators and generally with modifications adapted to the specific product under investigation. Two general procedures have been followed: (*1*) isolation of the hydroxy acid and cleavage with previously prepared and isolated lead tetraacetate; and (*2*) formation of hydroxy acids by oxidation in acetic acid solution and cleavage with lead tetraacetate formed *in situ* by addition of red lead. When the lead tetraacetate is to be prepared and isolated, the method of Oesper and Deasy[141] is recommended.

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[140] R. Criegee, *Ber.*, **64**, 260–266 (1931); *Ann.*, **481**, 263–302 (1930). R. Criegee, L. Kraft, and B. Rank, *ibid.*, **507**, 159–197 (1933).

[141] R. E. Oesper and C. L. Deasy, *J. Am. Chem. Soc.*, **61**, 972–973 (1939).

In 1935 Nunn and Smedley-Maclean[142] and, about the same time, Raudnitz, Schindler, and Petrů,[143] applied Criegee's method to the structural identification of fatty acids. According to the first-mentioned authors, both dihydroxystearic and sativic (tetrahydroxystearic) acids were found to react almost quantitatively with lead tetraacetate at 37°C. In both cases azelaic acid was isolated from the reaction mixture and identified by its melting point (106–107°C.). *n*-Hexanal obtained by oxidation of sativic acid and *n*-nonanal from dihydroxystearic acid were identified by means of their dinitrophenylhydrazones. These authors also applied the lead tetraacetate method to the cleavage of the hydroxy acids produced by alkaline permanganate oxidation of the unsaturated acids from linseed oil.

In an effort to locate the point of attachment of the hydroxyl groups, Raudnitz and co-workers[143] applied lead tetraacetate oxidation to aleuritic acid, a trihydroxypalmitic acid found in shellac. Nagel,[144] on the basis of oxidative cleavage with potassium permanganate, concluded that aleuritic acid was 9,10,16-trihydroxypalmitic acid, whereas Endemann[145] concluded, also on the basis of permanganate oxidation, that it was 10,11,15-trihydroxypalmitic acid. Since Criegee's method of oxidation is specific for 1,2-glycols it should be possible to differentiate between these two structures. 9,10,16-Trihydroxypalmitic acid should yield azelaic semialdehyde and 7-hydroxyheptanal, $CH_2(OH)(CH_2)_5CHO$, whereas 10,11,15-trihydroxypalmitic acid should yield sebacic semialdehyde, $CHO(CH_2)_8COOH$, and 5-hydroxyhexanal, $CH_3CH(OH)(CH_2)_3CHO$. Actually, Raudnitz and co-workers[143] found only the semialdehyde of azelaic acid as the acidic constituent of the oxidation of aleuritic acid and identified it in the form of the semicarbazone melting at 163°C. The neutral portion of the reaction products gave qualitative tests for the presence of aldehydes but no crystalline derivative could be isolated by means of the usual aldehyde reagents.

Hsing and Chang[146] oxidized 9,10-dihydroxystearic acid with lead tetraacetate and obtained as reaction products *n*-nonanal and azelaic semialdehyde in the form of semicarbazones, each in 85% yield. They also oxidized 9,10,12-trihydroxystearic acid (m.p. 111–12°C.), previously obtained by permanganate oxidation of ricinoleic acid, with lead tetraacetate in benzene solution. After four hours' reaction they were able to isolate azelaic semialdehyde in the form of the semicarbazone (m.p. 112–13°C.) in 90% yield. Like Raudnitz and co-workers, Hsing and Chang were un-

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[142] L. C. A. Nunn and I. Smedley-Maclean, *Biochem. J.*, **29**, 2742–2745 (1935).
[143] H. Raudnitz, H. Schindler, and F. Petrů, *Ber.*, **68**, 1675–1676 (1935).
[144] W. Nagel, *Ber.*, **60**, 605–609 (1927).
[145] H. Endemann, *Z. angew. Chem.*, **22**, 676–677 (1909).
[146] C.-Y. Hsing and K.-J. Chang, *J. Am. Chem. Soc.*, **61**, 3589 (1939).

able to isolate and identify the hydroxyaldehyde corresponding to the other fragment of the cleavage reaction.

Scanlan and Swern[147] applied Criegee's reaction to the cleavage of hydroxylated derivatives of oleic acid, ethyl oleate, and oleyl alcohol. Because lead tetraacetate is relatively unstable, the reagent was formed *in situ* by reaction of glacial acetic acid and red lead (Pb_3O_4). According to these authors, this method is particularly advantageous when applied to the hydroxylation products prepared by the action of hydrogen peroxide in glacial acetic acid (peracetic acid) on unsaturated compounds, since under these conditions neither the hydroxylated compound nor the lead tetraacetate requires isolation. However, all of the hydroxylated compounds obtained by oxidation with hydrogen peroxide in glacial acetic acid were the low melting forms. The high melting forms had to be prepared by alkaline permanganate oxidation. Both series of products were reported to behave in the same manner with respect to oxidative cleavage with lead tetraacetate.

Hilditch and Jasperson[148] measured the rate of consumption of lead tetraacetate when used in strictly comparable concentrations to oxidize various isomeric polyhydroxystearic acids, and found marked differences in the speed of oxidation of the different isomers. The rate of oxidation of the 9,10-dihydroxystearic acid (m.p. 95°C.) was far more rapid than that of the corresponding isomer (m.p. 132°C.). The two low melting forms of 9,10,12,13-tetrahydroxystearic acid were more rapidly oxidized than the corresponding high melting forms. These differences in the rates of oxidation of the pairs of isomeric hydroxy acids are similar to those observed in many pairs of cyclic glycols. Criegee[149] has shown, in the case of the isomeric cyclic glycols, that *cis*-glycols are attacked by lead tetraacetate more rapidly than the *trans*-isomerides. However, in the case of polyhydroxystearic acids produced by oxidation of polyunsaturated acids, the isomerism arises from the presence of asymmetric carbon atoms and the various forms are, therefore, racemic mixtures of optical isomers and not geometric isomers.

Dorée and Pepper[139] found that lead tetraacetate reacts with the *cis*- and *trans*-forms of 13,14-dihydroxybehenic acid (m.p. 101° and 132°C., respectively) to form in each case nonanal and brassylic semialdehyde. The relative oxidation rates of the two isomers were found to be markedly different, the low melting form oxidizing very much more rapidly than the high melting form. Since this behavior parallels that observed by Criegee and others with geometric isomers, it might be considered as evidence that

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[147] J. T. Scanlan and D. Swern, *J. Am. Chem. Soc.*, **62**, 2305–2309 (1940).
[148] T. P. Hilditch and H. Jasperson, *Nature*, **147**, 327 (1941).
[149] R. Criegee, *Ber.*, **65**, 1770–1772 (1932).

TABLE 122

MONO- AND DIBASIC ACIDS FORMED BY DISRUPTIVE OXIDATION OF MONOETHENOID FATTY ACIDS

Unsaturated acid		Monobasic acid		Dibasic acid	
Name	Formula	Name	Formula*	Name	Formula
Obtusilic	$CH_3(CH_2)_4CH:CH(CH_2)_2COOH$	Caproic	$CH_3(CH_2)_4COOH$	Succinic	$HOOC(CH_2)_2COOH$
Caproleic	$CH_2:CH(CH_2)_7COOH$	Formic	$HCOOH$	Azelaic	$HOOC(CH_2)_7COOH$
Undecenoic	$CH_2:CH(CH_2)_8COOH$	Formic	$HCOOH$	Sebacic	$HOOC(CH_2)_8COOH$
Lauroleic	$CH_3CH_2CH:CH(CH_2)_7COOH$	Propionic	CH_3CH_2COOH	Azelaic	$HOOC(CH_2)_7COOH$
Myristoleic	$CH_3(CH_2)_3CH:CH(CH_2)_7COOH$	Valeric	$CH_3(CH_2)_3COOH$	Azelaic	$HOOC(CH_2)_7COOH$
Palmitoleic	$CH_3(CH_2)_5CH:CH(CH_2)_7COOH$	Heptanoic	$CH_3(CH_2)_5COOH$	Azelaic	$HOOC(CH_2)_7COOH$
Petroselinic	$CH_3(CH_2)_{10}CH:CH(CH_2)_4COOH$	Lauric	$CH_3(CH_2)_{10}COOH$	Adipic	$HOOC(CH_2)_4COOH$
Oleic	$CH_3(CH_2)_7CH:CH(CH_2)_7COOH$	Nonanoic	$CH_3(CH_2)_7COOH$	Azelaic	$HOOC(CH_2)_7COOH$
Vaccenic	$CH_3(CH_2)_5CH:CH(CH_2)_9COOH$	Heptanoic	$CH_3(CH_2)_5COOH$	Hendecanedioic	$HOOC(CH_2)_9COOH$
Octadecenoic	$CH_3(CH_2)_4CH:CH(CH_2)_{10}COOH$	Caproic	$CH_3(CH_2)_4COOH$	Dodecanedioic	$HOOC(CH_2)_{10}COOH$
Gadoleic	$CH_3(CH_2)_9CH:CH(CH_2)_7COOH$	Undecanoic	$CH_3(CH_2)_9COOH$	Azelaic	$HOOC(CH_2)_7COOH$
Cetoleic	$CH_3(CH_2)_9CH:CH(CH_2)_9COOH$	Undecanoic	$CH_3(CH_2)_9COOH$	Hendecanedioic	$HOOC(CH_2)_9COOH$
Erucic	$CH_3(CH_2)_7CH:CH(CH_2)_{11}COOH$	Nonanoic	$CH_3(CH_2)_7COOH$	Brassylic	$HOOC(CH_2)_{11}COOH$
Selacholeic	$CH_3(CH_2)_7CH:CH(CH_2)_{13}COOH$	Nonanoic	$CH_3(CH_2)_7COOH$	Pentadecanedioic	$HOOC(CH_2)_{13}COOH$
Hexacosenoic	$CH_3(CH_2)_7CH:CH(CH_2)_{15}COOH$	Nonanoic	$CH_3(CH_2)_7COOH$	Heptadecanedioic	$HOOC(CH_2)_{15}COOH$
Tricosenoic	$CH_3(CH_2)_7CH:CH(CH_2)_{19}COOH$	Nonanoic	$CH_3(CH_2)_7COOH$	Heneicosanedioic	$HOOC(CH_2)_{19}COOH$

the hydroxy acids are geometric instead of optical isomers as just mentioned.

An attempt by Scanlan and Swern[150] to apply the peracetic-lead tetraacetate oxidation directly to olive, peanut, and lard oils was not successful, but when applied to castor oil the yield of oxidation products was higher than in the case of the lead tetraacetate oxidation of 9,10,12-trihydroxystearic acid obtained by hydroxylation of ricinoleic acid. The work of Scanlan and Swern furnishes an explanation of the failure of Raudnitz and co-workers[143] and of Hsing and Chang[146] to identify the aldehyde which is assumed to be formed during cleavage at the glycol configuration. Instead of the anticipated β-hydroxynonanal, Scanlan and Swern obtained approximately 63% of an unsaturated aldehyde, namely, α-nonenal, $CH_3(CH_2)_5CH{:}CH \cdot CHO$. The method of identification leaves no doubt as to the general structure of the aldehyde, *i. e.*, with respect to chain length, the presence of a double bond, and the terminal aldehyde group, but the position of the double bond does not appear to have been determined by irrefutable means. The unsaturated aldehyde was presumed to arise from a dehydration reaction occurring between the hydroxyl radical and the hydrogen attached to the twelfth and eleventh carbon atoms, respectively, either simultaneously with, or subsequent to, cleavage at the 9,10-double bond in accordance with the following equation:

$$CH_3(CH_2)_5CHOHCH_2CHOHCHOH(CH_2)_7COOH \xrightarrow{Pb(OCOCH_3)_4}$$

$$CH_3(CH_2)_5CH{:}CHCHO + CHO(CH_2)_7COOH$$

The production of such unsaturated aldehydes by dehydration seems to be firmly established, but under most dehydration conditions a mixture of $\Delta^{2,3}$- and $\Delta^{3,4}$-nonenal would be expected if dehydration occurred prior to cleavage. If β-hydroxynonanal was first formed and subsequently dehydrated the course of the dehydration may have been quite specific owing to the orienting effect of the aldehyde group.

Lead tetraacetate oxidation has been applied by Mendel and Coops[151] as a means of degrading higher fatty acids to the next lower homolog, *e. g.*, stearic to margaric, and palmitic to pentadecanoic. The method constitutes a means of preparing, in relatively good yield, the odd-carbon acid from the next higher even-carbon acid. The method involves the following steps: bromination of the original acid to produce the α-bromo acid; conversion of this acid to the corresponding α-hydroxy acid by esterification and reaction with potassium acetate in acetic acid; oxidation of the hydroxy acid to the aldehyde with lead tetraacetate in benzene solution;

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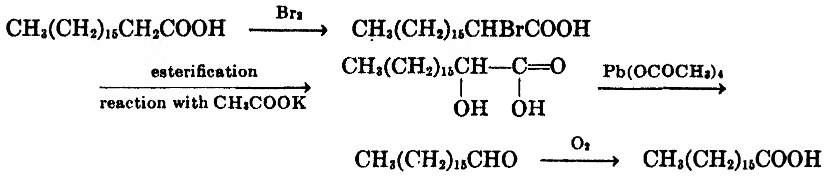
[150] J. T. Scanlan and D. Swern, *J. Am. Chem. Soc.*, **62**, 2309–2311 (1940).
[151] H. Mendel and J. Coops, *Rec. trav. chim.*, **58**, 1133–1143 (1939).

and air oxidation of the aldehyde to the desired acid. The following equations, using stearic acid, illustrate the steps in the process:



$$CH_3(CH_2)_{15}CH_2COOH \xrightarrow{Br_2} CH_3(CH_2)_{15}CHBrCOOH$$

$$\xrightarrow[\text{reaction with } CH_3COOK]{\text{esterification}} CH_3(CH_2)_{15}\underset{OH}{CH}-\underset{OH}{C}{=}O \xrightarrow{Pb(OCOCH_3)_4}$$

$$CH_3(CH_2)_{15}CHO \xrightarrow{O_2} CH_3(CH_2)_{15}COOH$$

The authors claim an over-all yield of the next lower homolog of approximately 84% by the use of this method of preparing higher odd-numbered carbon acids.

9. Products and Mechanisms Involved in Chemical Oxidation of Unsaturated Fatty Acids

(a) *Products Produced by Complete Cleavage of Double Bonds*

The various products which may be formed by chemical oxidation of the unsaturated fatty acids, together with some of their properties, are assembled in Tables 122 to 125.

If quantitative fission of the unsaturated acids given in Table 122 occurred as a result of oxidation by any one or any combination of the methods previously described, the corresponding pairs of mono- and di-

TABLE 123

PROPERTIES OF α,ω-DIBASIC ACIDS OBTAINED BY OXIDATION OF UNSATURATED FATTY ACIDS

Acid	Formula	M.p., °C.	B.p., °C.[a]	Soly. in water at 20°C., %	Ionisation constants	
					$k_1 \times 10^5$	$k_2 \times 10^6$
Oxalic	$(COOH)_2$	189.5	Sublimes	10.2	3800	43.7
Malonic	$CH_2(COOH)_2$	135.6	Decomposes	73.5	177.0	4.50
Succinic	$(CH_2COOH)_2$	185.0	235	6.8	7.36	5.34
Glutaric	$CH_2(CH_2COOH)_2$	97.5	304	63.9	4.60	5.29
Adipic	$(CH_2CH_2COOH)_2$	153.0	265^{100}	$1.5^{15°}$	3.90	4.87
Pimelic	$CH_2(CH_2CH_2COOH)_2$	105.5	272^{100}	5.0	3.33	4.71
Suberic	$(CH_2CH_2CH_2COOH)_2$	142.0	300	0.16	3.07	4.64
Azelaic	$CH_2(CH_2CH_2CH_2COOH)_2$	108.0	360	0.24	2.82	3.0
Sebacic	$(CH_2CH_2CH_2CH_2COOH)_2$	134.0	295^{100}	0.10	2.8	3.0
Undecanedioic	$CH_2(CH_2CH_2CH_2CH_2COOH)_2$	110				
Dodecanedioic	$(CH_2CH_2CH_2CH_2CH_2COOH)_2$	126				
Brassylic	$CH_2(CH_2CH_2CH_2CH_2CH_2COOH)_2$	112				

[a] Superscripts refer to pressure in millimeters of mercury.

basic acids given opposite each acid should be produced in equimolar quantities. A similar series of fission products could also be set down for the oxidation of the polyethenoid acids. However, the number of such fission products is increased in proportion to the number of double bonds in the carbon chain. For example, linoleic acid, if quantitatively split by oxidation at both double bonds without subsequent oxidation of the primary oxidation products, should produce one mole each of the following acids: caproic, $CH_3(CH_2)_4COOH$; malonic, $HOOCCH_2COOH$; and azelaic, $HOOC(CH_2)_7COOH$. Linolenic acid under the same conditions should produce one mole propionic (CH_3CH_2COOH), two moles malonic, and one mole azelaic acid. When the acid contains a conjugated system of double bonds complete fission of the conjugated portion of the C chain should produce

Table 124

ALDEHYDES PRODUCED BY PARTIAL OXIDATION OF UNSATURATED FATTY ACIDS

Aldehyde	Formula	M.p., °C.	B.p., °C.[a]
Methanal	$HCHO$	− 92	−21
Ethanal	CH_3CHO	−120	20.8
Propanal	C_2H_5CHO	...	49
Butanal	C_3H_7CHO	...	73
Pentanal	C_4H_9CHO	...	102
Hexanal	$C_5H_{11}CHO$	...	128
Heptanal	$C_6H_{13}CHO$	...	155
Octanal	$C_7H_{15}CHO$	...	$60–61^{9}$
Nonanal	$C_8H_{17}CHO$	...	$80–82^{15}$
Decanal	$C_9H_{19}CHO$	...	207–209
Hexadecanal	$C_{15}H_{31}CHO$	34	$200–201^{29}$
Octadecanal	$C_{17}H_{35}CHO$	63.5	$212–213^{22}$

[a] Superscripts refer to pressure in millimeters of mercury.

Table 125

ALDEHYDO ACIDS PRODUCED BY PARTIAL OXIDATION OF UNSATURATED FATTY ACIDS

Aldehydo acid	Formula
Glyoxylic acid	$OCHCOOH$
Malonic semialdehyde	$OCH(CH_2)COOH$
Succinic semialdehyde	$OCH(CH_2)_2COOH$
Glutaric semialdehyde	$OCH(CH_2)_3COOH$
Adipic semialdehyde	$OCH(CH_2)_4COOH$
Pimelic semialdehyde	$OCH(CH_2)_5COOH$
Suberic semialdehyde	$OCH(CH_2)_6COOH$
Azelaic semialdehyde	$OCH(CH_2)_7COOH$
Sebacic semialdehyde	$OCH(CH_2)_8COOH$
ω-Formyldecanoic acid	$OCH(CH_2)_9COOH$
ω-Formylundecanoic acid	$OCH(CH_2)_{10}COOH$
Brassylic semialdehyde	$OCH(CH_2)_{11}COOH$

oxalic acid, *e. g.*, elaeostearic acid should yield: one mole valeric acid, $CH_3(CH_2)_3COOH$; two moles oxalic acid, $(COOH)_2$; and one mole azelaic acid.

As previously mentioned, quantitative fission seldom occurs and in some cases the primary fission product may be partly or completely oxidized to one or more lower molecular weight acids. For example, valeric acid frequently appears where caproic acid is expected and oxalic acid appears where malonic acid is expected.

The properties of the monobasic acids formed by oxidative cleavage have been discussed elsewhere. Some of the properties of the dibasic acids are given in Table 123. Little is known concerning the dibasic acids having a chain length greater than sebacic acid. The melting points of the dibasic acids exhibit alternation similar to that observed with monobasic acids. Within the series of alternate pairs the melting point decreases with increasing molecular weight. Solubilities in water also exhibit alternation, the acids with an odd number of carbon atoms being more soluble than the adjacent even-numbered acids. Acids containing an even number of carbon atoms are more resistant to oxidation and are generally, but not necessarily, produced by further oxidation of odd-numbered dibasic acids. Except for oxalic acid the dibasic acids are obtained by crystallization from water without water of crystallization; oxalic acid adds two molecules of water. Except for oxalic and malonic acids they are readily distillable without decomposition. Compared with the monobasic aliphatic acids, dicarboxylic acids have higher dissociation constants[151a] and are therefore stronger acids.

The aldehydes (Table 124) produced on oxidation of the unsaturated acids are generally identified in the form of derivatives such as the hydrazones, phenylhydrazones, nitro- or dinitrophenylhydrazones, etc., or they may be further oxidized to the corresponding acids. The aldehyde acids (Table 125) are difficult to isolate in highly pure form. It is therefore preferable to employ the ester of the acid to be oxidized when it is desired to isolate a semialdehyde or to conduct the oxidation so as to produce the corresponding dibasic acid.

(*b*) *Products Produced by Partial Oxidation of Double Bonds*

In addition to the products obtained by oxidative cleavage, unsaturated acids form various partially oxidized products such as di- and polyhydroxy, hydroxyketo, diketo and oxido acids. Of this group of products the di- and polyhydroxy acids shown in Tables 126 and 127 are best known.

Although most of the polyhydroxy acids shown in Table 126 have long been known and many of their properties and those of their derivatives have been determined, there exist many unanswered questions concerning the exact stereo configuration of these compounds. Since all of these acids con-

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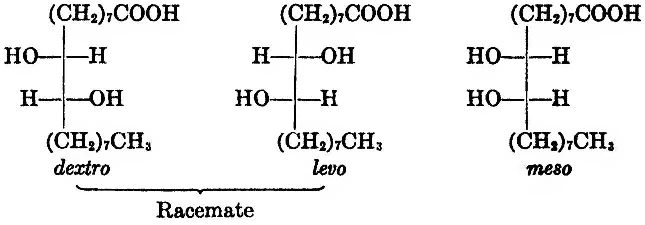
[151a] J. Greenspan, *Chem. Revs.*, **12**, 339–361 (1938).

tain two or more asymmetric carbon atoms they should exhibit optical activity, but no such activity has been conclusively demonstrated. All of the dihydroxy acids in Table 126 are theoretically capable of existing in four isomeric forms as illustrated in the following configurations for dihydroxystearic acid:



The *d*- and *l*-forms should have identical physical properties with the exception of their effect on plane polarized light. The racemate or *dl*-form and the *meso*-form should exhibit differences in such properties as melting point, solubility, refractive index, etc., but neither form should exhibit optical activity.

Table 126

MELTING POINTS OF ISOMERIC POLYHYDROXY ACIDS OBTAINED BY OXIDATION OF UNSATURATED FATTY ACIDS

Unsaturated acid	Hydroxy acid	Melting point, °C.
$\Delta^{9,10}$-Hexadecenoic, $C_{16}H_{30}O_2$	Dihydroxypalmitic	87, 125
Oleic (*cis*), $C_{18}H_{34}O_2$	Dihydroxystearic	95, 132
Elaidic (*trans*), $C_{18}H_{34}O_2$	Dihydroxystearic	95, 132
Petroselinic (*cis*-$\Delta^{6,7}$), $C_{18}H_{34}O_2$	6,7-Dihydroxystearic	115, 122
Petroselaidic (*trans*-$\Delta^{6,7}$), $C_{18}H_{34}O_2$	6,7-Dihydroxystearic	115, 122
$\Delta^{12,13}$-Octadecenoic, $C_{18}H_{34}O_2$	12,13-Dihydroxystearic	129.5
Erucic (*cis*-$\Delta^{13,14}$), $C_{22}H_{42}O_2$	Dihydroxybehenic	100, 130
Brassidic (*trans*-$\Delta^{13,14}$), $C_{22}H_{42}O_2$	Dihydroxybehenic	100, 130
Ricinoleic (*cis*), $C_{18}H_{33}O_2(OH)$	Trihydroxystearic	111, 142
Ricinelaidic (*trans*), $C_{18}H_{33}O_2(OH)$	Trihydroxystearic	111, 142
Linoleic, $C_{18}H_{32}O_2$	Tetrahydroxystearic	163.5, 174[a]
Linolenic, $C_{18}H_{30}O_2$	Hexahydroxystearic	175, 203
$\Delta^{6,7,9,10,12,13}$-Octadecatrienoic, $C_{18}H_{30}O_2$	Hexahydroxystearic	245

[a] Mixtures of these two forms have been shown to melt at temperatures between 153° and 161 °C.

Trihydroxystearic acid which contains three asymmetric carbon atoms can theoretically exist in eight optically isomeric forms or four racemic modifications. Tetrahydroxystearic acid contains four asymmetric carbon atoms and thus should give rise to sixteen optical isomers or eight racemic modifications. The hexahydroxy acids would have sixty-four optical isomers or thirty-two racemic modifications. In general, the straight chain hydroxy acids will contain one asymmetric carbon atom for each hydroxyl group which replaces one of the hydrogens of each methylene group. The number of optical isomers corresponding to each asymmetric carbon atom will be 2^n where n is the number of asymmetric carbon atoms or, in this case, substituted hydroxyl groups in the methylene carbon chain.

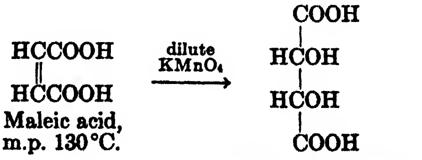
TABLE 127

PROPERTIES OF SOME POLYHYDROXY ACIDS OBTAINED BY OXIDATION OF UNSATURATED FATTY ACIDS

Acid	Crystal form	Solubility[a]				
		Water		Alcohol		Ether
		Cold	Hot	Cold	Hot	
Dihydroxystearic, 95°, 132°C.	Rhombic plates	I	I	DS	S	DS
Tetrahydroxystearic, 173°C.	Needles	I	DS	DS	S	I
Hexahydroxystearic, 203°C.	Rhombic plates	DS	S	DS	DS	I
Hexahydroxystearic, 173–175°C.	Needles	DS	ES	S	S	I

[a] I = insoluble. S = soluble. DS = difficultly soluble. ES = easily soluble.

Dihydroxy Acids Obtained by Oxidation of Monounsaturated Fatty Acids.—Only two dihydroxy acids have been observed among the oxidation products of monounsaturated acids and both are optically inactive. With a given oxidizing agent, one of these is derived from the *cis*-acid and one from the *trans*-acid. For example, oleic acid on oxidation with peracetic acid gives dihydroxystearic acid melting at 95°C., and oxidation of the *trans*-oleic or elaidic acid gives a dihydroxy acid melting at 132°. The formation of these two optically inactive dihydroxystearic acids might be explained on the assumption that one of them, say the low melting acid, is a *meso*-compound and the high melting compound a racemate. Such a relationship has been established[152] with respect to the oxidation of the isomeric, maleic, and fumaric acids. Careful oxidation of maleic acid with dilute permanganate yields *meso*-tartaric acid while under the same conditions fumaric acid yields *dl*-tartaric acid by the following equations:



$$\begin{array}{c} \text{HCCOOH} \\ \| \\ \text{HCCOOH} \end{array} \xrightarrow[\text{KMnO}_4]{\text{dilute}} \begin{array}{c} \text{COOH} \\ | \\ \text{HCOH} \\ | \\ \text{HCOH} \\ | \\ \text{COOH} \end{array}$$

Maleic acid, m.p. 130°C.

meso-Tartaric acid, m.p. 140°C.

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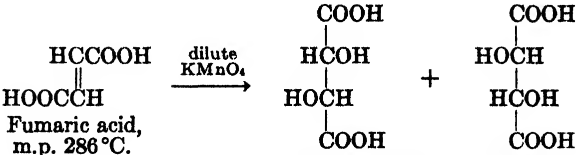
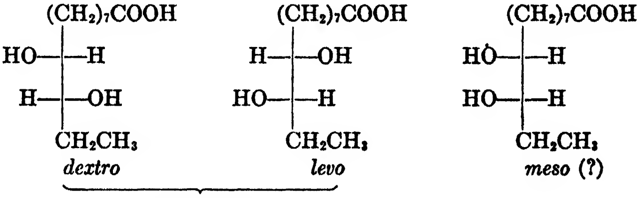
[152] A. Kekulé and R. Anschütz, *Ber.*, 13, 2150–2152 (1880); 14, 713–717 (1881).



Fumaric acid, m.p. 286 °C.

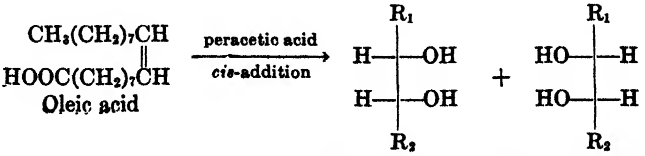
dl-Tartaric acid, m.p. 206 °C.

In the case of the postulated *meso*-dihydroxystearic acid, it is necessary to assume that the —$(CH_2)_7COOH$ group and —$(CH_2)_7CH_3$ group have equal and opposite effects on the optical rotation despite a difference of thirty units in their respective molecular weights. Although such an assumption is not unreasonable in the case of dihydroxystearic acid, it appears less plausible in the case of some of the 9,10-dihydroxy acids of lower molecular weight. Owing to the lack of symmetry in the 9,10-dihydroxylauric acids illustrated by the accompanying formulas, the possibility of internal compensation appears somewhat untenable:



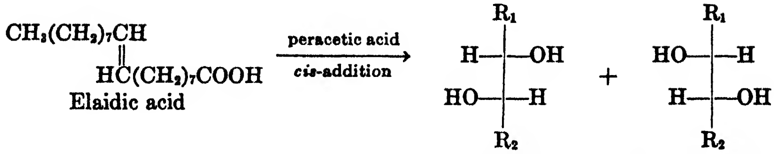
Racemate

There exists also another possible explanation of the formation of two optically inactive dihydroxy acids which does not assume the formation of a *meso*-compound. This postulate assumes that the hydroxyl groups enter the molecule at the same positions on the carbon tetrahedrons which were previously united by the double bond, thus producing a compound with the same stereo configuration as the original acid. The *cis*-addition, as it is generally called, produces two *dl*-modifications from a given pair of *cis*- and *trans*-unsaturated fatty acids as illustrated by the accompanying formulas. It is evident that *cis*-addition preserves the original configuration of the unsaturated acid and a *cis*-unsaturated acid produces what might be termed a "*cis*"-hydroxy acid; similarly a *trans*-unsaturated acid would produce a "*trans*"-hydroxy acid.



Oleic acid

dl-Dihydroxystearic acid, m.p. 95 °C.



dl-Dihydroxystearic acid, m.p. 132 °C.

Attempts have been made to resolve these racemic mixtures by way of the strychnine salts. Freundler[153] claimed the rotatory power of the individual optically active isomers was too small to permit their differentiation. Inoue and Suzuki[154] claimed to have resolved the dihydroxystearic acid, m.p. 132°C., into a *d*-dihydroxystearic acid having the rotation $[\alpha]_D$ +23.2° and an *l*-dihydroxystearic acid having the rotation $[\alpha]_D$ −23.6. Similarly, the dihydroxystearic acid, m.p. 95°, was resolved into a *d*-dihydroxystearic acid, $[\alpha]_D$ +27.6°, and an *l*-dihydroxystearic acid, $[\alpha]_D$ −27.45°. However, Toyama and Ishikawa[155] and also King[156] were unable to resolve either racemic mixture by means of strychnine salts.

Esafov[157] investigated the reactivity of the two forms of 9,10-dihydroxystearic acid in acetone and found that their relative reactivities were markedly different. The 9,10-dihydroxystearic acid (m.p. 95°C.) when allowed to stand for 12 days at room temperature in acetone solution containing 2% hydrochloric acid reacted almost quantitatively to form isopropylidenedihydroxystearic acid. Under the same conditions, 9,10-dihydroxystearic acid (m.p. 132°C.) reacted only to an extent of 12% to 16%. These results would be expected if the low melting form possessed a *cis*-configuration and the high melting form a *trans*-configuration. When the acetonated compounds were hydrolyzed in dilute aqueous alcoholic sulfuric acid solution, the acids were recovered without change in their original configurations.

A naturally occurring 9,10-dihydroxystearic acid melting at 141°C. has been isolated from castor oil. Its optical activity was too low to measure with certainty, but according to King[156] it must be a component of one or the other of the two known racemic dihydroxystearic acids produced on oxidation of oleic acid. King was able, by treatment of this acid with hydrogen chloride at 160°C., to convert it into a mixture of chlorohydroxy acids which when boiled with dilute alkali gave an optically active oxidostearic acid, m.p. 59.5°C. On hydrolysis of this compound, the racemic dihydroxystearic acid, m.p. 95°C., was obtained.

Polyhydroxy Acids from Linoleic and Linolenic Acids.—Oxidation under proper conditions of a diethenoid acid such as linoleic acid results in the

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[153] M. P. Freundler, *Bull. Soc. Chim.*, 13, 1052–1055 (1895).
[154] Y. Inoue and B. Suzuki, *Proc. Imp. Acad. Tokyo*, 7, 261–264 (1931).
[155] Y. Toyama and T. Ishikawa, *Bull. Chem. Soc. Japan*, 11, 735–741 (1936).
[156] G. King, *J. Chem. Soc.*, 1942, 387–391.
[157] V. I. Esafov, *J. Gen. Chem. U.S.S.R.*, 6, 1818–1822 (1936).

formation of hydroxy acids. Since these acids contain four asymmetric carbon atoms, sixteen optically active isomers, or eight inactive *dl*-mixtures or racemates are possible. The exact number of tetrahydroxy (sativic) acids which are produced on oxidation, for example by cold, dilute, alkaline permanganate of linoleic acid, is not known with certainty. It is generally held that only two such acids having melting points of 157° and 173°C., respectively, are formed from the *cis-cis*-$\Delta^{9,10,12,13}$-octadecadienoic acid. Even this is not certain, as Riemenschneider and co-workers[158] claim that the melting points of the two sativic acids are 163.5°C. for the α-form and 174°C. for the β-form and that the product melting at 156–157°C., generally isolated from the oxidation mixture of linoleic acid, is a 70:30 eutectic of the α- and β-sativic acids. According to the postulates of these authors, oxidation of natural or *cis-cis*-linoleic acid to tetrahydroxy acids leads to the formation of but two optically inactive or *dl*-mixtures of corresponding pairs of optically active isomers. The same reasoning applied to linolelaidic or *trans-trans*-linoleic acid would also produce two *dl*-mixtures of the alternate optically active isomers. It should be mentioned here that the literature contains numerous references to the production of a number of tetrahydroxy acids derived directly or indirectly from one or another of the four stereoisomeric linoleic acids. The melting points recorded for these tetrahydroxy acids are 122°, 126–127°, 134–135°, 144–146°, 155–159°, 163.5°, and 173°C. However, at the present time only two of these hydroxy acids can be related with certainty to the configuration of natural linoleic acid.

That only two hexahydroxystearic (linusic) acids, melting at 173–175°C. and 203°C., respectively, are obtained on oxidation of linolenic acid despite the theoretical possibility of the existence of thirty-two racemic forms is even more perplexing. The detection of only two isomeric hydroxy acids among the oxidation products of naturally occurring linoleic and linolenic acids may be the result of highly specific oxidation mechanisms, or the acids thus far identified may be complex mixtures extremely difficult to resolve. At the present time it is not possible to explain the fact that only two polyhydroxystearic acids are obtained by oxidation from linoleic and linolenic acids, and little can be said concerning the exact stereo configuration of even the two known forms.

Oxido or Epoxy Acids.—Oxidation of monounsaturated acids with perbenzoic or peracetic acid results in the formation of oxido or epoxy acids among which the following have been recognized: two *r*-oxidostearic acids melting at 55.5° and 59.5°C., respectively, *d*-oxidostearic (m.p. 59.5°C.), and *cis*- and *trans*-modifications of oxidobehenic acid melting at 63.5° and 70.5°C., respectively. The structures and interrelationships

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[158] R. W. Riemenschneider, D. H. Wheeler, and C. E. Sando, *J. Biol. Chem.*, **127**, 391–402 (1939).

of these acids have been discussed by King,[156] Dorée and Pepper,[139] and Atherton and Hilditch.[159]

Oxidostearic acids are obtained by oxidation of oleic and elaidic acids with perbenzoic acid while oxidobehenic acids are obtained by perbenzoic oxidation of erucic and brassidic acids. King investigated the relationship of oleic and elaidic acids, their oxido- and dihydroxy derivatives and their interconversion by way of the chlorohydrins. On the basis of this work he concluded the configurations of these compounds were best represented as shown in the formulas reproduced in Figure 73. In these formulas *a* = $CH_3(CH_2)_7$— and *b* = —$(CH_2)_7COOH$, *d* and *l* rotations are indicated by plus and minus signs, and the racemic forms by *r*. Atherton and Hilditch have disputed the configural relationships proposed by King for these prod-

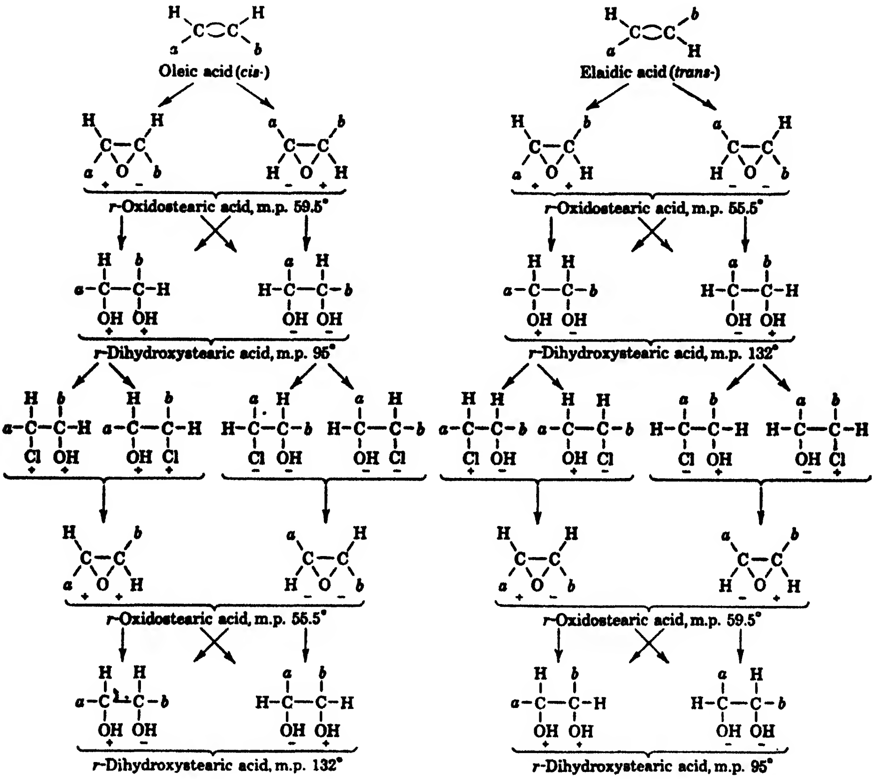

Fig. 73. Stereochemical relationships of the oxidation products of oleic and elaidic acids according to King.[156]

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[159] D. Atherton and T. P. Hilditch, *J. Chem. Soc.*, **1943**, 204–208.

ucts and have proposed in their place a somewhat different relationship, which is reproduced in Figure 74.

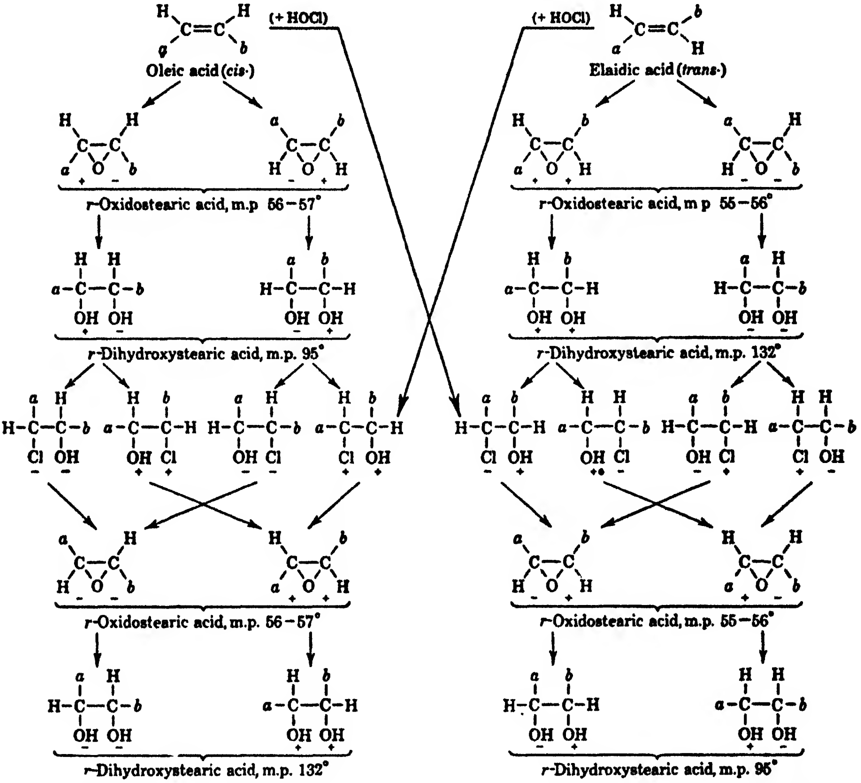

Fig. 74. Stereochemical relationships of the oxidation products of oleic and elaidic acids according to Atherton and Hilditch.[159]

(c) Mechanisms of Chemical Oxidation

For the most part the mechanisms involved in ordinary oxidation procedures with the unsaturated fatty acids are understandable. Little controversy exists with regard to the mechanisms by which unsaturated acids undergo oxidation with such reagents as ozone, chromic acid, and hydrogen peroxide. This is not generally true of the mechanisms involved in oxidation reactions involving per acids or potassium permanganate.

Ozone is generally assumed to consist of a three-membered ring which probably adds to the double bond of an unsaturated acid to form a five-membered heterocyclic ring containing two carbon atoms and three oxygen atoms. Hydrolysis of the heterocyclic product results in complete rupture of the ring to form shorter chain acids or aldehydes as has already been discussed.

Chromic acid or its equivalent, namely, potassium dichromate, in the presence of four moles of sulfuric acid and an oxidizable substance, yields three atoms of oxygen which will react with saturated, unsaturated, hydroxy, keto, and other acids to produce a variety of oxidation products. This reagent, and that prepared by addition of chromium trioxide to sulfuric acid, has not received extensive consideration in work on the elucidation of the structure of fatty acids.

Hydrogen peroxide appears to act as an oxidizing agent by liberating one atom of active oxygen, or as a hydroxylation agent by furnishing two hydroxyl groups depending on the menstruum, temperature, and presence or absence of such oxidation catalysts as osmium tetroxide, vanadium pentoxide, etc. In neutral, weakly alkaline, and weakly acidic solutions hydrogen peroxide is not generally an effective oxidizing agent for fatty acids. In concentrated acid solutions, and in such solutions in the presence of an oxidation catalyst, hydrogen peroxide appears to act as a hydroxylation agent. It is generally presumed that the hydrogen peroxide reacts with acid anhydrides to form per acids which react with unsaturated acids to form various oxidation products depending on the conditions of the reaction, but the mechanisms by which these reactions are accomplished are not as yet entirely understood.

Mechanism of Per Acid Oxidation.—An understanding of the mechanism of per acid oxidation is obscured by the lack of knowledge of whether all per acids are structurally the same, for example, persulfuric, peracetic, and perbenzoic, and also by the fact that the original oxidation may be accompanied with or followed by secondary hydrolytic reactions.

It was originally presumed that persulfuric and peracetic acids reacted with unsaturated fatty acids to form hydroxysulfonic or hydroxyacetoxy addition compounds which subsequently underwent hydrolysis to form polyhydroxy acids. It is quite probable that under certain conditions such reactions do actually occur. On the other hand, perbenzoic acid has generally been presumed to react simply by furnishing one atom of oxygen which adds to the double bond to form an oxido or epoxy acid. These oxido acids can in turn be hydrolyzed by acids or alkalies to form polyhydroxy acids. Recently, Findley, Swern, and Scanlan[160] have shown that oxido acids are also formed by peracetic acid oxidation of unsaturated acids provided the reaction is conducted in an inert solvent, or by other means of minimizing secondary hydrolysis.

It has also been observed that under certain conditions of oxidation and hydrolysis the hydroxy acids which were obtained represented inversion products, *i. e.*, high melting forms of hydroxy acids were obtained from the low melting forms of saturated acids and *vice versa*. Generally, peracetic

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[160] T. W. Findley, D. Swern, and J. T. Scanlan, *J. Am. Chem. Soc.*, 67, 412–414 (1945).

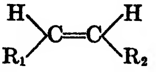
acid in the absence of a catalyst reacts with monounsaturated acids by *cis*-addition to form the corresponding dihydroxy acid. No inversion occurs during the reaction. Perbenzoic acid reacts similarly except that the product of reaction is an oxido acid which on acid hydrolysis forms the dihydroxy acid also corresponding to *cis*-addition. When, however, hydrolysis of the oxido acid is carried out with alkali at high temperatures, inversion occurs and the hydroxy acid corresponding to *trans*-addition is obtained. The inversion would therefore appear to be due to the action of alkali or to the high temperature or both.

If, however, an oxidation catalyst is present, peracetic acid reacts with unsaturated acids to give the dihydroxy acid corresponding to *trans*-addition. Thus, erucic acid gives the low melting dihydroxybehenic acid (101°C.) when oxidized with peracetic acid in the absence of a catalyst and the high melting form (132°C.) when oxidized in the presence of a catalyst such as osmium tetraoxide. With brassidic acid the reverse reactions occur. This action of the catalyst in producing inversion during oxidation requires further investigation and elucidation.

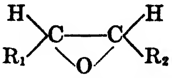
Mechanism of Potassium Permanganate Oxidation.—Potassium permanganate has been extensively employed for investigating the constitution of unsaturated fatty acids and has proved of inestimable value in this connection, but despite its utility the mechanism by which the reaction is accomplished is still incompletely understood. It reacts in alkaline and neutral solutions to liberate 1.5 atoms of oxygen and in acid solution to liberate five atoms of oxygen. In neutral, and especially in nonaqueous solution, it reacts in a manner similar to potassium dichromate but much more energetically. For example, when dry powdered permanganate is moistened with glycerin the mass presently bursts into flame. When it is in contact with the skin, oxidation of organic substances in the skin occurs, with the production of brown stains of manganese dioxide. In dilute solution and at low temperatures it reacts less energetically, but only under rigidly controlled conditions are highly specific and reproducible results obtained. Reaction of cold alkaline permanganate on monounsaturated acids generally leads to the production of hydroxy acids, while reactions in acidic media or aqueous and acetone solutions at elevated temperatures generally result in complete rupture of the double bond. In neither case is the mechanism of the reaction completely established.

To understand the reactions of potassium permanganate with unsaturated fatty acids they must be examined in relation to the reactions occurring with other oxidation reagents. The question which then arises is whether or not the first step is the same in all chemical oxidations of the double bond of a given unsaturated acid such as oleic irrespective of the oxidation agent, and whether the subsequent reactions follow the same or different paths once addition of oxygen occurs at the double bond.

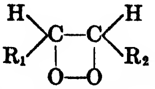
Omitting for the present the formation of a peroxido derivative at the methylene carbon adjacent to the double bond, at least five oxidation products have been isolated or their existence postulated as being derivable from an unsaturated fatty acid without fission of the carbon chain. These products are illustrated in the accompanying formulas for oleic acid and its derivatives in which $R_1 = CH_3(CH_2)_7—$ and $R_2 = —(CH_2)_7COOH$.



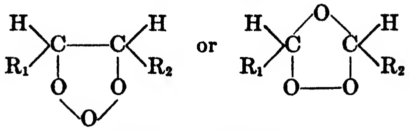
Oleic acid



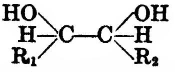
Oxidoleic acid



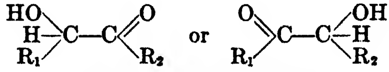
Cyclic peroxidoleic acid



Oleic acid ozonide



Dihydroxystearic acid



Hydroxyketostearic acid

All of these oxidation products exist in at least two modifications corresponding to the two stereoismeric or *cis*- and *trans*-unsaturated acids. Dissimilarly substituted oxidation products exist in two positionally isomeric forms, *e. g.*, 9-hydroxy-10-keto- and 9-keto-10-hydroxystearic acid.

With oxidation agents such as perbenzoic and peracetic acids, the stereo configurations of the parent unsaturated acids are preserved in the oxidation products. As has been previously mentioned, Dorée and Pepper[161] obtained the low melting oxido acid from erucic acid and the high melting oxido acid from brassidic acid on oxidation of the respective unsaturated acids with perbenzoic acid. Hydrolysis of the oxido acids in aqueous alcoholic hydrochloric acid gave the corresponding forms of the dihydroxybehenic acids. Similarly, when methyl erucate and methyl brassidate were oxidized in the same manner they gave the corresponding oxido acids. Likewise, when methyl erucate and methyl brassidate were reacted with hydrogen peroxide and acetic acid at 100°C. and saponified, they gave the corresponding dihydroxybehenic acids. No inversions were observed to occur at any stage in the reactions, *i. e.*, in all cases the low melting form of the unsaturated acid gave the low melting form of the oxido acid, and the low melting form of the oxido acid gave the low melting form of the dihydroxy acid, whereas with the high melting form of the unsaturated acid only high melting oxidation products were obtained.

In contrast to these reactions, oxidation of the same acids with alkaline

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[161] C. Dorée and A. C. Pepper, *J. Chem. Soc.*, **1942**, 477–483.

potassium permanganate results in an inversion at some stage of the oxidation as is evident from the fact that the dihydroxy acid which is obtained under these circumstances corresponds to the opposite stereoisomer of the parent acid. Oxidation of oleic acid with alkaline permanganate produces the dihydroxystearic acid melting at 132°C., while elaidic acid under the same condition yields the dihydroxystearic acid melting at 95°C. However, King[162] has reported that the same inversions occur during oxidation of oleic and elaidic acids in neutral solutions but to a considerably lesser extent since the primary products of oxidation under these conditions are hydroxyketo acids rather than dihydroxy acids.

Although it is agreed that an inversion must occur in the course of the oxidation, no agreement exists concerning the stage at which inversion occurs, the mechanism by which it occurs, or the specific agent responsible for the inversion. Also, it appears to be agreed that the inversion is practically quantitative, and only one form of the oxidation product is obtained from a given acid rather than an equilibrium mixture such as occurs in the inversion of oleic or elaidic acid under the catalytic influence of the oxides of nitrogen,[163] or in the case of the rearrangement of hydroxyketostearic acids under the influence of alkali.[162] In the latter case it was observed that treatment at room temperature of 9-hydroxy-10-ketostearic acid (m.p. 74°C.) with an excess of 0.1 *N* sodium hydroxide resulted in the gradual conversion of part of the original acid to 9-keto-10-hydroxystearic acid (m.p. 75.5°C.) which reaction reached equilibrium in 36 hours. When the temperature was raised to 100°C. the equilibrium mixture (m.p. 63–64°C.) was obtained in five minutes. It is of interest, therefore, to seek an explanation for the inversion occurring during alkaline permanganate oxidation and the fact that it is also quantitative.

It might be assumed that the oxygen liberated in alkaline permanganate solution adds to the double bond of a monoethenoid acid to form a peroxido or oxido acid which undergoes subsequent rapid reaction to form a dihydroxy acid. If such a reaction did occur it might be expected that *cis*-addition would result as in the case of the reaction with perbenzoic acid. Subsequent hydrolysis might then be accompanied by inversion due to the alkalinity of the medium. No such products have been observed during alkaline permanganate oxidation which may or may not be sufficient reason for assuming that the reaction does not occur through such an intermediate.

It might also be assumed that the high concentration of hydroxyl ions present in the alkaline permanganate reaction mixture results in direct hydroxylation of the double bond of an unsaturated acid. Such a reaction

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[162] G. King, *J. Chem. Soc.*, **1936**, 1788–1792. See T. P. Hilditch and H. Plimmer, *J. Chem. Soc.*, **1942**, 204–206.

[163] H. N. Griffiths and T. P. Hilditch, *J. Chem. Soc.*, **1932**, 2315–2324; *J. Soc. Chem. Ind.*, **53**, 75–81T (1934).

appears plausible in view of the fact that oxidation of these acids with neutral permanganate produces predominantly hydroxyketo derivatives with only a small proportion of dihydroxy acid. Further plausibility is rendered such a view by King's[162] observation that dihydroxy acids are not converted to hydroxyketo acids by further oxidation with neutral permanganate and that the only effect of this reagent on hydroxyketo acids under mild reaction conditions is to produce equilibrium with respect to the positionally isomeric pairs of these acids. However, even if alkaline potassium permanganate does actually result in direct hydroxylation of the unsaturated linkage it does not account for the fact that it is also accompanied by an inversion.

Hilditch and co-workers[159,164,165] hold that an inversion occurs during permanganate oxidation in alkaline solution and that the configurational course taken during the conversion of the double bond into a glycol by oxidation is controlled by the alkalinity of the medium. However, evidence is available to indicate that inversion occurs in neutral or even acid media. As has been previously mentioned, King[162] reported that with oleic and elaidic acids the same inversion occurred in substantially neutral solution (*p*H about 8.5) but to a considerably lesser extent than in alkaline solutions, and Dorée and Pepper observed that permanganate oxidation of erucic acid in neutral solution gave the high melting form of dihydroxybehenic acid. Furthermore, Dorée and Pepper[161] observed that oxidation with hydrogen peroxide in glacial acetic acid containing osmium tetroxide as a catalyst produced an inversion in the oxidation products of both erucic and brassidic acids.

The evidence for the inversion occurring as a result of the alkalinity of the permanganate reaction medium rests primarily on the behavior of chlorohydrins and oxido acids with respect to formation and rupture of oxido rings under various reagents. With strong alkali and high temperature, oxido acids react to form hydroxy acids representing inversion products of the parent unsaturated acids.[166] With aqueous alcoholic hydrochloric acid, the oxido ring is ruptured to form dihydroxy acids in which no inversion occurs.[161] With ethereal hydrogen chloride, the oxido ring is opened and chlorohydroxy acids are formed which in the presence of alkali undergo ring closure to produce the original oxido acid.[156] The foregoing observations are not only difficult to harmonize with respect to the role which alkali plays in determining the configuration of the dihydroxy acids formed by alkaline permanganate oxidation, but it is questionable whether they shed any direct light on the problem since oxido acids have never been shown to be intermediates in permanganate oxidation.

The most notable difference in the conditions prevailing in permanganate

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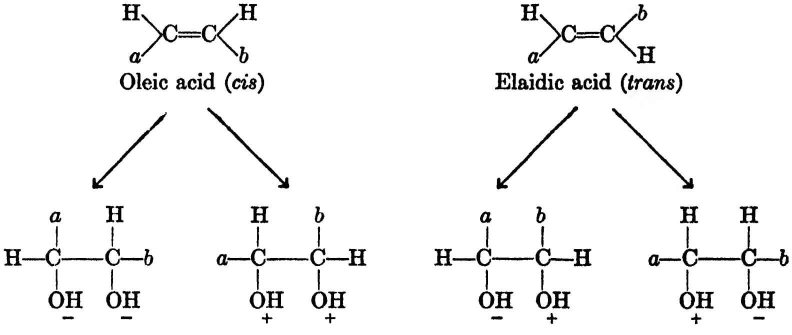
[164] T. P. Hilditch, *J. Chem. Soc.*, **1926**, 1828–1836.

[165] T. P. Hilditch and C. H. Lea, *J. Chem. Soc.*, **1928**, 1576–1583.

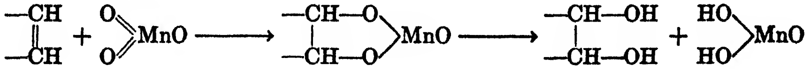
[166] K. H. Bauer and O. Bähr, *J. prakt. Chem.*, **122**, 201–213 (1929).

oxidations and per acid oxidations is the fact that the former are carried out in aqueous or aqueous alkali solutions, while the latter are carried out in nonaqueous or acidic media. Thus, it might be expected that hydroxyl ions influence the mechanism in the first case and hydrogen ions in the second. It might seem, therefore, that permanganate oxidation consisted of direct hydroxylation rather than some form of oxygen addition at the double bond and that this direct hydroxyl addition resulted in the formation of racemic mixtures of pairs of hydroxy acids corresponding to those presumed by Atherton and Hilditch[159] to result from monoethenoid acids if they proceeded by way of the corresponding racemic oxido acids. The dihydroxystearic acids resulting from the hydroxylation of oleic and elaidic acids could, according to this assumption, be represented by the accompanying formulas in which $a = CH_3(CH_2)_7—$ and $b = —(CH_2)_7COOH$. The (+) and (−) signs in the formulas are those arbitrarily assigned by Atherton and Hilditch to correlate the configural relationship and do not refer to the actual optical rotations. Although the reaction may be schematically represented in this manner, it still does not explain the cause of the inversion which occurs during permanganate oxidation or the cause of the same inversion occurring with peracetic acid in the presence of an oxidation catalyst.



r-Dihydroxystearic acid, m.p. 132 °C. *r*-Dihydroxystearic acid, m.p. 95 °C.

In order to explain their results on the oxidation of olefins with dilute permanganate solution, Böeseken and co-workers[167,168] assumed that manganese trioxide added to the double bond by *cis*-addition to form a heterocyclic ring containing an atom of manganese, and that this ring subsequently is opened by hydrolysis with the formation of a *cis*-diol according to the following scheme:



$$\begin{matrix}—CH\\ \| \\ —CH\end{matrix} + \begin{matrix}O\\ O\end{matrix}\!\!>\!MnO \longrightarrow \begin{matrix}—CH—O\\ | \\ —CH—O\end{matrix}\!\!>\!MnO \longrightarrow \begin{matrix}—CH—OH\\ | \\ —CH—OH\end{matrix} + \begin{matrix}HO\\ HO\end{matrix}\!\!>\!MnO$$

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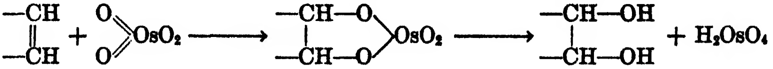
[167] J. Böeseken and J. van Giffen, *Rec. trav. chim.*, **39**, 183–186 (1920).

[168] J. Böeseken and C. de Graaff, *Rec. trav. chim.*, **41**, 199–207 (1922).

Similarly, Criegee[169] found that in the case of oxidation with osmium tetroxide such *cis*-addition actually occurred and subsequent hydrolysis produced a *cis*-diol as indicated in the following scheme:



When various olefins such as acenaphthylene, indene, $\Delta^{2,3}$-dihydronaphthalene, $\Delta^{9,10}$-octalin, stilbene, anethol, and crotonic acid, were treated with osmium tetroxide, crystalline addition products were obtained containing one mole of olefin per mole of osmium tetroxide. The addition product of osmium tetroxide and acenaphthylene was relatively stable, decomposing at 236°C. without melting. Hydrolysis of this and similar addition products under a variety of conditions always produced the *cis*-diol.

If a similar *cis*-addition of manganese oxide occurs in the case of oxidation of monoethenoid acids, such as oleic and erucic, with potassium permanganate, or addition of osmium oxide occurs during oxidation with hydrogen peroxide catalyzed by osmium tetroxide, then inversion must occur during subsequent hydrolysis of the cyclic addition product, and, as suggested by Hilditch, probably by the action of alkali.

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[169] R. Criegee, *Ann.*, **522**, 75–96 (1936).

CHAPTER XVI

OXIDATION BY ATMOSPHERIC OXYGEN (AUTOXIDATION)

1. Introduction

Atmospheric oxygen is the most universally prevalent as well as economically important oxidizing agent for fats and fatty acids. Its action on fats and fatty products may be beneficial and highly desirable or deleterious and equally undesirable, depending on the conditions and circumstances under which it occurs. It is advantageously employed in the production of "blown oils" and in various oxidation and polymerization products in the drying oil industry. The process of film formation in applied protective coatings is essentially an oxidative process. However, the ultimate failure of these same protective coatings is a result of prolonged and excessive oxidation. Rancidification and other forms of deterioration of many fats and fat-containing materials are likewise due to atmospheric oxidation. These reactions are highly undesirable and result in serious economic losses.

So far as we are aware both the favorable and unfavorable results of atmospheric oxidation follow from the same type of reactions between oxygen and the unsaturated constituents of fats or fatty acids, consequently an enormous amount of effort has been expended in attempting to unravel the mystery which still enshrouds the fundamental reactions involved in these processes. A vast literature has appeared on the subject but as yet no clear understanding of the complete reaction mechanism involved has appeared. Many theories have been advanced and much experimental evidence has been accumulated to substantiate one or another hypothesis. Some of the theories and experimental evidence have resulted in confusing rather than clarifying the problem, but gradually there has been adduced a few fundamental principles which will eventually lead to a complete understanding of these mechanisms.

Because of the spontaneous nature of the reaction between atmospheric oxygen and unsaturated fats and fatty acids, the process is frequently referred to as *autoxidation*. Without attempting to justify this terminology, it is used here because of its convenience and because it affords a means of avoiding the repetitious use of the cumbersome phrase "oxidation with atmospheric oxygen."

Light, heat, concentration of oxygen, moisture, and the presence of catalysts or inhibitors affect the reaction between oxygen and unsaturated fatty acids, often with seemingly very different results. However, it is probable that the same or very similar mechanisms are involved or would ultimately be involved if the reaction process were permitted to run its course. It is sometimes difficult to evaluate the effect of a specific environmental factor in the over-all oxidation process because in most cases several of these factors are simultaneously active. Of the several factors which may be operating, one may predominate under one set of conditions and quite a different one under another. For example, in a relatively thick layer of fat or fatty acid maintained in a completely filled glass container at room temperature and exposed to sunlight or ultraviolet light, the absorbed radiant energy may be the predominant factor influencing the oxidation reaction, and the temperature and concentration of oxygen may be quite secondary. On the other hand, in the process of blowing oils the temperature and concentration of oxygen are the predominant factors and the effect of light is quite secondary.

The effect of temperature on the oxidation mechanism and the products of oxidation of unsaturated fats or fatty acids is such that for practical purposes three temperature ranges are readily distinguished and many investigations have been confined to one or another of these ranges. These temperature ranges are generally: (*1*) atmospheric temperature or 0–40°C. (32–104°F.); (*2*) 90–120°C. (194–248°F.); (*3*) 200–300°C. (392–572°F.). Many of the oxidation reactions involved in the rancidification of fats occur at the lowest temperature mentioned. Blown oils, used in the drying oil industry, are generally prepared at temperatures between 90° and 120°C., and it is in this temperature range that most of the investigations on accelerated fat deterioration are conducted. The highest temperatures are employed in the manufacture of boiled oils, stand oils, and related polymerized fat products.

Catalysts or inhibitors of various types may be added to or may be present naturally in fats and oils, thus markedly influencing the reaction velocity. For example, traces of copper accidentally introduced in a fat or fatty acid generally increase the rate of oxidative rancidification. The addition of metal oxides or metallic salts in the manufacture of boiled oils accelerates the oxidation and subsequent polymerization reactions in this process, and similar use of these substances in protective coatings enhance their rate of drying and film formation. On the other hand, the presence of antioxidants acts to inhibit these same reactions.

In planning and executing an investigation in the autoxidation of fats, the careful worker attempts to minimize the number of variables which may affect the course of the reaction, or at least control them within relatively narrow limits. Thus, the effect of light may be avoided by excluding it entirely from the reaction, or the effect of heat may be minimized by maintaining a constant low temperature in the reacting system. Unfortunately the literature contains reports of many investigations in which little or no control was exercised over the various environmental factors, or if they were controlled the author failed to mention it. In such cases it is often difficult to evaluate the data reported or determine the validity of the conclusions drawn by the investigator.

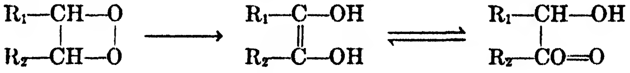
Underlying all investigations of the autoxidation of fats is a desire not only to learn the nature of the products formed but also to understand the mechanism involved in their production, since only by control of these mechanisms can the desired products be produced or the undesirable products be avoided. Natural fats are generally too complex to permit drawing far-reaching generalizations concerning the mechanisms involved in autoxidative processes. Hence, much work involving these reactions has been carried out with simple substances such as oleic, linoleic, or similar acids and their monoesters, especially since they can be obtained in relatively pure form. Generalizations made on the basis of the results with these simple substances have then been applied to natural fats. In some cases such generalizations may be valid but as in all cases of reasoning by analogy they may not be entirely justified. It should therefore be borne in mind that applying the results and conclusions derived from one substrate, *e. g.*, methyl oleate at 100°C., to a quite different substrate, *e. g.*, cottonseed or soybean oil, at room temperature, may not be entirely justified. It is known, for example, that peroxido acids or esters are relatively unstable at 100–110°C., whereas at room temperature they are relatively stable, therefore quite different end products may be produced under the two reaction conditions. Of course, if the time be sufficiently extended at the lower temperature the same end result might ultimately be achieved. However, if these limitations are borne in mind it is entirely possible to proceed from the simple to the more complex with reasonable prospects of ultimately resolving the whole of the complicated phenomenon involved in the autoxidation of fats.

2. Development of the Concepts of Autoxidation

Any explanation of the process of autoxidation must begin, as in all related oxidation reactions, with an understanding of the nature of first addition of oxygen to the double bond. Until this initial step is known with certainty the subsequent steps of the process must remain more or less speculative. It is for this reason that every theory which has been evolved with regard to the autoxidation of fats has been founded on some concept concerning the initial addition of oxygen to the unsaturated linkage and upon the chemical nature of the product thus formed.

The first observation of autoxidation of a carbon-to-carbon double bond has been attributed to Schönbein[1] the discoverer of ozone, who investigated the reactions of a variety of oxidizing agents with unsaturated substances such as almond oil and turpentine. However, the modern theories of autoxidation are generally assumed to date (about 1900) from the work of Bach[2] and of Engler and co-workers[3–5] who investigated the role of organic peroxides in slow oxidation processes and introduced the term *activated oxygen.* Prior to the publications of Bach and of Engler, molecular oxygen was presumed to be broken down, at least to a small extent, into atomic oxygen in a manner analogous to the liberation of oxygen from hydrogen peroxide, and that this *active oxygen* was presumed to be responsible for the slow oxidation observed in various unsaturated organic substances. Bach and Engler, however, believed that autoxidation by atmospheric oxygen was molecular and not atomic in nature, *i. e.*, that a molecule of oxygen added at the double bond to form a peroxidized compound corresponding to the formula $R_1—O—O—R_2$ and that this compound, like hydrogen peroxide, could in turn oxidize another oxidizable substance. The *activated oxygen* was not considered to be a free oxygen atom, but was rather, chemically bound in such a manner that it could readily be liberated to enter into autoxidative reactions.

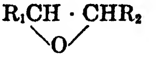
In an attempt to explain the action of driers in the formation of linseed oil films and the reactions occurring between the oil and protein in the chamoising process, Fahrion[6] assumed that an autoxidation occurred in the fatty acid to form a cyclic peroxide which underwent rearrangement to a dihydroxyethylenic or a hydroxyketo configuration as follows:



$$\begin{array}{l} R_1—CH—O \\ \quad\ \ | \qquad | \\ R_2—CH—O \end{array} \longrightarrow \begin{array}{l} R_1—C—OH \\ \qquad \| \\ R_2—C—OH \end{array} \rightleftharpoons \begin{array}{l} R_1—CH—OH \\ \qquad | \\ R_2—CO{=}O \end{array}$$

It was also presumed that the cyclic peroxide might give rise to more stable products corresponding to the formulas:

$R_1COCH_2R_2$ and



$$\underset{\diagdown O \diagup}{R_1CH\cdot CHR_2}$$

Ellis[7] developed the theory of tautomeric ketohydroxy-dihydroxy rearrangement especially with reference to the drying of linseed oil films. The detection of considerable quantities of hydroxyl and keto groups in films of

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[1] C. F. Schönbein, *J. prakt. Chem.*, **74,** 328–340 (1858); see **75,** 73–78 (1858).

[2] A. Bach, *Compt. rend.*, **124,** 951–954 (1897); *J. Russ. Phys.-Chem. Soc.*, **29,** 373 1897).

[3] C. Engler and J. Weissberg, *Ber.*, **31,** 3046–3055, 3055–3059 (1898).

[4] C. Engler and W. Wild, *Ber.*, **30,** 1669–1681 (1897). See C. Engler and J. Weissberg, *Kritische Studien über die Vorgänge der Autoxydation*, Vieweg, Braunschweig, 1904.

[5] C. Engler, *Ber.*, **33,** 1090–1096, 1097–1109, 1109–1111 (1900).

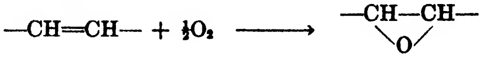
[6] W. Fahrion, *Z. angew. Chem.*, **22,** 2083–2097 (1909); *Chem.-Ztg.*, **28,** 1196–1200 (1904).

[7] G. W. Ellis, *J. Soc. Chem. Ind.*, **44,** 401–408T, 463–468T, 469–472T, 486T (1925); **45,** 193–199T (1926); *Biochem. J.*, **26,** 791–800 (1932).

this type was advanced as proof of the correctness of the theory. According to Ellis, autoxidation occurs as a result of addition of oxygen to the double bond with the formation of a dihydroxy compound which subsequently rearranges, in part at least, to a hydroxyketo compound according to the following scheme:

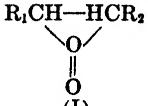
$$R_1CH{-}CHR_2 \xrightarrow{O_2} R_1C(OH){=}C(OH)R_2 \longrightarrow R_1CO{-}CH(OH)R_2$$

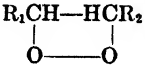
In 1909, Fokin[8] proposed a theory in which the first step in the autoxidation of an ethylenic bond was presumed to occur through the formation of an ethylene oxide ring:



Fatty acids or esters containing this oxirane or ethylene oxide ring have been variously referred to as monoxides, epoxides, and oxido compounds. This configuration is now known to be formed during oxidation of monoethenoid acids with perbenzoic, peracetic, and Caro's acid[9] and many of these oxido acids have been isolated and characterized. In substantiation of the theory of ethylene oxide formation during autoxidation, Fokin considered it from the kinetic point of view and adduced considerable experimental data which was amenable to kinetic treatment.

Staudinger[10] proposed a theory of autoxidation based on the assumption that the peroxido reaction originally proposed by Bach and by Engler was probably not the first, but the second step in the autoxidation of ethylenic compounds. He assumed that a molecule of oxygen added at the ethylene bond to form a moloxide, probably corresponding to formula I, which subsequently underwent a rearrangement to form a peroxido compound (II):


(I)


(II)

This theory was predicated on an investigation of the autoxidation of *asym*-diphenylethylene, $(C_6H_5)_2C{:}CH_2$. Diphenylethylene peroxide was isolated and found to be relatively stable, whereas the product of first addition of oxygen, which could not be isolated, was unstable and exploded when heated in a steel bomb to 40–50°C. In a footnote, Staudinger points out that the *moloxide* having a structure corresponding to the four-membered heterocyclic ring should be designated as *peroxide* and its unknown precursor as a *moloxide*.

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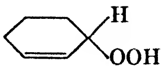
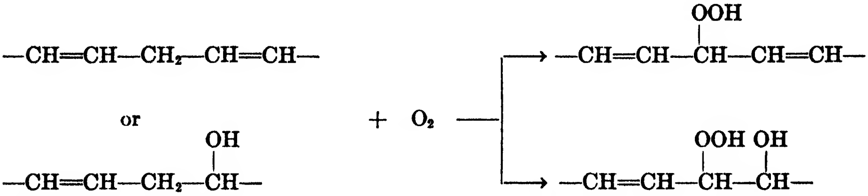
[8] S. Fokin, *Z. angew. Chem.*, **22**, 1451–1459, 1492–1502 (1909).
[9] D. Atherton and T. P. Hilditch, *J. Chem. Soc.*, **1943**, 204–208.
[10] H. Staudinger, *Ber.*, **58**, 1075–1079 (1925).

In 1936, Criegee[11,12] suggested that cyclohexene autoxidized to form a hydroperoxide having the structure:



and Rieche[13,14] suggested that unsaturated fats and oils probably behaved similarly. Rieche suggested that the autoxidation of mono- or polyunsaturated substances may occur through the formation of oxygen-activated methylene groups according to the following scheme:



$$\begin{array}{c} -CH{=}CH{-}CH_2{-}CH{=}CH- \\ \text{or} \\ -CH{=}CH{-}CH_2{-}\overset{OH}{\overset{|}{C}}H- \end{array} + O_2 \longrightarrow \begin{cases} -CH{=}CH{-}\overset{OOH}{\overset{|}{C}}H{-}CH{=}CH- \\ -CH{=}CH{-}\overset{OOH}{\overset{|}{C}}H{-}\overset{OH}{\overset{|}{C}}H- \end{cases}$$

The hydroperoxidic nature of autoxidation has received substantiation in the behavior of cyclohexene,[11,12,15] tetralin,[12,16] and other unsaturated compounds[17-19] which may be considered as being analogous to unsaturated fatty acids.

To Farmer and his co-workers[20-24] is due the credit for developing the hydroperoxide hypothesis of autoxidation, especially in its application to fatty acids, and for substantiating it with convincing experimental evidence. According to Farmer, the autoxidation of practically all unconjugated olefinic compounds proceeds by addition of a molecule of oxygen to the carbon atom adjacent to the double bond to form a hydroperoxide having an intact double bond, thus:

$$-CH_2{-}CH{=}CH- + O_2 \longrightarrow -CH(OOH){-}CH{=}CH-$$

Methyl oleate, for example, produces, according to Farmer, a mixture of mono- and dihydroperoxides in which the hydroperoxide groups are at-

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[11] R. Criegee, *Ann.*, **522,** 75–96 (1936).

[12] R. Criegee, H. Pilz, and H. Flygare, *Ber.*, **72,** 1799–1804 (1939).

[13] A. Rieche, *Die Bedeutung der organischen Peroxyde für die chemische Wissenschaft und Technik.* Enke, Stuttgart, 1936.

[14] A. Rieche, *Angew. Chem.*, **50,** 520–524 (1937).

[15] H. N. Stephens, *J. Am. Chem. Soc.*, **50,** 568–571 (1928).

[16] H. Hock and W. Susemihl, *Ber.*, **66,** 61–68 (1933).

[17] H. Hock and O. Schrader, *Naturwissenschaften*, **24,** 159 (1936).

[18] H. Hock, *Oel Kohle Erdoel Teer*, **13,** 697–700 (1937).

[19] H. Hock and K. Gänicke, *Ber.*, **71,** 1430–1437 (1938).

[20] E. H. Farmer, *Trans. Faraday Soc.*, **38,** 340–348 (1942); **42,** 228–236 (1946); *Rubber Chem. Tech.*, **19,** 267–276 (1946).

[21] E. H. Farmer, G. F. Bloomfield, A. Sundralingam, and D. A. Sutton, *Trans. Faraday Soc.*, **38,** 348–356 (1942).

[22] E. H. Farmer, *Trans. Faraday Soc.*, **38,** 356–361 (1942).

[23] E. H. Farmer and D. A. Sutton, *J. Chem. Soc.*, **1943,** 119–122.

[24] E. H. Farmer and D. A. Sutton, *J. Chem. Soc.*, **1943,** 122–125.

tached to the eighth or eleventh carbon atom or to both, as indicated by:

$CH_3(CH_2)_6CH(OOH)CH{=}CH(CH_2)_7COOCH_3$

$CH_3(CH_2)_7CH{=}CHCH(OOH)(CH_2)_6COOCH_3$

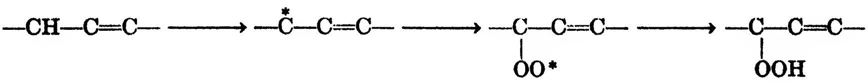
$CH_3(CH_2)_6CH(OOH)CH{=}CHCH(OOH)(CH_2)_6COOCH_3$

Each of these hydroperoxides contains either (*a*) one atom of active oxygen and one atom of active hydrogen, or (*b*) two atoms of active oxygen, and (*c*) an intact double bond.

Ordinarily the concentration of the hydroperoxide in the reacting system is presumed to be quite small owing to the relative instability of the product and its tendency to undergo secondary reactions. Farmer and Sutton hold that in the case of oleic acid a concentration of hydroperoxide corresponding to a consumption of about 1.5% of oxygen at room temperature can be obtained before appreciable decomposition ensues.

Although all the hydroperoxides are relatively unstable, several—those derived from cyclohexene, 1-methylcyclohexene, 1,2-dimethylcyclohexene, and methyl oleate—can be obtained in relatively pure form by fractional distillation at very low pressures. Oxygen absorption and hydroperoxide formation are promoted by sunlight and ultraviolet light, catalysts, and increased temperature. However, certain catalysts (iron salts) also promote the decomposition of the hydroperoxides, as is the case with elevated temperatures and prolonged irradiation. Therefore, optimum conditions of temperature, catalyst, and irradiation are essential to maximum production and minimum decomposition of hydroperoxides where their isolation is desired. The same type of oxygen addition is assumed to occur in the case of linoleic, linolenic, and the polyene fish-oil acids.[25] In the case of the fish-oil acids, the absorption of oxygen and formation of hydroperoxides is extremely rapid in diffused light at room temperature but decay is also relatively rapid.

Of the various mechanisms by which hydroperoxide formation may occur, Farmer and co-workers[21,25] incline to the view that olefinic peroxidation occurs by way of a free-radical mechanism in which the olefin passes through the stages:



$$-CH-C{=}C- \longrightarrow -\overset{*}{C}-C{=}C- \longrightarrow -\underset{\substack{|\\ OO^*}}{C}-C{=}C- \longrightarrow -\underset{\substack{|\\ OOH}}{C}-C{=}C-$$

in which the free radical center is indicated by an asterisk. In the case of unconjugated unsaturation of the methylene-interrupted type such as is characteristic of most unconjugated drying oil acids (linoleic, linolenic, etc.), the first step of peroxidation is assumed to consist in the severance

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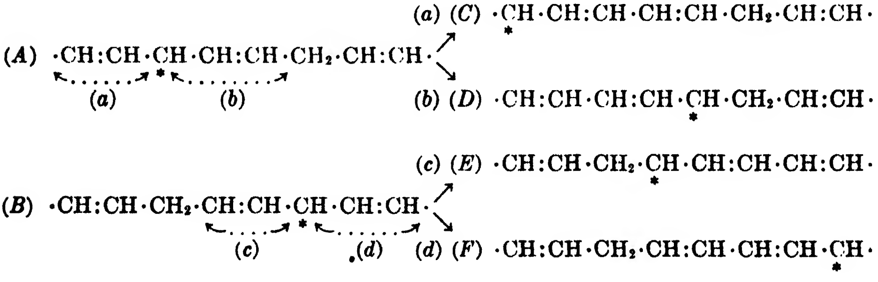
[25] E. H. Farmer, H. P. Koch, and D. A. Sutton, *J. Chem. Soc.*, **1943**, 541–547.

(presumably with the aid of molecular oxygen) of a thermally or photochemically activated α-methylene C to H bond, leaving an olefinic free radical. Since resonance may be expected between the two three-carbon forms $-\overset{3}{C}H{=}\overset{2}{C}H-\underset{*}{\overset{1}{C}H}-$ and $-\underset{*}{\overset{3}{C}H}-\overset{2}{C}H{=}\overset{1}{C}H-$, the addition or substitution of a molecule of oxygen would most probably result with equal frequency in the production of peroxido groups (—OOH) at positions 1 and 3 and permit the double bond to remain at the original position or to appear at the adjacent C—C bond.

According to Farmer,[25] in the case of the methylene-interrupted type of unsaturation just considered, the most reactive methylene groups are those flanked on either side by a double bond, and if the two methylene groups of this type in ethyl linolenate were to be attacked singly by oxygen, the original radical forms (*A*) and (*B*) would be supplemented by products (*C*) to (*F*):



(*a*) (*C*) $\cdot\underset{*}{CH}\cdot CH{:}CH\cdot CH{:}CH\cdot CH_2\cdot CH{:}CH\cdot$

(*A*) $\cdot CH{:}CH\cdot\underset{*}{CH}\cdot CH{:}CH\cdot CH_2\cdot CH{:}CH\cdot$

(*a*) (*b*)

(*b*) (*D*) $\cdot CH{:}CH\cdot CH{:}CH\cdot\underset{*}{CH}\cdot CH_2\cdot CH{:}CH\cdot$

(*c*) (*E*) $\cdot CH{:}CH\cdot CH_2\cdot\underset{*}{CH}\cdot CH{:}CH\cdot CH{:}CH\cdot$

(*B*) $\cdot CH{:}CH\cdot CH_2\cdot CH{:}CH\cdot\underset{*}{CH}\cdot CH{:}CH\cdot$

(*c*) (*d*)

(*d*) (*F*) $\cdot CH{:}CH\cdot CH_2\cdot CH{:}CH\cdot CH{:}CH\cdot\underset{*}{CH}\cdot$

The hydroperoxides derived from products (*C*) to (*F*) would then show diene conjugation. Similarly, if both the reactive methylene groups were attacked consecutively by oxygen, which would happen frequently only in advanced stages of oxidation, five other (di-)peroxido-forms would become possible, three showing diene conjugation, one triene conjugation, and the last the original state of unconjugation. If on each occasion that a hydrogen atom is detached from just one of the active methylene groups of a linolenic acid molecule the tendency for the radical center so formed to migrate to left or right is assumed to be about equal to the tendency for it to retain its original position, then it will follow that only half the radical molecules that are ultimately successful in combining with oxygen and hydrogen to give monohydroperoxido compounds will yield conjugated forms; if, however, all of the three resonance forms derivable by loss of a hydrogen atom from a pentadiene system, $-CH{=}CH-CH_2-CH{=}CH-$, are to be regarded as possessing equal stability, the proportion of conjugated to unconjugated forms will rise to about 2:1.

If the above-described free-radical mechanism of autoxidation is correct, double bond shifts quite likely occur in the autoxidation of mono-olefinic substances, since they too possess a three-carbon grouping, —CH=CH—CH—; thus, methyl oleate should give the peroxido forms:

$$-\overset{11}{C}=\overset{10}{C}-\overset{9}{C}(OOH)-\overset{8}{C}- \quad \text{and} \quad -\overset{11}{C}-\overset{10}{C}(OOH)-\overset{9}{C}=\overset{8}{C}-$$

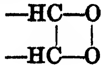
as well as:

$$-\overset{11}{C}(OOH)-\overset{10}{C}=\overset{9}{C}-\overset{8}{C}- \quad \text{and} \quad -\overset{11}{C}-\overset{10}{C}=\overset{9}{C}-\overset{8}{C}(OOH)-$$

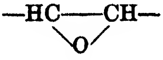
From absorption spectra data, the authors[25] conclude that no distinction can be made between photochemical and thermal oxidation as far as the mechanism of hydroperoxide formation is concerned.

It is interesting to note that Meyer[26] found that oleic acid, when photochemically oxidized in the Warburg apparatus in the presence of chlorophyll, absorbed 0.5 mole of oxygen with practically no decrease in iodine value. Meyer interpreted his results as indicating that oxidation occurred with the formation of hydroxyoleic acid. Decenoic and undecenoic acids, in each of which the double bond is attached to the terminal carbon atom, were entirely resistant to autoxidation under the same conditions. Böeseken and Geersteranus[27] have likewise reported a similar stability of terminal double bonds to oxidation. The resistance to autoxidation of acids having a double bond attached to the terminal carbon atom would be expected on the basis of the mechanism proposed by Farmer and may therefore be considered as additional evidence in its favor.

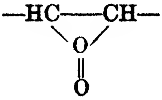
It is apparent from the foregoing review of the various hypotheses of autoxidation that the first step in the addition of oxygen to an ethylenic bond of an unsaturated fatty acid has been assumed to occur with the formation of one or another of four different primary reaction products: (*a*) cyclic peroxide, (*b*) epoxide, (*c*) moloxide, and (*d*) hydroperoxide. These products have been assigned the structures illustrated in the accompanying formulas:



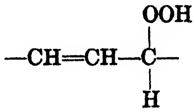
(*a*)



(*b*)



(*c*)



(*d*)

Each of the foregoing hypotheses has had numerous adherents and a vast amount of experimental work and discussion has been offered in their support. It is impossible to refer to all or even a considerable portion of the literature on the subject but a few of the more pertinent contributions are referred to in the following pages.

3. Ethylene Oxide Hypothesis

Experimental evidence in support of Fokin's proposal that ethylenic bonds are autoxidized to form ethylene oxide (oxido, epoxide) groups,

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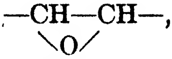
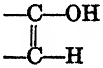
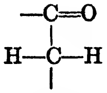
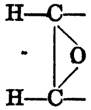
[26] K. Meyer, *Cold Spring Harbor Symposia Quant. Biol.*, 3, 341–349 (1935).
[27] J. Böeseken and M. W. M. Geersteranus, *Rec. trav. chim.*, 51, 551–556 (1932).


$\underset{\diagdown O \diagup}{—CH—CH—}$, is the least extensive of the various hypotheses. Aside from Fokin's[8] own work, some support for this theory is found in the work of Szent-Györgyi[28] who investigated the autoxidation of linolenic acid in the presence of sulfhydryl groups as catalyst. The linolenic acid was dissolved in ether and filter paper was saturated with the ethereal solution and the ether allowed to evaporate. The paper, saturated with linolenic acid, was placed in a closed glass cylinder with 30 ml. of a 10% solution of thioglycolic acid in 0.03 *N* acetic acid and connected with a gasometer filled with oxygen. The consumption of oxygen was measured, and at the end of the oxidation the paper was removed from the cylinder and extracted with petroleum naphtha. The reaction mixture was separated into (*a*) the unaltered petroleum naphtha-soluble product (original linolenic acid), (*b*) the petroleum naphtha-insoluble oxidation products, and (*c*) the thioglycolic acid.

The molecular weight of the oxidation product was found by titration to be 293, indicating that only one atom of oxygen was absorbed per mole of linolenic acid oxidized. According to Szent-Györgyi, one of the double bonds must have yielded an oxygenated product corresponding to one of the following formulas:

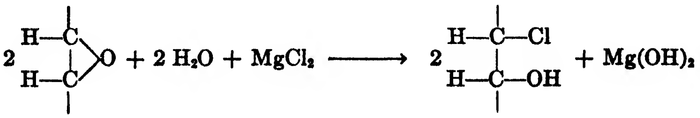

Enol


Ketone


Ethylene oxide

The absence of hydroxyl groups in the oxidation product was demonstrated by acetylation experiments. No red color was obtained with ferric chloride indicating the absence of a keto group which was also confirmed by the failure of the oxidation product to form a hydrazone when treated with phenylhydrazine. These reactions, according to the author, left only the possibility of ethylene oxide formation.

Ethylene oxides are known to react with concentrated magnesium chloride solutions according to the scheme:



The magnesium hydroxide normally precipitates in such a reaction and can be quantitatively separated and determined. However, in the case of linolenic or a similar acid, the inorganic hydroxides react to form soaps

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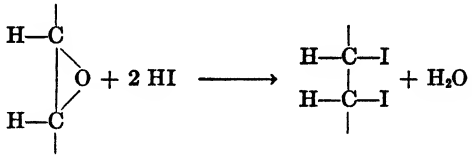
[28] A. v. Szent-Györgyi, *Biochem. Z.*, 146, 245–253, 254–258 (1924).

and thus complicate the determination. By a modification of the method, Szent-Györgyi obtained results which he considered as proof of the presence of the ethylene oxide group. Tollen's silver reagent is reduced by aldehydes and ethylene oxides and the linolenic oxidation product was found to strongly reduce this reagent in the cold.

After hydrolysis of the oxidation product with 10% sulfuric acid in methyl alcohol, the molecular weight was found to be 551 or approximately twice that of the original acid.

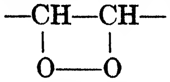
According to Szent-Györgyi, the iodine number of the oxido acid should remain the same as the unoxidized acid since hydriodic acid reacts with the ethylene oxide in the same way as with a double bond:



Within experimental limits, the iodine value by the Hübl and the Hübl-Waller methods of the original and oxidized linolenic acids were the same.

Szent-Györgyi concluded from these experiments that, in the catalytic oxidation of linolenic acid under the influence of sulfhydryl groups, the primary oxidation product is not a peroxide but an ethylene oxide (oxido acid). However, some of Szent-Györgyi's experimental evidence, for example, failure to observe a change in iodine value of the oxidized product, would be expected on the basis of Farmer's hydroperoxide structure for this product. Furthermore, the fact that the oxido acids of a number of the unsaturated acids are well-known crystalline products and the further fact that they have in no case been isolated from the products appearing in the early stages of autoxidation is rather convincing evidence against their formation at this stage of the oxidation.

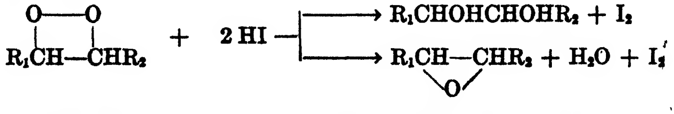
4. Cyclic Peroxide Hypothesis

Although the majority of workers in the field have accepted, at least until very recently, the theory of the formation of a heterocyclic peroxide of the formula  $\begin{array}{c}-\mathrm{CH}-\mathrm{CH}-\\ |\qquad|\\ \mathrm{O}-\!\!-\mathrm{O}\end{array}$ as the primary step in the autoxidation process, all the evidence relative to the existence of fatty acid peroxides containing such a configuration is indirect, since no product containing this grouping has ever been isolated and identified from an oxidized fat or fatty acid. Such peroxidized unsaturated compounds (ergosterol, rubrene, tetrahydronaphthalene, etc.) as have been obtained in pure form possess a structure different from that assumed for the fatty acid peroxides. Hydrogen peroxide and inorganic peroxides generally do not contain a heterocyclic ring. The per acids, such as peracetic and perbenzoic, likewise are quite dissimilar to the postulated peroxidized fatty acids. Benzoyl peroxide, which is often used as a comparative substance in investigations of peroxidized fatty acids, does not contain a heterocyclic ring and is a relatively stable solid melting at 108°C. Dihydroxydiheptyl peroxide, used by Franke and Jerchel and others as a comparative standard, is similar to the postulated fatty acid peroxides with respect to its chain length but it, too, lacks a heterocyclic ring and is a readily crystallizable solid.

The existence of fatty acid cyclic peroxides has been assumed on the basis of certain analytical data which have been interpreted as substantiating the existence of such a configuration in autoxidized unsaturated acids. These analytical determinations include iodine, thiocyanogen, and diene values, total absorbed oxygen, peroxide value, molecular weight, saponification, hydroxyl, and carbonyl values. If the autoxidized acid or ester contained but a single oxidation product and the methods gave quantitative results, the structure of the primary autoxidation product might be deduced on the basis of these data, at least for the simpler unsaturated acids. However, as a general rule, all of these methods have been applied to autoxidized acids or esters in which oxidation has proceeded to the point where there exists in the reaction mixture a number of oxidation, degradation, or polymerization products, and consequently, the interpretation of the analytical data becomes extremely complicated. Furthermore, there is some doubt that all of the methods are entirely quantitative and specific in their application, especially in the presence of the considerable number of oxidation and degradation products which may exist in the reacting system.

(a) *Quantitative Determination of Fatty Acid Peroxides by Iodimetry*

Although a number of qualitative reagents for peroxides are known to give apparently similar reactions, iodimetric methods are primarily applied in estimating the content of peroxides in an autoxidized fat or fatty acid. The methods are all based on the assumption that potassium iodide, barium iodide, or hydriodic acid liberate iodine in contact with peroxidized fats or fatty acids according to one of the following equations:



$$\underset{R_1CH-CHR_2}{O-O} + 2\,HI \begin{cases} \longrightarrow R_1CHOHCHOHR_2 + I_2 \\ \longrightarrow \underset{\diagdown O \diagup}{R_1CH-CHR_2} + H_2O + I_2 \end{cases}$$

The liberated iodine is then titrated with sodium thiosulfate solution. It is interesting to note that neither of the products postulated as being formed by the reaction of hydriodic acid and peroxidized oleic acid has been isolated from the reaction although both are crystalline compounds at room temperature. Although all of the iodimetric methods used, namely those of Lea,[29] Wheeler,[30] and Franke and Jerchel,[31] are presumed to react quantitatively and may do so under most conditions, they probably do not do so in all cases.

Method of Lea.—One gram of the oil or fat is weighed into a numbered and tared Pyrex test tube approximately 17 mm. in diameter. Powdered potassium iodide (about 1 g.) is added, followed by 20 ml. of a mixture of glacial acetic acid and chloroform or carbon tetrachloride (2:1 by volume). A rubber stopper, bored with one hole, is fitted, and nitrogen or carbon dioxide passed into the air space above the liquid for about one minute to displace most of the air. The tube is then heated in an inclined position over a small flame applied to its lower end, a finger resting lightly over the hole in the stopper, and the tube rotated slowly to prevent cracking. As soon as the solution is bubbling fairly freely, the tube is plunged into a boiling water bath. The liquid boils smoothly, chloroform vapor expelling any remaining traces of air. When vapor begins to issue from the tube, as felt by condensation on the stopper, the finger is removed and a glass plug forced in. This operation is preferably carried out with the liquid frothing nearly to the top of the tube. In the presence of nonfatty material, the tube is now shaken for a few seconds to insure complete extraction of the fat. Otherwise it is simply cooled under the tap and the contents poured into about 30 ml. of water. The tube is rinsed out with a little water and the free iodine titrated with 0.002 N sodium thiosulfate, starch solution being added as the end point is approached. 1 ml. of 0.002 N thiosulfate per gram is equivalent to 1 millimole, or 2 milliequivalents of peroxide, 16 mg. of *active* oxygen, or 32 mg. of total peroxide oxygen per kilogram of fat.

Method of Wheeler.—Three to 10 g. of oil is dissolved in 50 ml. of a mixture of glacial acetic acid and chloroform (3:2 by volume) and 1 ml. of saturated potassium iodide solution is added. The mixture is stirred by giving a rotary motion to the flask. Exactly one minute after addition of the potassium iodide 100 ml. of water is added and the liberated iodine titrated with 0.1 or 0.01 N sodium thiosulfate, depending on the amount of iodine liberated. The end point is obtained by the use of starch as an indicator. Vigorous shaking is necessary to remove the last traces of iodine from the layer of chloroform. If W g. of oil require T ml. of thiosulfate of normality N, the peroxide content, expressed as millimoles of peroxide per kilogram of oil, is given by:

$$M = \frac{T \times N \times 500}{W}$$

M, in this case, is exactly equivalent to the "ml. of 0.002 N thiosulfate per gram" used by Lea.

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[29] C. H. Lea, *Rancidity in Edible Fats.* Chemical Pub. Co., New York, 1939.

[30] D. H. Wheeler, *Oil & Soap*, **9**, 89–97 (1932).

[31] W. Franke and D. Jerchel, *Ann.*, **533**, 46–71 (1937). W. Franke and J. Monch, *Ann.*, **556**, 200–223 (1944).

Method of Franke and Jerchel.—The autoxidized fat or fatty acid is dissolved in chloroform or carbon tetrachloride, or in the case of highly oxidized products a mixture of the two solvents may be used. Five ml. of a mixture of hydriodic acid (sp. gr. 1.96) and dilute acetic acid (3:7) is added. The air in the flask is displaced with nitrogen or carbon dioxide, after which the flask is tightly closed and allowed to stand at room temperature in diffused light. After one hour, at which time reaction is complete, 20 ml. of water and starch solution is added and the flask vigorously shaken. The liberated iodine is titrated with 0.1 *N* sodium thiosulfate.

Modifications of these methods have been proposed and are used to some extent, *e. g.*, Taffel and Revis[32] employ solid barium iodide or a 50% solution of potassium iodide in glacial acetic acid but without either chloroform or carbon tetrachloride.

As previously mentioned, all of these methods are presumed to react quantitatively and, in fact, do when applied under rigidly specified conditions to the determination of certain well-known peroxido compounds such as benzoyl peroxide, dihydroxydiheptyl peroxide, etc. When applied to oxidized fats or fatty acids, concordant results are not obtained with the various methods. All of them are affected by temperature to a marked degree and the same method does not respond in the same manner with fatty substances of different degrees of unsaturation, oxidation, and polymerization. This latter behavior is explained by the assumption that secondary products of oxidation interfere with the determination. Generally, it is assumed that these reagents give no reaction with perfectly fresh (unoxidized) fats, but Franke and Jerchel found that some iodine was liberated from hydriodic acid by the purest unsaturated acids they could prepare and they therefore introduced a blank correction to compensate for this reaction.

All of these reagents react with oxidized fats and fatty acids in varying degrees but it is by no means certain that the reaction is with a heterocyclic peroxide. These reagents could react with a hydroperoxide such as postulated by Rieche[13,14] and Farmer[20,21] or perhaps even with a moloxide such as is postulated by Staudinger.

Hydriodic Acid Method of Goldschmidt and Freudenberg.—Among the evidence frequently cited for the validity of peroxide formation as the first step of autoxidation is the work of Goldschmidt and Freudenberg[33] who investigated the autoxidation of pure linolenic acid and methyl linolenate in the absence of a solvent and in carbon tetrachloride and acetic acid solutions. The oxidation was conducted in the presence of a cobalt catalyst using a special apparatus which could be shaken and which permitted the oxygen consumption to be measured. The content of

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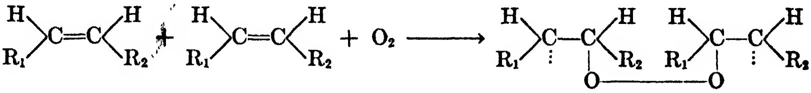
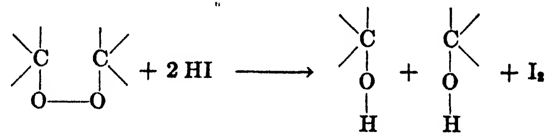
[32] A. Taffel and C. Revis, *J. Soc. Chem. Ind.*, 50, 87–91T (1931).
[33] S. Goldschmidt and K. Freudenberg, *Ber.*, 67, 1589–1594 (1934).

double bonds in the original and autoxidized product was determined by the Wijs iodine method. Comparison of the two values showed that for each mole of oxygen consumed one double bond disappeared. A simultaneous polymerization of linolenic acid with the disappearance of a double bond did not occur, but it was assumed that the molecular size could have been increased by autoxidation if oxygen had added to the double bond according to the following scheme:



However, further oxidation of such a product would result in the formation of additional carboxyl groups and no increase in the acid number was observed. Estimation of the active hydrogen by Zerewitinoff's method gave no evidence of the formation of hydroxyl groups. It was therefore concluded that the chief product of autoxidation was direct addition of oxygen to form a peroxide. The determination of peroxide oxygen was carried out by warming the oxidation product with a mixture of hydriodic acid and acetic acid and determining the amount of liberated iodine. It was assumed that the simultaneous absorption of free iodine at any unsaturated bonds proceeds so slowly under these conditions that it can be neglected. According to Goldschmidt and Freudenberg, the reduction of the peroxide by hydriodic acid can occur only according to one of the two following schemes:

(*1*)



(*2*)

The analytical data obtained by Goldschmidt and Freudenberg are reproduced in Table 128. Inspection of these data indicates that addition of the residual iodine values and the values obtained for the hydriodic acid peroxide number of the autoxidized acid or ester are, within experimental limits, equal to the iodine number of the unoxidized substance. On the basis of these results, the authors concluded that autoxidation of linolenic acid and methyl linolenate resulted only in the formation of peroxides. They also concluded that these peroxides were relatively stable from the fact that after standing for many days the peroxide value determined by their method remained relatively constant. Actually these data represent excellent corroboration for the hydroperoxide hypothesis discussed later.

TABLE 128

ANALYTICAL DATA FOR AUTOXIDIZED POLYETHYLENIC ACIDS AND ESTERS[a]

Substance	Oxidised by	Original product	Oxidised product		
		Iodine value	Iodine value	HI peroxide value	Total I and HI peroxide values
Methyl linolenate	Shaking in air	259	163	89	252
Linolenic acid	Shaking in air	274	135	150	285
Linseed oil	Shaking in air	180	131	22	153
Linseed oil	Shaking in air	180	132	24	156
Linseed oil	Shaking in air	180	132	22	154
Methyl linolenate	Standing in air	259	220	40	260
Linolenic acid	Standing in air	274	121	148	269

[a] S. Goldschmidt and K. Freudenberg, *Ber.*, 67, 1589–1594 (1934).

(*b*) *Oxygen Absorption Method*

Franke and Jerchel,[31] like many others, hold that the primary formation of peroxides affords the only logical explanation of autoxidation. They consider the formation of an oxido compound (Fokin's ethylene oxide) as the primary step in autoxidation as improbable for the following reasons. The substantiating evidence of Szent-Györgyi is considered invalid on the basis that the use of thioglycollic acid as an oxidation catalyst interferes with the detection of peroxides and Ellis'[34] oxidoleic and oxidelaidic acids may be dismissed from consideration on the basis that they are secondary and not primary products of oxidation. They also consider Rieche's hypothesis of an oxygen-activated methylene group (Farmer's hydroperoxide) as equally improbable as a primary autoxidation product.

In substantiation of the cyclic peroxide hypothesis, Franke and Jerchel investigated the reactions of oleic, ricinoleic, linoleic, and linolenic acids with oxygen in the presence of various catalysts such as cobalt nitrate, proline, and hemin. Oxygen absorption was determined by means of a modified Barcroft method. Generally, 0.5 g. of the fatty acid and 5 mg. of proline or cobalt nitrate dissolved in 0.1 ml. of methyl alcohol or 5 mg. of hemin in 0.02 ml. of pyridine were placed in the reaction vessel. The consumption of oxygen at 37°C. was followed manometrically.

When the consumption of oxygen in milliliters was plotted against time in hours for the four fatty acids, it was found that up to 100 hours complete saturation of all the double bonds did not occur in any case and none of the reactions showed any evidence of reaching completion as may be seen from Figure 75. It is evident from the curves shown in Figure 75 that the initial rate of oxygen absorption increases with the increase in the number of double bonds in the fatty acid. After the absorption of one mole of oxygen

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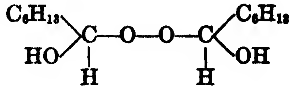
[34] G. W. Ellis, *Biochem. J.*, 26, 791–800 (1932); 30, 753–761 (1936).

in the case of linoleic acid, and two moles in the case of linolenic acid, the curves for these acids resemble those of oleic and ricinoleic acids.

In addition to determining the oxygen absorption, Franke and Jerchel also determined the decrease in iodine value by the Hübl method, and the amount of peroxides formed in the oxidized fatty acids. Dihydroxydiheptyl peroxide:[35]



was used as a comparative standard for the peroxide determination instead of benzoyl peroxide since the former reacted with their method more nearly like the fatty acid peroxides than did the latter.

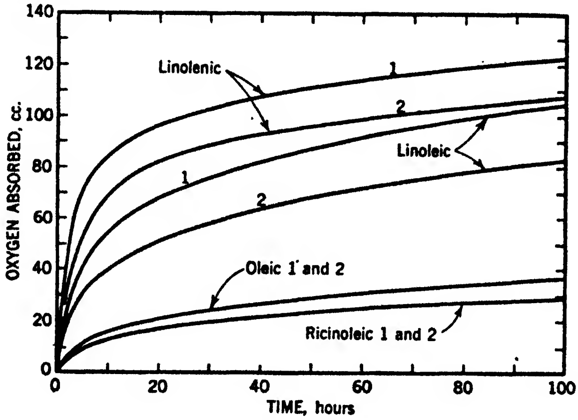


Fig. 75. Oxygen absorption curves obtained by Franke and Jerchel[31] with 500 mg. of fatty acid and 5 mg. of cobalt nitrate in 0.1 ml. of methanol at 37 °C. 40 cc. of oxygen is equivalent to one double bond per mole. (1) Substrates on 24 sq. cm. of filter paper. (2) Liquid substrate.

As a result of a series of investigations in which various oxidation products, for example, dihydroxymaleic acid, oxalacetic acid, acetaldehyde, pyroracemic acid, etc., were added to the unoxidized or autoxidized fatty acids, they concluded that the peroxide and iodine methods gave reliable results in the early stages of oxidation, but that in the later stages when secondary products of oxidation were present the methods became increasingly unreliable. Therefore, the results and the conclusions drawn from the investigation of the early stages of oxidation were dependable, but those of later stages of oxidation need to be accepted with reservations.

[35] A. Rieche, *Alkylperoxide und Ozonide; Studien über peroxydischen Sauerstoff.* Steinkopff, Dresden, 1931.

Graphic comparisons were made of the variations of peroxide and iodine values as functions of the percentages of oxygen consumed for each of the acids investigated. Oleic and ricinoleic acids were found to behave similarly when autoxidized in the presence of cobalt nitrate, both exhibiting the same rate and amount of absorption. With increasing absorption of oxygen, the ratio of peroxides formed to oxygen consumed decreased rapidly. The absorption of oxygen was paralleled with a decrease in iodine value up to 25% after which the iodine value fell less rapidly. The authors interpreted these results as indicating that secondary oxidation of peroxides occurred and the fact that both oleic acid, containing the group —CH_2CH—$CHCH_2$—, and ricinoleic acid, containing the group —$CH(OH)CH_2CH$—$CHCH_2$—, behaved in the same manner was evidence against Rieche's theory of an activated —CH_2— group.

In the case of linoleic and linolenic acids in the presence of cobalt nitrate, proline, and hemin as catalysts, peroxide formation and oxygen absorption were found to be theoretical up to 25% absorption after which the rate of peroxide formation rapidly decreased. The iodine values decreased proportionally up to 60% absorption of oxygen and then decreased rapidly. Franke and Jerchel interpreted these results to indicate that peroxides are formed exclusively, at first, on absorption of oxygen, after which they are decomposed to form hydroxy ketones, —COCH(OH)—, as postulated by Morrell and coworkers.[36–38] Evidence obtained by hydrogenation of the oxidation products and estimation of hydroxyl groups was also cited in substantiation of the correctness of these views. The authors also attempted to show that the various double bonds of linoleic and linolenic acids responded differently to oxidation and that the resultant peroxide possessed different stabilities.

Henderson and Young[38a] investigated the rate of autoxidation of pure oleic acid as a function of oleic acid concentration and oxygen pressure. Palmitic acid, tripalmitin, *n*-decane, and biphenyl were used as diluents in varying the mole fraction of oleic acid between the limits of 0.988 and 0.240. The partial pressure of the oxygen was varied from 1.0 to 0.21 atmosphere. It was observed that the fraction of the total oxygen absorbed and remaining as peroxide is determined by the moles of oxygen absorbed per mole of oleic acid (initial) and is independent of the variations in initial concentration of oleic acid and oxygen pressure up to 0.3 mole of oxygen absorbed per mole of oleic acid.

These authors concluded that peroxide formation is the first reaction in the oxidation of oleic acid since it was observed that as the oxygen absorp-

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[36] R. S. Morrell and S. Marks, *J. Oil Colour Chem. Assoc.*, **12**, 183–205 (1929); *J. Soc. Chem. Ind.*, **50**, 27–36T (1931).

[37] S. Marks and R. S. Morrell, *Analyst*, **54**, 503–508 (1929).

[38] R. S. Morrell, *Chemistry & Industry*, **56**, 795–798 (1937).

[38a] J. L. Henderson and H. A. Young, *J. Phys. Chem.*, **46**, 670–684 (1942).

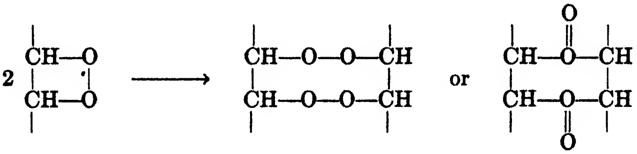
tion approached zero, the double bond destruction is proportional to the oxygen absorbed. However, the isolation by Farmer and Sutton[23] of peroxidized methyl oleate having an intact double bond invalidates this deduction. Although the nature of the autoxidation product may be questioned, Henderson and Young's kinetic equation for the absorption of oxygen by oleic acid between the end of the induction period and prior to the onset of appreciable secondary reaction is probably correct, since it is deduced from a plot of the oxygen consumption versus peroxide formed as determined by the Wheeler method. The rate curve was expressed as:

$$-\frac{dO_2}{dt} = k_1 + k_2\,(\text{peroxide})\,(O_2)^{1/2}$$

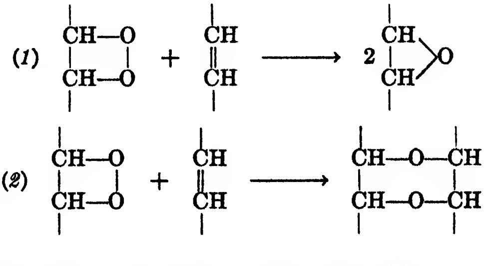
For oxygen pressures between 0.5 and 1.0 atmosphere the average value for k_1 was found to be 2.2 whereas k_2 was found to be 226.

(*c*) *Secondary Reactions of Cyclic Peroxides*

Some authors[33,39] are of the opinion that the unsaturated molecules are more or less completely converted to peroxides while others incline to the belief that the peroxides merely represent transient intermediate products which undergo more or less rapid transformation to other products. According to Fahrion[40] and Marcusson,[41] two peroxide molecules interact to form oxide bridges:



Fahrion, and also Orlov,[42] speculated on the possibility that a reaction might occur between the primary peroxide and an unattached double bond to produce two molecules of an oxide or a 1,4-dioxane ring compound as follows:



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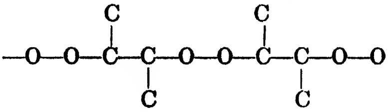
[39] S. Coffey, *J. Chem. Soc.*, **119**, 1152–1161, 1408–1415 (1921).
[40] W. Fahrion, *Die Chemie der trocknenden Öle*, Springer, Berlin, 1911; *Z. angew. Chem.*, **23**, 722–726 (1910).
[41] J. Marcusson, *Z. angew. Chem.*, **38**, 148–149 (1925).
[42] E. I. Orlov, *J. Russ. Phys.-Chem. Soc.*, **42**, 658–676 (1910); **44**, 1576–1658 (1912).

However, neither Fahrion[40] and Marcusson,[41] nor Eibner and Munzert[43] and Elm,[44] in the course of investigations on the drying of linseed oil films, could find any experimental evidence to substantiate the formation of such products.

According to Eibner, and more recently according to Rieche,[45] polymerization of the primary peroxide, or of Staudinger's[46] moloxide, is assumed to occur with the formation of compounds of the general structure:

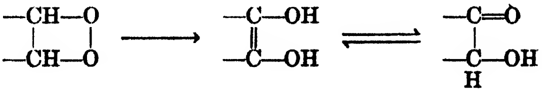


$$-O-O-\overset{C}{C}-\underset{C}{C}-O-O-\overset{C}{C}-\underset{C}{C}-O-O$$

Tschirch and Barben[47] advanced the idea that the primary peroxide is decomposed by water to produce an oxido compound, ozone, and hydrogen peroxide. The latter two products were presumed to react in turn with more unsaturated linkages to form other oxidation products. Browne[48] advanced a similar hypothesis in which he postulated a reaction between the peroxide and water with the liberation of an atom of active oxygen according to the following scheme:

However, Browne inclines to the view that the unsaturated acid is oxidized to an oxido acid with the liberation of an atom of active oxygen and that the oxido acid is hydrolyzed by water to form two moles of short chain acids.

Ellis[49] postulated an intramolecular rearrangement of the primary peroxide to a tautomeric ketohydroxy-dihydroxy system and in support of this hypothesis he identified appreciable quantities of hydroxyl and keto groups in dried linseed oil films, presumably formed according to the following scheme:



According to Ellis, linoxyn, for example, contains seven hydroxyl and six carbonyl groups.

This hypothesis finds further support in the work of Morrell and co-

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[43] A. Eibner and H. Munzert, *Chem. Umschau Fette Öle Wachse Harze*, **33**, 188–194, 201–208, 213–216 (1926).

[44] A. C. Elm, *Ind. Eng. Chem.*, **23**, 881–887 (1931).

[45] A. Rieche, *Angew. Chem.*, **50**, 520–524 (1937).

[46] H. Staudinger, *Ber.*, **58**, 1075–1079 (1925). H. Staudinger and L. Lautenschläger, *Ann.*, **488**, 1–8 (1931).

[47] A. Tschirch and A. Barben, *Schweiz. Apoth. Ztg.*, **62**, 281–285, 293–295 (1924).

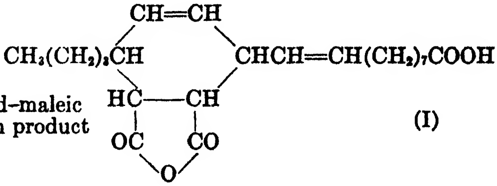
[48] C. A. Browne, *Ind. Eng. Chem.*, **17**, 44–47 (1925).

[49] G. W. Ellis, *J. Soc. Chem. Ind.*, **45**, 193–199T (1926).

workers,[36–38, 50–59] who published an extensive series of researches on the oxidation of drying oils which have been widely referred to and generally accepted as substantiating the cyclic peroxide theory of autoxidation. Their work has been largely confined to investigations on the oxidation of elaeostearic and related acids containing a system of three conjugated double bonds, and especially to the behavior of the maleic anhydride addition products of these acids.

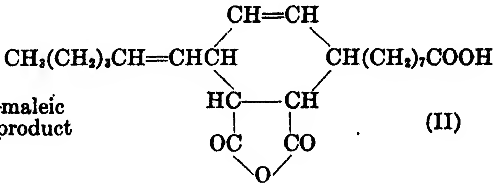
The basic principle involved in the work reported by Morrell consists in the preparation and isolation of the maleic anhydride addition products of α- and β-elaeostearic acids and subjection of these products to autoxidation and analysis. Morrell assumed that α-elaeostearic acid (m.p. 49°C.) is *trans*-9,10-*cis*-11,12-*cis*-13,14-octadecatrienoic acid and β-elaeostearic acid (m.p. 71.5°C.) is *cis*-9,10-*cis*-11,12-*trans*-13,14-octadecatrienoic acid. Therefore, with maleic anhydride they are presumed to produce reaction products corresponding to formulas I and II.

α-Elaeostearic acid-maleic anhydride reaction product



(I)

β-Elaeostearic acid-maleic anhydride reaction product



(II)

Each of these substances has a double bond as a component of the hydrobenzene ring and another double bond in the aliphatic side chain. In the case of the product derived from the α-acid the side chain double bond occurs at the 9,10-position and in the β-acid product at the 13,14-position of the original acid. Morrell and co-workers found that these two double

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[50] R. S. Morrell and S. Marks, *J. Soc. Chem. Ind.*, **50**, 27–36T, (1931).

[51] R. S. Morrell and W. R. Davis, *ibid.*, **55**, 237–246T, 261–265T, 265–267T (1936).

[52] R. S. Morrell, *J. Oil Colour Chem. Assoc.*, **10**, 186–201 (1927).

[53] R. S. Morrell and W. R. Davis, *J. Soc. Chem. Ind.*, **55**, 101–103T (1936).

[54] R. S. Morrell and W. R. Davis, *Trans. Faraday Soc.*, **32**, 209–219 (1936).

[55] R. S. Morrell and E. O. Phillips, *J. Soc. Chem. Ind.*, **57**, 245–247 (1938); **58**, 159–162 (1939); **59**, 144–148 (1940).

[56] R. S. Morrell and E. O. Phillips, *Fette u. Seifen*, **46**, 541–546 (1939).

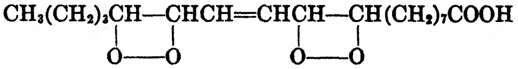
[57] R. S. Morrell and E. O. Phillips, *J. Oil Colour Chem. Assoc.*, **23**, 103–121, 233–237 (1940).

[58] R. S. Morrell and E. O. Phillips, *Paint Tech.*, **7**, 130–132, 169–170, 187 (1942).

[59] R. S. Morrell, T. R. Bolam, W. R. Davis, S. Marks, E. O. Phillips, and W. S. Sim, *Trans. Faraday Soc.*, **38**, 362–366 (1942).

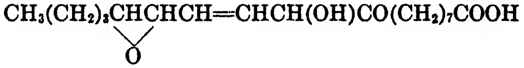
bonds autoxidized at markedly different rates, the β-form oxidizing readily and the α-form with difficulty.

Examination of the autoxidation products of the two addition products led Morrell to believe that oxidation occurred to form a 9,10-peroxido derivative in the case of the α-acid addition product, and a 13,14-peroxido derivative in the case of the β-acid addition product. The theory was extended to apply to the original acids in which case it was assumed that the first product of autoxidation of elaeostearic acid is a 9,10,13,14-diperoxido derivative having the structure:



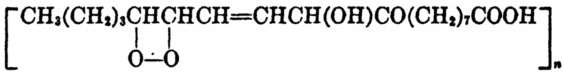
$$\mathrm{CH_3(CH_2)_3\underset{\substack{|\qquad|\\ O\!-\!\!-\!O}}{CH-CH}CH{=}CH\underset{\substack{|\qquad|\\ O\!-\!\!-\!O}}{CH-CH}(CH_2)_7COOH}$$

The secondary step in the autoxidation reaction was presumed to produce, in the case of the 9,10-peroxido group, an equilibrium mixture of tautomeric ketols and unsaturated diol with possibly some oxido formation at the 13,14-peroxide:



$$\mathrm{CH_3(CH_2)_3\underset{\diagdown\!\diagup\\ O}{CHCH}CH{=}CHCH(OH)CO(CH_2)_7COOH}$$

while the 13,14-peroxido group generally entered into polymerization reactions:



$$\left[\mathrm{CH_3(CH_2)_3\underset{\substack{|\;\;|\\ O\!-\!O}}{CHCH}CH{=}CHCH(OH)CO(CH_2)_7COOH}\right]_n$$

The extent to which one or another of these reactions predominated was presumed to depend on the temperature, solvent, catalyst, and probably other factors.

The more recent work of Farmer and co-workers[20-25] has led to considerable questioning[60] concerning the validity of Morrell's conclusions. The principal basis of disagreement has been the failure to isolate pure oxidation products corresponding to the structures assigned to them by Morrell and the lack of specificity of the analytical methods employed. Furthermore, it is possible, on the basis of the work of Robertson, Hartwell, and Kornberg,[61] that the peroxides of α-elaeostearic and other conjugated unsaturated acids differ from those of the nonconjugated acids. These authors found that, when peroxidation occurred in nonconjugated acids, the peroxidized product, with the exception of ricinoleic and undecenoic acids, were capable of oxidizing β,β′-dichloroethyl sulfide to β,β′-dichloroethyl sulfoxide. Peroxidized conjugated acids and oils containing these acids were, however, incapable of effecting this oxidation.

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[60] C. E. Hollis, *J. Oil Colour Chem. Assoc.*, **27**, 67–91 (1944).

[61] W. v. B. Robertson, J. L. Hartwell, and S. Kornberg, *J. Am. Chem. Soc.*, **66**, 1894–1897 (1944).

Treibs,[62] likewise, observed a marked difference in the reaction of hydroxylamine and lead tetraacetate, which latter reacts in a specific manner with hydroperoxides, RH—O—OH, and autoxidized elaeostearic acid as compared to autoxidized linoleic and linolenic acids. In fact, Treibs favors the view that, even in the case of autoxidized linoleic and linolenic acids, both hydroperoxides and cyclic (Treibs's ethylene) peroxides are produced.

5. Hydroperoxide Hypothesis

All of the oxidation products of the naturally occurring monounsaturated acids and esters having a chain length of C_{18} or greater which have been isolated in pure form are crystalline solids at room temperature—*e. g.*, oxidoleic acid, oxidoerucic acid, dihydroxystearic acid, hydroxyketostearic acid, *et al.* In all of these compounds in which the double bond of the unsaturated acid has been saturated with oxygen the resulting product is a solid at ordinary temperatures. On the other hand, ricinoleic acid and related acids containing a double bond and a hydroxyl group are liquids at the same temperatures. This property of liquidity at ordinary temperature of long chain fatty acids is associated with the presence of one or more double bonds, and when the double bonds disappear as a result of saturation with oxygen the resulting product is no longer liquid at room temperature. The addition of one oxygen atom at the double bond, as in the case of oxidation of oleic to oxidoleic acid, is sufficient to raise the melting point above room temperature. It would be logical to assume, therefore, that the addition of two atoms of oxygen to a double bond to form a heterocyclic peroxido fatty acid would also result in raising the melting point of the product above room temperature. However, up to the present no such solid peroxido fatty acid has been isolated as a product of autoxidation of the C_{18} or related unsaturated fatty acids.

(*a*) *Isolation of Hydroperoxides*

The most fundamental advance in the chemistry of autoxidation of fats and fatty acids was made by Farmer and Sutton[63] in 1942 when they isolated for the first time a moderately pure peroxidized methyl oleate. The product which was obtained by molecular distillation of partially oxidized methyl oleate was stated not to exceed 70% in purity, but refractionation produced a final product which analysis indicated to be nearly 100% pure methyl peroxido oleate. By application of a combination of low temperature crystallization and molecular distillation, similar products of 90% to 95% purity have been isolated in the author's laboratory.[63a] In every case

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[62] W. Treibs, *Ber.*, **77**, 69–71 (1944).

[63] E. H. Farmer and D. A. Sutton, *J. Chem. Soc.*, **1943**, 119–122.

[63a] C. E. Swift, F. G. Dollear, and R. T. O'Connor, *Oil & Soap*, **23**, 355–359 (1946).

they have possessed the properties and responded to the reactions described by Farmer and Sutton for their product.

The peroxidized methyl oleate was found by analysis to contain one mole of oxygen per mole of ester and an intact double bond. As was to be expected, it was an oily liquid at ordinary temperatures and, in fact, failed to crystallize even at relatively low temperatures. Peroxidized methyl linoleate prepared in the author's laboratory by low temperature crystallization exhibited similar properties with regard to its physical state.

If, as Farmer and others have shown, the isolated peroxidized methyl oleate contains two atoms of oxygen and one double bond, the product cannot contain a heterocyclic ring which heretofore has been generally accepted as adequately representing the structure of the first oxidation product of unsaturated acids. The structures (see pp. 456–459) proposed by Rieche[13,14] and Farmer and co-workers[20–25] for the primary product of autoxidized unsaturated fatty acids is in accord with the observed properties of the isolated product. Moreover, on reduction with aluminum amalgam the product gave methylhydroxy oleate. The latter product, after hydrogenation, was presumed to consist of a mixture of 8-hydroxy- and 11-hydroxymethyl stearate as indicated in the following equations:

$$(1)\quad \mathrm{C_8H_{17}CH{:}CHCH\cdot OOH(CH_2)_6COOCH_3 \xrightarrow{2\,H_2} C_{10}H_{21}CHOH(CH_2)_6COOCH_3}$$

$$(2)\quad \mathrm{C_7H_{15}CH\cdot OOHCH{:}CH(CH_2)_7COOCH_3 \xrightarrow{2\,H_2} C_7H_{15}CHOH(CH_2)_9COOCH_3}$$

These facts provide definite evidence that the primary product of autoxidation of methyl oleate is a mixture of two isomeric monohydroperoxides each containing a molecule of oxygen and an intact double bond.

Further substantiation of the identity of this compound was obtained by Atherton and Hilditch[64] who subjected peroxidized methyl oleate to further oxidation with powdered potassium permanganate. The autoxidation of methyl oleate was conducted at 20°C. until a peroxide value of 920 was obtained. The autoxidized fraction was adsorbed on silica gel and eluted with acetone. Following the oxidation of the eluted adsorbate (peroxidized methyl ester) with potassium permanganate, four acids, suberic, octanoic, azelaic, and nonanoic, predicted by Farmer as the fission products of hydroperoxido oleic acid, were isolated and identified.

Sutton[65] subjected methyl elaidate to autoxidation at 35°C. while irradiating it with ultraviolet light and observed that it formed hydroperoxido esters as in the case of methyl oleate. Aeration was continued until the ester absorbed 0.2 mole of oxygen, 90% of which was found to be in the form

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[64] D. Atherton and T. P. Hilditch, *J. Chem. Soc.*, **1944**, 105–108; T. P. Hilditch, *Nature*, **157**, 586 (1946); F. D. Gunstone and T. P. Hilditch, *J. Chem. Soc.*, **1945**, 836–841; **1946**, 1022–1025.

[65] D. A. Sutton, *J. Chem. Soc.*, **1944**, 242–243.

of a peroxide. The oxidized methyl elaidate was hydrogenated in the presence of Adam's catalyst to convert the unreacted elaidate to stearate and the peroxidized fraction to hydroxy stearate. After saponification and acetylation, the acetoxy derivative was separated by fractional crystallization. The crude acetoxystearic acid was converted to hydroxystearic acid. Since peroxidation could have occurred at the eighth, ninth, tenth and eleventh carbon atoms, any one or any mixture of corresponding hydroxystearic acids could have formed.[25] An apparently pure hydroxystearic acid (m.p. 79°C.) was isolated but the position of the hydroxyl group was not established.

Bolland and Koch[66] have shown that the primary product of the thermal reaction between ethyl linoleate and molecular oxygen is the formation of a monohydroxy peroxide. The latter product was found on spectrographic analysis to contain at least 70% of conjugated diene isomers resulting from rearrangement of the unsaturated system $—C{=}C—C—C{=}C—$. Evidence was also obtained that one of the first decomposition products contained a ketonic group.

The experimental evidence which has been amassed in the short time following the isolation of the methyl hydroperoxido oleate by Farmer appears to render the cycloperoxide theory of autoxidation untenable and establishes the formation of the hydroperoxide theory as the only tenable alternative. Acceptance of the hydroperoxide reaction as the first stage of the addition of oxygen to unsaturated fatty acids necessitates a reinterpretation of a considerable amount of previous experimental work and vitiates much of the speculation and conclusions concerning the subsequent stages of the autoxidation reaction.

(b) *Secondary Reactions of Hydroperoxides*

Having established the identity of the first reaction product of autoxidation as a hydroperoxide, Farmer and co-workers proceeded to the consideration of the probable nature of the secondary autoxidation reaction and products. It is difficult to paraphrase or improve upon Farmer's discussion of these secondary reactions and it is therefore quoted here from his original work[67] as follows:

> "Except with the most stable hydroperoxides, and then only under optimum conditions of operation, peroxide decay occurs side by side with new peroxidation. Thus in polyenes—especially long-chain polyenes such as rubber—hydroperoxide groups and their oxygeno-derivatives inevitably occur in the same molecule. This mixing of peroxidic and secondary groupings is aided by the usual very uneven dis-

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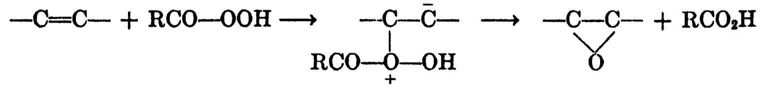
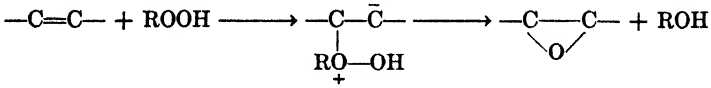
[66] J. L. Bolland and H. P. Koch, *J. Chem. Soc.*, 1945, 445–447; J. L. Bolland and G. Gee, *Trans. Faraday Soc.*, 42, 236–243, 244–252 (1946).

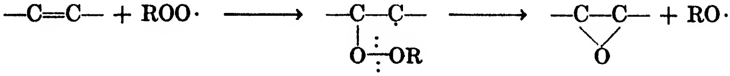
[67] E. H. Farmer, G. F. Bloomfield, A. Sundralingam, and D. A. Sutton, *Trans. Faraday Soc.*, 38, 348–356 (1942).

tribution of oxidative attack over the olefinic molecules present. The principal, and doubtless the most invariable, feature of secondary autoxidative changes is that the hydroperoxide groups themselves revert to hydroxyl groups (in some circumstances to keto groups) and concurrently the active oxygen is used in oxidising either the adjacent or some remote double bond—the latter perhaps in another molecule. This oxidative action may proceed as far as chain-scission at the double bonds, or may oxygenate and so saturate the double bonds without severing them. Chain-scission reactions can occur with embarrassing facility in rubber after even slight oxygenation; in a less serious degree they occur unavoidably in the polyene fish-oil acids and the shorter polyisoprenes. It is impossible at present to distinguish between thermal and photochemical secondary decompositions. The basic reactions, so far as they are at present known, seem to be the following:—

"*1.* Interaction of a hydroperoxide group with a double bond, giving a hydroxyl group at the former and an epoxy group at the latter. This reaction is in part comparable with the action of an organic peracid at an ethylenic bond (equation *a*), and since it can be brought about at will by heating an olefin hydroperoxide with an olefin, may be represented as in (*b*). But since the change appears to occur with greater facility during the actual autoxidation reaction than subsequently by thermal decomposition of the isolated hydroperoxide, it may possibly be brought about during the autoxidation in a more direct way, *e. g.*, by the interaction of a radical peroxide with a double bond as shown in (*c*). This reaction is of "intermolecular" type, occurring between a peroxide group in one molecule and either a double bond in another molecule, or a remote double bond in the same molecule.

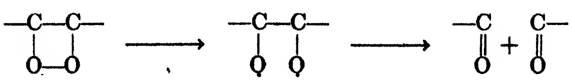
(*a*)

$$-C{=}C- + RCO{-}OOH \longrightarrow \underset{RCO-\underset{+}{O}-OH}{-C-\bar{C}-} \longrightarrow \underset{O}{-C-C-} + RCO_2H$$

(*b*)

$$-C{=}C- + ROOH \longrightarrow \underset{\underset{+}{RO}-OH}{-C-\bar{C}-} \longrightarrow \underset{O}{-C-C-} + ROH$$

(*c*)

$$-C{=}C- + ROO\cdot \longrightarrow \underset{O\,\vdots\,OR}{-C-\dot{C}-} \longrightarrow \underset{O}{-C-C-} + RO\cdot$$

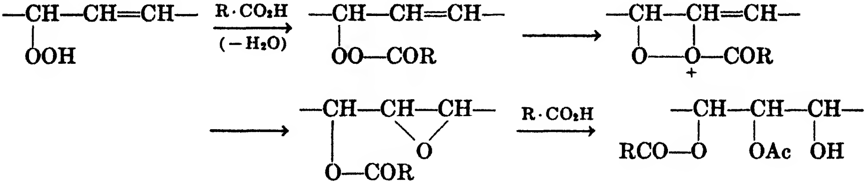
$$RO\cdot + -CH_2-C{=}C- \longrightarrow ROH + \dot{C}H-C{=}C-$$

"*2.* Scission of the carbon chain at the double bond occurs with considerable ease, both during the autoxidation reaction (*i. e.*, perhaps as the result of irradiation), and subsequently by thermal decomposition. The precise mechanism of this change in either case remains still to be determined. There is insufficient evidence at present for rejecting finally the possibility that in some very small degree scission can occur during the original autoxidation by momentary formation and immediate decomposition of a cyclic peroxide, thus:

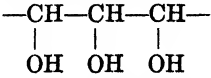

$$\underset{O-O}{-C-C-} \longrightarrow \underset{\dot{O}\;\;\dot{O}}{-C-C-} \longrightarrow \underset{O}{\overset{-C}{\|}} + \underset{O}{\overset{C-}{\|}}$$

but this mechanism cannot apply to thermal decompositions of the hydroperoxide.

"*3.* In the presence of organic acids or their anhydrides autoxidation occurs readily. This may be represented for the free acid:

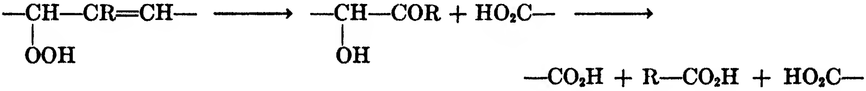


"*4.* By the decomposition of the hydroperoxide in presence of mineral acid a reaction analogous to the foregoing and yielding a saturated triol,



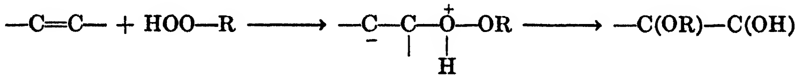
$\text{—}\underset{\text{OH}}{\text{CH}}\text{—}\underset{\text{OH}}{\text{CH}}\text{—}\underset{\text{OH}}{\text{CH}}\text{—}$, occurs.

"*5.* Subsidiary scission can occur between an ethylenic bond and an α-carbon atom:



$$\text{—}\underset{\text{OOH}}{\text{CH}}\text{—CR=CH—} \longrightarrow \text{—}\underset{\text{OH}}{\text{CH}}\text{—COR} + \text{HO}_2\text{C—} \longrightarrow \text{—CO}_2\text{H} + \text{R—CO}_2\text{H} + \text{HO}_2\text{C—}$$

"*6.* Polymerisation occurs by the interaction of —OOH groups and double bonds. This appears to give mainly *dimerides* of ether type, possibly to be represented as involving the reaction



$$\text{—C=C—} + \text{HOO—R} \longrightarrow \text{—}\underset{-}{\text{C}}\text{—}\underset{|}{\text{C}}\text{—}\overset{+}{\underset{\text{H}}{\text{O}}}\text{—OR} \longrightarrow \text{—C(OR)—C(OH)}$$

In addition, radical forms, RO·, produced by thermal (or possibly photochemical) dissociation of the hydroperoxides, and radical forms, ROO·, produced in the primary peroxidation reaction, probably take part in the process by reacting with other olefinic systems present.

"*7.* In the presence of iron salts, and in some cases as the result of spontaneous or violent thermal decomposition, hydroperoxides give unsaturated ketones. This is comparable to the spontaneous formation of esters from the peroxides of ethers [$\text{RCH(OOH)—OR}' \rightarrow \text{RCO—OR}' + H_2O$].

"*8.* In the presence of alkalies extensive hydrolysis of the hydroperoxide groups occurs ($\text{ROOH} + H_2O \rightarrow \text{ROH} + H_2O_2$) with concomitant oxidative degradation of the double bonds by the hydrogen peroxide liberated."

The new concepts and substantiating evidence introduced by Farmer and his co-workers have not solved all of the numerous problems inherent in the process of autoxidation of fats and fatty acids, but they have cleared away many misconceptions, brought a considerable degree of order into a field which was becoming increasingly chaotic, and provided a sound basis for future work as well as a firmer belief that continued intensive effort will eventually lead to a complete solution of this important problem.

CHAPTER XVII

BIOLOGICAL OXIDATION

1. Introduction

Ingested and stored fats serve the animal organism as a source of energy which is released during their oxidation to form shorter chain compounds, carbon dioxide, and water. Although the subject of numerous investigations, no completely satisfactory answer has been obtained concerning the mechanism by which the oxidation process occurs in the animal organism. Still less is known concerning the process in plants. Many seed kernels are known to contain a relatively large and often a predominant amount of fat or oil which decreases more or less rapidly during germination. The disappearance of these stored fats probably occurs partly by oxidation to carbon dioxide and water with the liberation of energy, and partly by elaboration of other fats in the new plant. Few hypotheses have been offered to explain the oxidation of the fatty reserves in plants and these have generally been extensions or elaborations of the hypotheses proposed to explain the oxidation of fats in animal organisms.

Since the ingested or stored fats are complex substances containing glycerol residues and saturated and unsaturated acids of various chain lengths, it is probable that a number of mechanisms are involved in their metabolism. It is not known with certainty whether fats are oxidized *per se* or are hydrolyzed prior to oxidation. Likewise, it is not known whether the liberated unsaturated acids are hydrogenated to form saturated acids prior to oxidation or whether saturated acids are first dehydrogenated and then oxidized.

Theoretically any or all of these reactions are possible since both plants and animals contain various enzyme systems capable of producing such transformations. Unfortunately only little attention has been devoted to the investigation of the enzyme systems which may be involved in the complete metabolism of the fats in plants and animals.

It is generally assumed that the fat is first hydrolyzed by lipolytic enzymes to produce glycerol and free fatty acids, and that each constituent is then oxidized. The glycerol portion of the fat molecule is presumed to be oxidized in a manner wholly analogous to the oxidation of carbohydrates.[1]

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[1] R. S. Hubbard and F. R. Wright, *J. Biol. Chem.*, 50, 361–402 (1922).

2. β-Oxidation

The oldest and perhaps most widely held theory of fatty acid oxidation by animal organisms is based on the classical work of Knoop,[2] Embden and co-workers,[3,4] Dakin,[5] and others. These investigators demonstrated that benzoic, C_6H_5COOH, and phenylacetic, $C_6H_5CH_2COOH$, acids are unattacked when fed to animals. Benzoic acid is eliminated either as such or conjugated with glycine in the form of hippuric acid in accordance with the following equation:

$$C_6H_5COOH + CH_2NH_2COOH \longrightarrow C_6H_5CONHCH_2COOH + H_2O$$

Phenylacetic acid is also conjugated with glycine and eliminated as phenaceturic acid:

$$C_6H_5CH_2COOH + CH_2NH_2COOH \longrightarrow C_6H_5CH_2CONHCH_2COOH + H_2O$$

However, phenylpropionic, $C_6H_5CH_2CH_2COOH$, was found to be eliminated as hippuric acid, phenylbutyric, $C_6H_5CH_2CH_2CH_2COOH$, as phenaceturic acid, and phenylvaleric, $C_6H_5CH_2CH_2CH_2CH_2COOH$, as hippuric acid. These results are summarized in Table 129.

TABLE 129

FATE OF INGESTED PHENYL-SUBSTITUTED ACIDS

Acid fed	Formula	Oxidation product	Excreted as
Benzoic	C_6H_5COOH	Not oxidized	Hippuric
Phenylacetic	$C_6H_5CH_2COOH$	Not oxidized	Phenaceturic
Phenylpropionic	$C_6H_5CH_2CH_2COOH$	C_6H_5COOH	Hippuric
Phenylbutyric	$C_6H_5CH_2CH_2CH_2COOH$	$C_6H_5CH_2COOH$	Phenaceturic
Phenylvaleric	$C_6H_5CH_2CH_2CH_2CH_2COOH$	C_6H_5COOH	Hippuric

In each case the β-carbon atom is presumed to be attacked according to the following mechanism:

$$PhCH_2CH_2COOH \xrightarrow{+O} PhCHOHCH_2COOH \xrightarrow{+O} PhCOCH_2COOH$$
$$\longrightarrow PhCOCH_3 \longrightarrow PhCOOH$$

According to this mechanism of oxidation the carboxyl carbon atom and the adjacent methylene carbon atom are removed by conversion to carbon dioxide and water leaving a new carboxyl in the position corresponding to

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[2] F. Knoop, *Beitr. chem. Physiol. Path.*, 6, 150–162 (1905). See F. Knoop, *Oxydationen im Tierkörper, ein Bild von den Hauptwegen physiologischer Verbrennung*, Enke, Stuttgart, 1931.

[3] G. Embden, H. Salomon, and F. Schmidt, *Beitr. chem. Physiol. Path.*, 8, 129–155 (1906).

[4] G. Embden and A. Marx, *Beitr. chem. Physiol. Path.*, 11, 318–322 (1908).

[5] H. D. Dakin, *J. Biol. Chem.*, 4, 419–435 (1908); 5, 173–185, 303–309 (1908); 6, 203–219, 221–233 (1909); 9, 123–128 (1911).

the β-position in the unoxidized acid. This process is presumed to continue until the entire carbon chain is consumed.

Raper and Wayne[6] repeated and confirmed the experiments with phenyl-substituted acids and extended it to include phenylcaproic acid. Quick[7] demonstrated that the total benzoic acid or phenylacetic acid eliminated in combination with glycine and glycuronic acids after feeding phenyl-substituted fatty acids represents practically a quantitative transformation. Other supporting evidence is adduced from the fact that the oxidation of a fat is incomplete in diabetic patients since β-hydroxybutyric acid and acetoacetic acid presumably derived from fats are found in the urine of individuals suffering from diabetes.

The principal objections to these experiments and their interpretation are that they have been confined to short chain fatty acids, that fats are ingested as glycerides and not as free acids, that the presence of the phenyl group in the carbon chain may specifically influence the course of oxidation, and that it involves only saturated acids whereas ingested fats are composed predominantly of unsaturated acids. Furthermore, it has not been possible to recover any of the two-carbon fragments produced by β-oxidation of normal fatty acids, substituted (hydroxy, branched chain, etc.) fatty acids, or odd-numbered carbon acids. Only acetoacetic and β-hydroxybutyric acids have thus far been detected. Also no experimental evidence is available to prove that the acids containing two less carbon atoms than the ingested acid are produced in the living organisms.

3. ω-Oxidation

In contrast to the theory of β-oxidation, Verkade and co-workers[8-12] have experimentally demonstrated that oxidation can and does occur elsewhere in the hydrocarbon chain, namely at the terminal or ω-carbon atom. These investigators have shown that when glycerides of fatty acids containing eight to eleven carbon atoms are ingested, dicarboxylic acids are formed and are excreted in quantity.

In other cases dicarboxylic acids were not found owing, according to Verkade, to the fact that secondary β-oxidation occurred in these cases, *i. e.*, because biterminal or bilateral β-oxidation of the dicarboxylic acid occurred. In fact Verkade inclined to the belief that all normal saturated

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[6] H. S. Raper and E. J. Wayne, *Biochem. J.*, **22**, 188–197 (1928).

[7] A. J. Quick, *J. Biol. Chem.*, **77**, 581–593 (1928).

[8] P. E. Verkade and J. van der Lee, *Biochem. J.*, **28**, 31–40 (1934).

[9] P. E. Verkade, *Chem. Weekblad.*, **28**, 470–474, 477–484 (1931).

[10] P. E. Verkade, M. Elzas, J. van der Lee, H. H. de Wolff, A. Verkade-Sandbergen, and D. van der Sande, *Z. physiol. Chem.*, **215**, 225–257 (1933).

[11] P. E. Verkade and J. van der Lee, *Z. physiol. Chem.*, **225**, 230–244 (1934); **227**, 213–222 (1934).

[12] P. E. Verkade, J. van der Lee, and A. J. S. van Alphen, *Z. physiol. Chem.*, **237**, 186–190 (1935); **247**, 111–114 (1937); **250**, 47–56 (1937).

dicarboxylic acids are subject to biterminal β-oxidation. Artom[13] believes that β-oxidation may occur at both ends of the hydrocarbon chain.

Verkade's biterminal oxidation may be illustrated by the behavior of tricaprin which when ingested was found to produce sebacic, suberic, and adipic acids in the urine. Triundecylin when ingested resulted in the elimination of hendecanedioic, azelaic, and pimelic acids. These acids would be produced by the following reactions.

$$CH_3(CH_2)_8COOH \xrightarrow{\omega} HOOC(CH_2)_8COOH \xrightarrow{\beta} HOOC(CH_2)_6COOH \xrightarrow{\beta} HOOC(CH_2)_4COOH$$

$$CH_3(CH_2)_9COOH \xrightarrow{\omega} HOOC(CH_2)_9COOH \xrightarrow{\beta} HOOC(CH_2)_7COOH \xrightarrow{\beta} HOOC(CH_2)_5COOH$$

This mechanism does not require that the glyceride be split prior to the initiation of oxidation since the terminal methyl group is readily available and oxidation can proceed prior to or simultaneous with lipolysis. Furthermore, oxidation of terminal methyl groups in the animal organism is known to occur with other substances. Kuhn, Köhler, and Köhler[14] have shown that polyene acids undergo ω-oxidation. Thus, sorbic acid, $CH_3CH{:}CHCH{:}CHCOOH$, when ingested was found to be partly excreted as muconic acid, $HOOCCH{:}CH \cdot CH{:}CHCOOH$. Ingestion of camphor resulted in the excretion of the corresponding dicarboxylic acid.[15] Kuhn found that geraniol and citral were eliminated in the form of their dicarboxylic acids. It is interesting to note that in all of these compounds oxidation occurred without involving the double bonds.

Flaschenträger and Bernhard[16] claimed to have demonstrated the existence of ω-oxidation in fat metabolism but believe it occurs to only a small degree, not more than one per cent, whereas β-oxidation is the predominant reaction.

4. Multiple Oxidation

A considerable amount of experimental evidence has been accumulated in recent years which casts doubt on the hypothesis of β-oxidation in the living organism. Deuel and co-workers[17,18] found that when ethyl butyrate and ethyl caproate were fed to rats the same quantities of acetone bodies and acetoacetic acid were found in the urine, whereas the caprylic

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[13] C. Artom, *Z. physiol. Chem.*, **245**, 276–277 (1937).

[14] R. Kuhn, F. Köhler, and L. Köhler, *Z. physiol. Chem.*, **247**, 197–219 (1937).

[15] Y. Asahina and M. Ishidate, *Ber.*, **68**, 947–953 (1935).

[16] B. Flaschenträger and K. Bernhard, *Helv. Chim. Acta*, **18**, 962–972 (1935).

[17] J. S. Butts, C. H. Cutler, L. Hallman, and H. J. Deuel, Jr., *J. Biol. Chem.*, **109**, 597–613 (1935).

[18] H. J. Deuel, Jr., L. F. Hallman, J. S. Butts, and S. Murray, *J. Biol. Chem.*, **116**, 621–639 (1936).

ester yielded twice these amounts indicating fission into two four-carbon fragments which would occur in the case of both β- and δ-oxidation. Ethyl palmitate, ethyl oleate, and ethyl stearate gave three different four-carbon fragments.

Jowett and Quastel[19] reinvestigated the oxidation of fatty acids by means of liver slices and found that even-numbered carbon acids produced considerable quantities of acetone bodies whereas the odd-numbered acids produced little of these bodies. To explain these observations, and those of Deuel and co-workers, Jowett and Quastel proposed the theory of multiple alternate oxidation of the long chain fatty acids, according to which oxidation may occur simultaneously at the β-position and at each alternate carbon atom in the chain as indicated in the formula for lauric acid:

$$\mathrm{CH_3CH_2} \vdots \mathrm{CH_2CH_2} \vdots \mathrm{CH_2CH_2} \vdots \mathrm{CH_2CH_2} \vdots \mathrm{CH_2CH_2} \vdots \mathrm{CH_2COOH}$$

That such a type of reaction occurs in long hydrocarbon chains when subjected to catalytic oxidation is well substantiated in the catalytic air-oxidation method of producing fatty acids from petroleum. A similar type of degradation appears to occur in the oxidation of hydrocarbon chains by hot chromic–sulfuric acid. Experiments involving catalytic air oxidation at relatively low temperatures conducted in the author's laboratory with the object of shortening the hydrocarbon chain of stearic acid indicate that the molecule is simultaneously attacked along the entire chain but apparently at relatively different rates.

5. Dehydrogenation and Oxidation

Because of the difficulty of oxidation of the saturated carbon chains *in vitro,* it might be considered relatively difficult in the living organism. Also, in view of the greater ease of oxidation of unsaturated linkages in hydrocarbon chains *in vitro,* it is not unreasonable to assume that the saturated acids might first be dehydrogenated to unsaturated acids. On the other hand, it is conceivable that oxidation might occur readily at body temperatures under the influence of enzymes as it certainly does in the case of sugars and other carbohydrates, but here the carbon chain is already in a highly oxidized state. Furthermore, although dehydrogenation of long hydrocarbon chains probably occurs less readily *in vitro* than does oxidation, it could possibly do so readily through the action of enzymes *in vivo.*

Leathes[20] and Leathes and Meyer-Wedell[21] observed that the liver of rats fed on cod liver oil contained fatty acids of higher iodine value than those present in the ingested oil. They therefore suggested that β-oxida-

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[19] M. Jowett and J. H. Quastel, *Biochem. J.*, **29**, 2143–2158, 2159–2180, 2181–2191 (1935).

[20] J. B. Leathes, *Lancet*, **176**, 593–599 (1909). See *Ergeb. Physiol.*, **8**, 356–370 (1909); *Arch. exptl. Path. Pharmakol.*, Suppl. Binding, **1909**, 327–348.

[21] J. B. Leathes and L. Meyer-Wedell, *J. Physiol.* (*Proc.*), **38**, xxxviii–xi (1909).

tion may be preceded by desaturation in the liver and addition of a molecule of water at the 2,3-position with the formation of a β-hydroxy acid according to the following scheme:

$$RCH_2CH_2COOH \xrightarrow{-H_2} RCH{:}CHCOOH \xrightarrow{H_2O} RCHOHCH_2COOH$$

In substantiation of this idea Mazza[22] observed that dead bacteria and liver extracts actively dehydrogenated stearic and $\Delta^{9,10}$-oleic acids, but were without action on $\Delta^{2,3}$-oleic acid. $\Delta^{2,3}$-Unsaturation cannot be detected by ordinary iodine determinations such as were applied by Leathes and Meyer-Wedell, but can be by hydrogenation methods used by Mazza.

Raper[23] found, on feeding coconut oil to cats or dogs, that the volatile acids of the liver possessed a higher iodine value than those present in the original oil.

In contrast to the theory of dehydrogenation, Mottram[24] found that the liver of the plaice contained acids more saturated than those which were present in the ingested food. Banks and Hilditch[25] presented evidence to indicate that hydrogenation rather than dehydrogenation occurred in the case of the pig depot fats. Lovern[26] found that in the tunny the degree of unsaturation in the C_{18} acids decreased as the content of stearic acid increased and suggested that the increase of stearic acid was at the expense of the ethylenic bonds to preserve an approximately constant content of saturated acids. Hilditch and Longenecker[27] expressed a somewhat similar idea in regard to the ox depot fats in which the increase in stearic acid was balanced by a decrease in oleic acid, thus maintaining a constant ratio of C_{16} to C_{18} acids.

The work of Burr and his associates[28–30] on the deficiency disease caused by lack of certain essential unsaturated acids (linoleic, linolenic, and arachidonic) when experimentally omitted from the diet, would seem to indicate that the animal organism lacks both a mechanism of synthesis of these acids from carbohydrates and also a means of producing them by dehydrogenation from ingested or stored fats.

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[22] F. P. Mazza, *Arch. ital. biol.*, **94**, 69–71 (1935); *Arch. sci. biol. Italy*, **21**, 320–331 (1936); **22**, 307–325 (1936); *Boll. soc. ital. biol. sper.*, **11**, 143–145, 157–158 (1936).

[23] H. S. Raper, *J. Biol. Chem.*, **14**, 117–134 (1913).

[24] V. H. Mottram, *J. Physiol.*, **45**, 363–369 (1912).

[25] A. Banks and T. P. Hilditch, *Biochem. J.*, **26**, 298–308 (1932).

[26] J. A. Lovern, *Biochem. J.*, **30**, 2023–2026 (1936).

[27] T. P. Hilditch and H. E. Longenecker, *Biochem. J.*, **31**, 1805–1819 (1937).

[28] G. O. Burr and M. M. Burr, *J. Biol. Chem.*, **82**, 345–367 (1929); **86**, 587–621 (1930).

[29] G. O. Burr, M. M. Burr, and W. R. Brown, *Proc. Soc. Exptl. Biol. Med.*, **28**, 905–907 (1931).

[30] G. O. Burr and A. J. Beber, *J. Nutrition*, **14**, 553–566 (1937).

CHAPTER XVIII

NITROGEN DERIVATIVES OF ALIPHATIC ACIDS

1. Classification

Aliphatic acids containing nitrogen, as well as nitrogen compounds which contain aliphatic acid residues, are found in nature, but they are seldom encountered in fats and oils except in their unrefined state. Various types of nitrogen compounds occur as impurities in crude fats and oils as a result of the method of extraction, but they are generally completely removed during subsequent refining. An exception to this statement is the occurrence of certain phospholipids in some fats and oils and possibly of very small amounts of nitrogenous unsaponifiable constituents which are not entirely removed by refining.

Although not generally found in fats and oils *per se*, many of the nitrogen derivatives of the aliphatic acids are of considerable interest and economic importance and have, therefore, been the object of much research and even of considerable industrial activity. In fact, the investigation of the effect on the properties of aliphatic acids produced by the introduction of nitrogen into their structures, and the possibility of using fatty acids as raw materials for the preparation of industrially important nitrogen derivatives, have in recent years attracted the attention of a number of investigators. The fatty acids afford an excellent raw material for the synthesis of a variety of nitrogen-containing compounds, many of which possess distinctive properties and are, therefore, finding increasing employment in a number of industrial processes and products.

The saturated fatty acids present four points of attack for the introduction of nitrogen or nitrogen-containing radicals, namely, the hydrogen of the carboxyl group, the hydroxyl of the carboxyl group, the carbonyl group of the carboxyl, and the hydrogens of the hydrocarbon chain. The unsaturated fatty acids possess a fifth point of attack, namely, the double bond. The substitution of nitrogen in fatty acids in place of these atoms or radicals results in the production of derivatives which form homologous series corresponding to the aliphatic acid series from which they are derived.

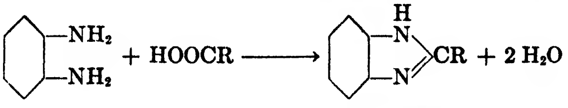
The simplest series of such nitrogen derivatives are the *ammonium salts* of the normal saturated acids which are entirely analogous to the alkali metal salts. Another series comprises the acid *amides*, $RCONH_2$, in which the NH_2 group replaces the hydroxyl group of the fatty acids. Substitution of a hydrogen in the hydrocarbon chain by NH_2 gives rise to the *amino acids*, such as $RCH(NH_2)COOH$, of which an extremely large number are theoretically possible owing to increasing capacity for the production of isomers with increasing chain length. Three other classes of aliphatic nitrogen derivatives, two of which may be formed from fatty acids, are represented by: the *amines*, RCH_2NH_2; the *nitriles*, RCN; and the *nitroparaffins*, RCH_2NO_2. Related to the aliphatic amides are the hydrazides, $RCONHNH_2$, and the acid azides, $RCON_3$.

Numerous nitrogenous derivatives of fatty acids can be prepared in the form of esters simply by introducing nitrogen-containing radicals in place of the hydrogen of the carboxyl or by reaction of the fatty acid chlorides with nitrogen-containing compounds. For example, the fatty acids react with aromatic amines to form *anilides* and with aromatic *diamines* to form heterocyclic nitrogen compounds. The anilides may also be formed by the reaction of acid chlorides and anhydrides with aromatic amines. These reactions may be illustrated by the following equations:

$$C_6H_5NH_2 + HOOCR \longrightarrow C_6H_5NHOCR + H_2O$$

$$2\,C_6H_5NH_2 + ClOCR \longrightarrow C_6H_5NHOCR + C_6H_5NH_2{\cdot}HCl$$

$$C_6H_5NH_2 + O(OCR)_2 \longrightarrow C_6H_5NHOCR + RCOOH$$



o-Phenyldiamine 2-Alkylbenzimidazole

Many other nitrogen-containing compounds which may be considered as being formed indirectly from fatty acids are known but are not considered here because they are of theoretical interest only or are of minor economic importance.

2. Aliphatic Amino Acids

(*a*) *Natural Amino Acids*

When one or more hydrogens of the hydrocarbon chains of the normal aliphatic acids is replaced with an NH_2 group, the resulting compound is termed an *amino* acid. If the NH_2 group is attached to the carbon atom next to the carboxyl of a normal aliphatic acid, the substituted acid is designated *α-amino* acid. If it is attached to the second carbon atom removed from the carboxyl, it is designated *β-amino* acid, and so on as the point of attachment is moved along the carbon chain. If two amino groups are attached to two different carbon atoms in the aliphatic chain the resulting acid is known as a *diamino* acid.

The α-amino acids which are characterized by the presence of the terminal —CH(NH$_2$)COOH group are of special importance and interest because of their widespread occurrence in the proteins of plants and animals. In fact, they represent the building stones of all proteins and are produced from them by appropriate hydrolysis. Two of the simplest α-amino aliphatic acids, namely, glycine or α-aminoacetic acid, and alanine or α-aminopropionic acid, are among the commonest amino acids found in proteins. On the other hand, α-aminocaproic acid or norleucine is known to occur in only a few proteins. Generally, the naturally occurring aliphatic amino acids contain one or more side chains or groups such as hydroxy, methyl, or imino, in addition to the amino group. For example, isoleucine or α-amino-β-methyl-*n*-valeric acid, and leucine or α-amino-isocaproic acid, which are isomeric with norleucine, contain a methyl group at the β- and γ-carbon atoms, respectively. The important naturally occurring aliphatic amino acids are listed in Table 130. All of the other essential amino acids contain either a benzene, phenolic, or heterocyclic ring in their molecules.

TABLE 130

ALIPHATIC AMINO ACIDS FOUND IN PROTEINS

Amino acid	Formula
Alanine, α-aminopropionic	$CH_3CH(NH)_2COOH$
Arginine, α-amino-δ-guanidino-*n*-valeric	$NH_2C(NH)NH(CH_2)_3CH(NH_2)COOH$
Aspartic acid, α-aminosuccinic	$HOOCCH_2CH(NH_2)COOH$
Cystine, di-(α-amino-β-thiopropionic)	$[SCH_2CH(NH_2)COOH]_2$
Glutamic acid, α-aminoglutaric	$HOOC(CH_2)_2CH(NH_2)COOH$
Glycine, α-aminoacetic	CH_2NH_2COOH
β-Hydroxyglutamic acid, α-amino-β-hydroxyglutaric	$HOOCCH_2CH(OH)CH(NH_2)COOH$
Isoleucine, α-amino-β-methyl-*n*-valeric	$CH_3CH_2CH(CH_3)CH(NH_2)COOH$
Leucine, α-amino-isocaproic	$(CH_3)_2CHCH_2CH(NH_2)COOH$
Lysine, α-amino-ε-amino-*n*-caproic	$NH_2(CH_2)_4CH(NH_2)COOH$
Methionine, α-amino-γ-methylthiol-*n*-butyric	$CH_3S(CH_2)_2CH(NH_2)COOH$
Norleucine, α-amino-*n*-caproic	$CH_3(CH_2)_3CH(NH_2)COOH$
Serine, α-amino-β-hydroxypropionic	$HOCH_2CH(NH_2)COOH$
Threonine, α-amino-β-hydroxybutyric	$CH_3(OH)CH(NH_2)COOH$
Valine, α-amino-isovaleric	$(CH_3)_2CHCH(NH_2)COOH$

Despite the fact that all of the naturally occurring α-amino acids listed in Table 130 are derivatives of simple aliphatic acids, few of them can be readily prepared directly from the corresponding fatty acid. Various methods have been devised for the synthesis of the natural amino acids, but a number of them are still quite unsatisfactory.[1,2]

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[1] C. A. Schmidt, *The Chemistry of the Amino Acids and Proteins*, C. C Thomas, Springfield, Ill., 1938. *Addendum to the Chemistry of the Amino Acids and Proteins*, 1943. See also R. J. Block, *Chem. Revs.*, 38, 501–571 (1946).

[2] A. H. Blatt, *Organic Syntheses*, Collective Vol. II. Wiley, New York, 1943.

(*b*) *Synthetic Amino Acids*

The simple unsubstituted α-amino aliphatic acids can be prepared by several methods, one of which may be considered as beginning with the corresponding fatty acid. In this synthesis, the fatty acid is converted to the α-bromo acid by means of phosphorus and bromine and the α-bromo acid reacted with ammonia to form the α-amino acid according to the following equations:

$$RCH_2COOH \xrightarrow{Br_2 + P} RCHBrCOBr \xrightarrow{\text{hydrolysis}} RCHBrCOOH \xrightarrow{2\ NH_3} RCHNH_2COOH + NH_4Br$$

Although this reaction results in the formation of the desired α-amino acid, there are also produced di- and tri-substituted products of ammonia. It is, therefore, preferable to treat the halogen-substituted fatty acid, or better still, the monoester with potassium phthalimide instead of ammonia.

Another method of preparing the simple α-amino aliphatic acids is known as the cyanohydrin synthesis which employs the next lower aliphatic aldehyde. Aldehyde-ammonia is formed by the reaction of alcoholic ammonia or an ammonium salt with an aldehyde and this product is in turn reacted with anhydrous hydrocyanic acid, or with a solution of an alkali metal cyanide. On hydrolyzing the resulting aminocyanohydrin with a strong acid or base, an amino acid, with one more carbon atom than the original aldehyde, is formed. The reactions may be represented by the following equations:

$$RCHO + NH_3 \longrightarrow RCH(NH_2)OH$$

$$RCH(NH_2)OH + HCN \longrightarrow RCH(NH_2)CN$$

$$RCH(NH_2)CN \xrightarrow[HBr]{2\ H_2O} RCH(NH_2)COOH + NH_4Br$$

By means of these and other syntheses a number of α-amino aliphatic acids have been prepared. Practically all of the homologs, as well as positional isomers, from acetic to valeric have been synthesized, but beyond these the series has not been appreciably extended.

The introduction of the amino group into the aliphatic chain profoundly alters the character of the fatty acid. The introduction of the NH_2 group in the place of hydrogen at the α-carbon atom produces an asymmetric carbon atom and hence confers optical activity on all of the α-amino acids except glycine (α-aminoacetic acid). The lower members are colorless crystalline solids, but with increasing chain length they tend to become waxy in nature. The melting points of the amino acids are markedly higher than those of the fatty acids from which they are derived as may be seen from the data in Table 131. The lowest members in the series are moderately soluble in water, but the solubility decreases as the

TABLE 131

PROPERTIES OF FATTY ACIDS AND CORRESPONDING AMINO ALIPHATIC ACIDS

Fatty acid	M.p., °C.	B.p., °C.	Solubility[a]			Amino acid	M.p., °C.	Solubility[a]		
			Water	Alcohol	Ether			Water	Alcohol	Ether
Acetic	16.6	118.1	Completely	Completely	Completely	α-Aminoacetic	233 d.[b]	25.3^{25}	0.04^{25}	
Propionic	−22	141.1	Completely	Completely	Completely	α-Aminopropionic	295	16.6^{25}	0.08^{25}	Insoluble
						β-Aminopropionic	196	Very slightly	Very slightly	Insoluble
Butyric	− 7.9	163.5	$5.62^{-1.1}$	Completely	Completely	α-Aminobutyric	285 d.	28	0.18^{78}	Insoluble
						β-Aminobutyric	184	100	Insoluble	Insoluble
						γ-Aminobutyric	193	Very slightly	Insoluble	Insoluble
Valeric	−34.5 (−59)	187	3.7^{16}	Completely	Completely	α-Aminovaleric	291.5	10.7^{5}	Slightly	Insoluble
						γ-Aminovaleric	193	Very slightly	Slightly	Insoluble
						δ-Aminovaleric	157	Very slightly	Slightly	Insoluble
Caproic	− 1.5	205.8	0.4	Slightly	Slightly	α-Aminocaproic	327 d.	1.18^{25}	0.26^{25} (75%)	Insoluble
Caprylic	16.5	239.7	0.25^{100}	Completely	Completely	α-Aminocaprylic	263.5	0.6^{100}	Very slightly	Very slightly

[a] Superscripts refer to temperatures in degrees Centigrade.
[b] d. = decomposes.

series is ascended. Unlike the aliphatic acids which are soluble in alcohol and ether, the corresponding amino acids are only very slightly soluble or completely insoluble in these media.

The amino acids are amphoteric owing to the presence of the basic amino group and the acidic carboxyl group. Little can be said concerning the properties of the amino acids of the long chain fatty acids since they are but little known. It may be surmised, however, that they would display a variety of properties depending on the chain length of the fatty acid and the point of attachment of the amino groups. These properties would be still further modified by the presence of unsaturation in the hydrocarbon chain.

3. Acid Amides

Replacement of the hydroxyl group in the carboxyl of the aliphatic acids results in the formation of the corresponding amides, $RCONH_2$. This substitution may be accomplished by appropriate treatment of the ammonium salts, esters, halides, and anhydrides of the fatty acids. The resulting products possess markedly different properties compared with those of the fatty acid from which they are derived. These properties render the acid amides useful as waterproofing agents, protective coatings, paper sizes, plasticizers, lubricant modifiers, etc., and also as chemical intermediates for the preparation of other fatty acid derivatives such as the aliphatic nitriles.

(*a*) *Properties of the Acid Amides*

The effect produced on the properties of aliphatic acids by substitution of an amino group for the hydroxyl group is evident in the differences in the melting and boiling points of the fatty acids and corresponding amides shown in Table 132. With the exception of formamide, the fatty acid amides are crystalline solids at ordinary temperatures, consequently the liquid acids are often converted into amides for purposes of identification by melting and mixed melting points. However, their utility as a means of identifying acids is limited in many cases by the relatively small differences in the melting points of adjacent members of the series. The lower members of the series are soluble in water but become increasingly insoluble as the series is ascended. For example, normal caproamide is soluble in hot water but stearamide is insoluble in the same medium.

The basic properties of the amino group are practically neutralized by the "acidic" properties of the acyl group, RCO—; hence the amides can be titrated in glacial acetic acid with perchloric acid.[3] They also behave as weak acids, especially when dissolved in liquid ammonia and in

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[3] N. F. Hall, *J. Am. Chem. Soc.*, **52**, 5115–5128 (1930).

TABLE 132

COMPARISON OF MELTING AND BOILING POINTS OF FATTY ACIDS AND AMIDES

Fatty acid	Melting point, °C.		Boiling point, °C.[a]	
	Acid	Amide	Acid	Amide
Formic	8.4	2.5	100.5	200 d.
Acetic	16.6	82	118.1	222
Propionic	−22	80	141.1	213
Butyric	− 7.9 (−4.7)	116	163.5	216
Valeric	−34.5 (−59)	109 (115)	187	168
Caproic	− 1.5 (−9.5)	101	205.8	255
Heptanoic	−10.5	95	223.0	...
Caprylic	16.5	97	239.7	...
Nonanoic	12.5	99	255.6	...
Capric	31.3	108	270.0	...
Undecanoic	29.3	103	284.0	...
Lauric	44.0	110	298.9	$200^{12.5}$
Tridecanoic	41.5	...	312.4	...
Myristic	53.9	103	326.2	...
Pentadecanoic	52.3	...	339.1	...
Palmitic	63.1	106	351.5	236^{12}
Margaric	61.3	...	363.8	...
Stearic	69.6	109	376.1	251^{12}
Nonadecanoic	68.6	...	299^{100}	..
Arachidic	75.3	108	328	..

[a] Superscripts refer to pressures in millimeters of mercury. d. = decomposes.

this medium they will neutralize metal amides. These reactions may be represented by the following equations:

$$RCONH_2 \xrightarrow[HOAc]{HCl} RCONH_2 \cdot HCl$$

$$RCONH_2 \xrightarrow[NH_3]{NaNH_2} RCONHNa + NH_3$$

MacKenzie and Rawles[4] found that fatty acid amides reacted with oxalic acid in a manner analogous to hydrochloric acid. Whereas hydrochlorides are formed by the reaction of dry hydrochloric acid with amides in ether solution, oxalates are formed by the reaction of anhydrous oxalic acid with amides in minimum quantities of ethyl acetate. All of the oxalate salts of the first six members (formamide to *n*-caproamide) of the series are relatively stable, crystalline compounds having sharp melting points, and are readily titratable with sodium hydroxide.

(*b*) *Preparation of Acid Amides*

The aliphatic acid amides may be formed directly from the acids or indirectly from acid anhydrides, acid halides, ammonium salts, amines, etc. One of the oldest known methods of forming aliphatic acid amides is by heating the ammonium salt of the acid. The amide is formed by

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[4] C. A. MacKenzie and W. T. Rawles, *Ind. Eng. Chem., Anal. Ed.,* 12, 737–738 (1940).

loss of water according to the equation:

$$RCOONH_4 \longrightarrow RCONH_2 + H_2O$$

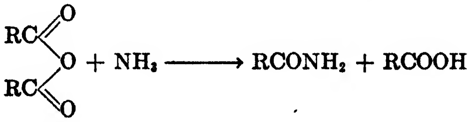
Another simple and well-known method of forming fatty acid amides consists in the partial hydrolysis of nitriles with alkaline hydrogen peroxide at 45–55°C. or with mineral acids according to the equation:

$$R{-}C{\equiv}N + H_2O \longrightarrow R{-}CONH_2$$

Conversion of nitriles to amides is also easily effected with concentrated sulfuric acid. The production of acid amides from the acid halides, anhydrides, and esters (glycerides) by ammonolysis is, however, the most important and generally useful method for the preparation of amides either in the laboratory or on an industrial scale.

Uncatalyzed Ammonolysis.—When acid halides, anhydrides, or esters react with water, they are hydrolyzed with the formation of free acids. Analogous reactions occur when the same compounds are treated with ammonia except that amides instead of free acids are formed. This reaction with ammonia, analogous to hydrolysis and alcoholysis, is termed ammonolysis. The reactions with ammonia are illustrated by the following equations:

$$RCOCl + 2\,NH_3 \longrightarrow RCONH_2 + NH_4Cl$$



$$(RCO)_2O + NH_3 \longrightarrow RCONH_2 + RCOOH$$

$$RCOOR' + NH_3 \longrightarrow RCONH_2 + R'OH$$

The preparation of acid amides from acids by treatment with thionyl chloride or phosphorus pentachloride to form acid chlorides, and reaction of the latter with ammonia, represents a simple and widely applicable method for the preparation of amides. Both saturated and unsaturated acid amides can be prepared by these reactions. The amides of most of the normal saturated acids from formic to stearic have been prepared by this method, as well as many unsaturated acid amides, such as oleic, elaidic, erucic, brassidic, undecenoic, etc. The chlorides of the lower members of the series react to form amides if they are merely allowed to stand in strong solutions of ammonia. The reactivity in aqueous solution decreases as the series is ascended, but vigorous reaction occurs in liquid ammonia.

From the industrial point of view, preparation of acid amides from the fatty acid esters is more important than from the acid chlorides. When a monoester or triglyceride is reacted with ammonia there is produced, beside the amide, the corresponding alcohol. Unless the alcohol is removed from the reaction mixture, equilibrium is established and conversion of the ester to amide is incomplete. The ammonolysis of esters in liquid ammonia has been the subject of research since 1901 when Bartow and McFarland[5] first noted that acid chlorides when slowly dropped into liquid ammonia reacted vigorously and that ethyl esters appeared to be unattacked under the same conditions.

When the ethyl esters of formic, acetic, propionic, valeric, and caprylic acids were dropped into liquid ammonia (−33°C.) and the mixture allowed to stand until the ammonia evaporated, no reaction occurred. With ethyl nonanoate (pelargonate) partial reaction resulted. When ethyl acetate and ethyl nonanoate were sealed in tubes with liquid ammonia (1:4 by volume) and allowed to stand at room temperature for 12 hours, no reaction occurred beyond that observed at −33°C. When the temperature was raised to 60–70°C., slight reaction occurred with ethyl acetate but not with the higher ethyl ester. Glattfeld and Macmillan[6] also found that butyl acetate did not react with liquid ammonia at −33°C. Philippi and Galter[7] found that ethyl oleate and ethyl elaidate failed to react with liquid ammonia at room temperature after standing for either 300 hours or 3 weeks.

Catalyzed Ammonolysis.—Owing to the slowness of the ammonolysis at relatively low temperatures the effect of catalysts was investigated especially by Oda and by Audrieth and co-workers. Oda and Wada[8] found that zinc chloride, calcium chloride, activated carbon, precipitated silica, benzene, ethanol, and ethyl ether failed to effect acceleration of the ammonolytic reaction. However, when ethyl acetate was reacted with liquid ammonia in the presence of ammonium chloride as catalyst, 43% of acetamide was formed,[9] whereas little reaction occurred in the absence of ammonium chloride even after heating for 24 hours at 130°C.

Audrieth and co-workers[10–13] investigated the catalytic activity of a number of ammonium salts and especially of ammonium chloride which was found to catalyze effectively the reaction of a wide variety of esters with liquid ammonia. Ammonium chloride was shown to be an acid catalyst in liquid ammonia and hence the analog of hydrochloric acid in hydrolysis of esters. Balaty, Fellinger, and Audrieth[13] applied the ammonium chloride catalyzed ammonolysis reaction to the preparation of

[5] E. Bartow and D. F. McFarland, *Kansas Univ. Quart.*, **10**, 79–85 (1901).

[6] J. W. E. Glattfeld and D. Macmillan, *J. Am. Chem. Soc.*, **58**, 898–901 (1936).

[7] E. Philippi and E. Galter, *Monatsh.*, **51**, 253–266 (1929).

[8] R. Oda and S. Wada, *J. Soc. Chem. Ind. Japan*, Suppl. binding, **37**, 294 (1934).

[9] H. Oeda, *Bull. Chem. Soc. Japan*, **11**, 385–389 (1936).

[10] C. Slobutsky, L. F. Audrieth, and R. W. Campbell, *Proc. Natl. Acad. Sci. U.S.*, **23**, 611–615 (1937).

[11] L. L. Fellinger and L. F. Audrieth, *J. Am. Chem. Soc.*, **60**, 579–581 (1938).

[12] L. F. Audrieth and J. Kleinberg, *J. Org. Chem.*, **3**, 312–316 (1938).

[13] V. F. Balaty, L. L. Fellinger, and L. F. Audrieth, *Ind. Eng. Chem.*, **31**, 280–282 (1939).

the mixed amides of olive, corn, soybean, castor, linseed, perilla, and tung oils and lard. The reaction was carried out at 25° and 165°C. for periods varying from 24 to 164 hours. Although reaction was observed to occur in the absence of ammonium chloride, the yields of amides were always appreciably greater when the catalyst was present.

Oda[14] and Oda and Wada[8] found that olive, coconut, castor, fish, spermaceti, tung, and linseed oils were converted to amides by heating in an autoclave at 100° to 150°C. with liquid ammonia for one-half to one hour.

The commercial production of amides from fatty acid anhydrides, halides, and esters, including natural oils, by reaction with liquid ammonia is covered by patents.[15] Production of the amides of coconut oil fatty acids is cited as an example. Coconut oil is mixed with an excess of liquid ammonia in an autoclave and allowed to stand for twelve hours at room temperature. The amides separate from the reaction mixture in acicular crystals and are removed by filtration and washed with liquid ammonia. The filtrate and wash liquors are distilled to recover the ammonia and glycerol. Other natural fats and oils may be similarly treated to produce the corresponding amides and anhydrous glycerol.

Stearic acid, when reacted in a similar manner at 70°C. for 24 hours, produces anhydrous ammonium stearate which on further heating is converted by dehydration to stearamide. The acid amide obtained from oleic acid resembles talc and may be used as a paper size; that from ricinoleic acid is used as a plasticizer and lubricant.

The patents provide for the use of catalysts for the ammonolysis of esters and natural fats and oils but do not mention them specifically. The reaction may also be carried out at superatmospheric pressures and in the vapor phase. Since many investigators have shown that esters or natural oils do not react rapidly with liquid ammonia between -33°C. and room temperature it would appear that either catalysts or high pressures are required for the commercial production of amides from these reactants. The advantage of the ammonolysis reaction lies in the simultaneous production of anhydrous alcohols and acid amides.

(c) *Diamides and Polyamides*

Dibasic acids form amides containing two amino groups in place of the two hydroxyls of the carboxyl groups. Succinamide, for example, is formed by the same methods as apply in the preparation of the amides of monobasic acids. On heating succinamide above its melting point it loses am-

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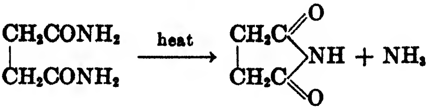
[14] R. Oda, *Sci. Papers Inst. Phys. Chem. Research Tokyo,* **24,** No. 510, 171–173 (1934).

[15] W. J. Hund and L. Rosenstein (to Shell Development Co., San Francisco, Calif.), U. S. Pat. 2,070,991 (Feb. 16, 1937). W. J. Hund and L. Rosenstein (to N. V. de Bataafsche Petroleum Maatschappij), British Pat. 445,148 (April 3, 1936), French Pat. 790,002 (Nov. 12, 1935).

monia and forms the corresponding imide:



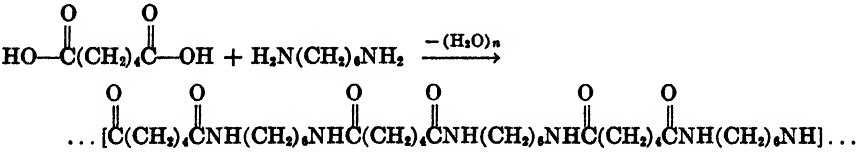
The hydrogen of the amino group in mono- and diamides is reactive and can be replaced with other groups. For example, *N*-methylacetamide, $CH_3NHCOCH_3$, can be considered as acetamide in which one of the hydrogen atoms of the amino group has been replaced by a methyl group. It can, of course, be considered as being acetylmethylamine. The NH group occurring in the derivatives of the two above-mentioned amides is referred to as an imido or imino group. Similar groups are produced by condensation (polymerization) reactions of amino aliphatic acids and fatty acid amides.

Carothers and Hill[16] prepared linear polymers of low molecular weight (2500–5000) having the formula:

$$[\text{—}NH(CH_2)_5CONH(CH_2)_5CO\text{—}]_n$$

by heating ε-aminocaproic acid, $NH_2(CH_2)_5COOH$. By further heating the low molecular weight polymer in a molecular still at a temperature around 200°C., these polymers underwent further reaction to form superpolymers having molecular weights of the order of 10,000 to 25,000. Similar condensation polymers are formed when dibasic acids are heated with amines, such as hexamethylenediamine.

When adipic acid, $HOOC(CH_2)_4COOH$, is heated with hexamethylenediamine, $NH_2(CH_2)_6NH_2$, dehydration occurs with the formation of a linear polymer:



$$HO\text{—}\overset{\overset{\displaystyle O}{\|}}{C}(CH_2)_4\overset{\overset{\displaystyle O}{\|}}{C}\text{—}OH + H_2N(CH_2)_6NH_2 \xrightarrow{-(H_2O)_n}$$

$$\ldots[\overset{\overset{\displaystyle O}{\|}}{C}(CH_2)_4\overset{\overset{\displaystyle O}{\|}}{C}NH(CH_2)_6NH\overset{\overset{\displaystyle O}{\|}}{C}(CH_2)_4\overset{\overset{\displaystyle O}{\|}}{C}NH(CH_2)_6NH\overset{\overset{\displaystyle O}{\|}}{C}(CH_2)_4\overset{\overset{\displaystyle O}{\|}}{C}NH(CH_2)_6NH]\ldots$$

The condensation that occurs by heating the constituents in an autoclave produces polymers which contain multiple peptide linkages as indicated in the formula above. One polymer obtained in this manner melts at about 263°C. and can be formed into threads by extruding the molten mass through fine dies into an atmosphere of nitrogen. The polypeptide linkages of this polyamide are analogous to those found in the protein of silk and hence it would be expected that fibers produced from it would resemble silk in many of its properties. Actually this is the case, especially after the extruded fiber is cold-drawn to increase its luster, tensile strength,

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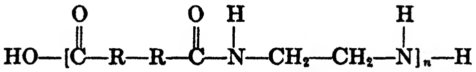
[16] W. H. Carothers and J. W. Hill, *J. Am. Chem. Soc.*, **54**, 1566–1579 (1932).

and elasticity. The polyamides produced from adipic acid and hexamethylenediamine form the various types of fibers and bristles which are produced commercially under the names nylon, Exton, etc.

Dimeric and trimeric fatty acids or esters formed by heat polymerization of linoleic and other polyethenoid acids, also react with diamines, such as ethylenediamine, to produce polyamides. Norelac,[17] a heat- and water-resistant resin, is produced by heating a mixture of dimeric and trimeric fatty acids to 150°C. in an atmosphere of nitrogen with 70% aqueous ethylenediamine. The reaction proceeds with loss of water from the reaction mixture followed by dehydration of the diamine salt to the polyamide. The reaction mixture is heated for about two hours during which time the temperature is raised to 170°C. Then, over a period of ninety minutes, the pressure on the reaction mixture is slowly reduced to 13 mm. and the temperature raised to 200°C. After holding the charge for ten minutes under these conditions, the product is discharged from the reaction vessel and allowed to cool under a blanket of carbon dioxide.

Dimeric and trimeric fatty acids or esters obtained from soybean, linseed, perilla, and similar oils may be reacted with ethylene diamine to form a variety of polyamides having correspondingly different properties. The polyamides formed with ethylenediamine and dimeric fatty acids are assumed to be linear polymers corresponding to the formula:



$$HO—[\overset{O}{\overset{\|}{C}}—R—R—\overset{O}{\overset{\|}{C}}—\overset{H}{\overset{|}{N}}—CH_2—CH_2—\overset{H}{\overset{|}{N}}]_n—H$$

4. Hydrazides and Azides

Hydrazine, $H_2N—NH_2$, reacts in a manner analogous to ammonia with aliphatic esters and acid chlorides to form hydrazides:

$$R\overset{O}{\overset{\|}{C}}—OCH_3 + H_2N—NH_2 \longrightarrow R\overset{O}{\overset{\|}{C}}—NHNH_2 + CH_3OH$$

The acid hydrazides are of themselves not particularly important compounds but they serve as intermediates for the preparation of azides, and what is more important, as one of the two best means of producing pure amines. The preparation of amines by the Hoffmann method of treating an acid amide with sodium hypochlorite or hypobromite is well established. The second method, known as the Curtius reaction, involves the production of the hydrazide of an acid by treatment with hydrazine, reacting of the hydrazide with nitrous acid to produce the acid azide, and heating the azide to convert it to the amine. The reactions involved may be represented by the following equations:

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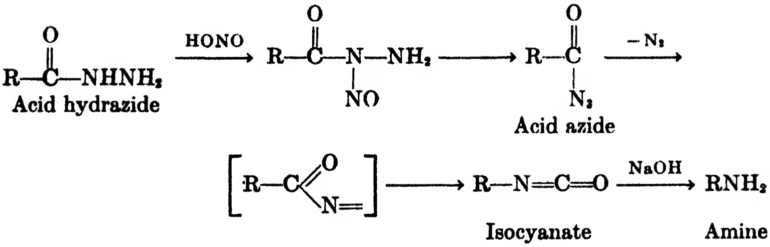
[17] J. C. Cowan, A. J. Lewis, and L. B. Falkenburg, *Oil & Soap*, 21, 101–107 (1944).



Our knowledge of the acid hydrazides and their reactions is due entirely to the exhaustive investigations of Theodor Curtius who published the results of many investigations on the subject over a period of more than a quarter of a century beginning in 1894.[18] During this interval he prepared the acid hydrazides of many of the aliphatic mono-, di-, and tribasic acids, hydroxy acids, alkoxy acids, alkyl and aryl substituted acids, and their derivatives.

The reactions of the acid hydrazides are similar to those of the acid amides. They are more readily hydrolyzed than the corresponding amides, possess reducing action, form stable salts with strong acids, and, as previously mentioned, react with nitrous acid to form azides.[19]

The acid azides may be considered as the acyl derivatives of hydrazoic acid, HN_3. They may be formed by the action of sodium azide on acid halides or by treatment of the acid hydrazides with nitrous acid (Curtius reaction). On heating with water they are converted to amines:

$$R-\overset{\overset{\displaystyle O}{\|}}{C}-N_3 \xrightarrow{H_2O} RNH_2 + CO_2 + N_2$$

and react with alcohol to form urethans:

$$R-\overset{\overset{\displaystyle O}{\|}}{C}-N_3 \xrightarrow{C_2H_5OH} RNH-\overset{\overset{\displaystyle O}{\|}}{C}-OC_2H_5 + N_2$$

The successive reactions from ester to hydrazide, to azide, to amine are particularly useful in descending a series of sensitive compounds such as the polypeptides.[20]

5. Aliphatic Nitriles

The alkyl nitriles or alkyl cyanides are the esters of hydrocyanic acid. They are characterized by the presence of the radical —C≡N and are isomeric with the isocyanides or carbylamines which contain the radical —N═C. When referred to as derivatives of hydrocyanic acid they are

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[18] T. Curtius, "Hydrazide und Azide organischen Säuren," *J. prakt. Chem.*, **50** to **95** (1894–1917).

[19] T. Curtius, *J. prakt. Chem.*, **95**, 168–256 (1917).

[20] T. Curtius, *J. prakt. Chem.*, **91**, 1–38, 39–102 (1915)

designated as cyanides, *e. g.*, methyl cyanide, ethyl cyanide, propyl cyanide, etc. As nitriles, they are designated by names derived from acids having the same number of carbon atoms, namely, acetonitrile, propionitrile, butyronitrile, etc. The lower members of the series, acetonitrile to lauronitrile, are colorless liquids of peculiar but not unpleasant odors and are appreciably less toxic than the isomeric isonitriles which have extremely unpleasant odors and are highly toxic. The lower members are, in general, excellent solvents for many organic substances and salts.

The alkyl nitriles are of interest because they possess properties making them of use *per se* and as intermediates for other reactions. Some of the higher alkyl nitriles have been shown by Ralston and Barrett[21] to possess insect-repellent activity, and after polymerization, either alone or mixed with mineral oils, they possess excellent lubricating properties under extremely high pressures.[22,23] They are claimed to act as good plasticizers for rubber,[24] can be cracked to form mixtures of lower molecular weight nitriles and hydrocarbons,[25] and may be reduced to primary amines.[26]

(*a*) *Properties of Nitriles*

Among the derivatives of the aliphatic acids few have been so systematically investigated with respect to their physical properties as the alkyl nitriles. The considerable data now available with respect to the physical constants of a large number of *n*-alkyl nitriles are due almost entirely to the efforts of Merckx *et al.*, Daragan, and Ralston and co-workers.

Merckx, Verhulst, and Bruylants[27] prepared the series of alkyl nitriles from C_2 to C_{14} and determined their boiling points, densities at three temperatures, and indices of refraction at 15° and 30°C., and calculated the corresponding molecular refractivities, and the refractometric constant of the CH_2 group. The boiling points for the series $C_7H_{15}CN$ to $C_{13}H_{27}CN$ were determined at 10 mm. pressure, but those of the lower members were determined in the vicinity of atmospheric pressure.

The densities of the first thirteen members of the series of *n*-alkyl nitriles for three temperatures and the refractive indices at 30°C. are given in Table 133. In the original publication of Merckx *et al.*[27] the refractive indices for each of the alkyl nitriles are given for eight different wave lengths of light and the molecular refractivities are given for two temperatures and four wave lengths. The refractometric constant corresponding

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[21] A. W. Ralston and J. P. Barrett, *Oil & Soap*, **18**, 89–91 (1941).

[22] A. W. Ralston, C. W. Christensen, E. J. Hoffman, W. M. Selby, and V. Conquest, *Natl. Petroleum News*, **28**, No. 50, 59–62 (1936).

[23] A. W. Ralston (to Armour and Co.), U. S. Pat. 2,116,472 (May 3, 1938).

[24] A. W. Ralston, *Oil & Soap*, **19**, 212–213 (1942).

[25] A. W. Ralston, H. J. Harwood, and W. O. Pool, *J. Am. Chem. Soc.*, **59**, 986–993 (1937).

[26] H. P. Young, Jr. (to Armour and Co.), U. S. Pat. 2,355,356 (Aug. 8, 1944).

[27] R. Merckx, J. Verhulst, and P. Bruylants, *Bull. soc. chim. Belg.*, **42**, 177–198 (1933).

to the CH_2 group was also calculated for each of these temperatures and wave lengths. Daragan,[28] using the same series of nitriles used by Merckx *et al.*, extended the determinations of densities and refractive indices to higher temperature ranges (20° to 95°C.).

TABLE 133

DENSITIES AND REFRACTIVE INDICES OF THE NORMAL ALKYL NITRILES[a]

Nitrile	Density			Refractive index, n_D^{30}
	0°C.	15°C.	30°C.	
CH_3CN	0.80377	0.78743	0.77125	1.33934
C_2H_5CN	0.80199	0.78673	0.77163	1.36132
C_3H_7CN	0.80919	0.79542	0.78172	1.37954
C_4H_9CN	0.81636	0.80348	0.79060	1.39307
$C_5H_{11}CN$	0.82171	0.80942	0.79711	1.40298
$C_6H_{13}CN$	0.82524	0.81348	0.80176	1.41037
$C_7H_{15}CN$	0.82871	0.81739	0.80586	1.41632
$C_8H_{17}CN$	0.83180	0.82061	0.80946	1.42140
$C_9H_{19}CN$	0.83429	0.82332	0.81236	1.42579
$C_{10}H_{21}CN$	0.83621	0.82538	0.81464	1.42929
$C_{11}H_{23}CN$	0.83815	0.82744	0.81682	1.43240
$C_{12}H_{25}CN$	.....	0.82937	0.81885	1.43512
$C_{13}H_{27}CN$	.....	.....	0.82067	1.43741

[a] R. Merckx, J. Verhulst, and P. Bruylants, *Bull. soc. chim. Belg.*, **42**, 177–198 (1933).

Dorinson and Ralston[29] determined the refractive indices, variation of refractive index with temperature, and the molecular refractivities of the liquid forms of the entire series of alkyl nitriles from butyronitrile to stearonitrile over the temperature range 20–75°C. The values of the refractive indices, obtained by Dorinson and Ralston by means of an Abbe type refractometer equipped with jacketed prisms through which water was circulated to control the temperature, are reproduced in Table 134. The refractive indices recorded in Table 134 were read directly on the refractometer and are not corrected for the effect of temperature on the prism of the instrument.

The freezing or melting points of only a few members of the series of alkyl nitriles have been determined (Table 135), while data with respect to the boiling points at 760 mm. pressure are available for the entire series from aceto- to stearonitrile. Ralston, Selby, and Pool[30] have not only determined the boiling points of all members of the series from capro- to stearonitrile over a wide range of pressures, but they also have constructed the corresponding vapor pressure curves. These data are repro-

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[28] B. Daragan, *Bull. soc. chim. Belg.*, **44**, 597–624 (1935).
[29] A. Dorinson and A. W. Ralston, *J. Am. Chem. Soc.*, **66**, 361–362 (1944).
[30] A. W. Ralston, W. M. Selby, and W. O. Pool, *Ind. Eng. Chem.*, **33**, 682–683 (1941).

Table 134

REFRACTIVE INDICES OF NORMAL ALIPHATIC NITRILES (UNCORRECTED)[a]

Nitrile	Refractive indices, n_D									
	20.0°	25.0°	30.0°	35.0°	40.0°	45.0°	50.0°	55.0°	65.0°	75.0°
Butyro-	1.3842	1.3820	1.3798	1.3773	1.3754	1.3729	1.3706	1.3862	1.3636	1.3590
Valero-	1.3972	1.3950	1.3929	1.3908	1.3887	1.3864	1.3843	1.3820	1.3774	1.3727
Capro-	1.4069	1.4049	1.4028	1.4008	1.3986	1.3966	1.3944	1.3921	1.3878	1.3834
Heptano-	1.4144	1.4124	1.4104	1.4083	1.4064	1.4044	1.4022	1.4000	1.3960	1.3917
Caprylo-	1.4204	1.4183	1.4164	1.4145	1.4124	1.4104	1.4085	1.4063	1.4021	1.3980
Nonano-	1.4254	1.4235	1.4216	1.4197	1.4176	1.4157	1.4137	1.4115	1.4075	1.4035
Capri-	1.4296	1.4276	1.4256	1.4237	1.4218	1.4199	1.4180	1.4159	1.4119	1.4080
Undecano-	1.4330	1.4312	1.4293	1.4273	1.4254	1.4236	1.4217	1.4197	1.4156	1.4118
Lauro-	1.4360	1.4341	1.4322	1.4304	1.4286	1.4267	1.4248	1.4227	1.4188	1.4149
Tridecano-	1.4387	1.4368	1.4349	1.4330	1.4312	1.4294	1.4275	1.4254	1.4216	1.4177
Myristo-	1.4410	1.4392	1.4373	1.4354	1.4335	1.4317	1.4298	1.4279	1.4240	1.4202
Pentadecano-	....	1.4413	1.4395	1.4376	1.4356	1.4338	1.4320	1.4300	1.4261	1.4224
Palmito-	....	....	....	1.4396	1.4377	1.4358	1.4340	1.4319	1.4281	1.4244
Margaro-	....	....	....	....	1.4392	1.4373	1.4355	1.4336	1.4298	1.4260
Stearo-	....	....	....	....	....	1.4389	1.4370	1.4351	1.4313	1.4276

[a] A. Dorinson and A. W. Ralston, *J. Am. Chem. Soc.*, 66, 361–362 (1944).

Table 135

FREEZING AND BOILING POINTS OF THE NORMAL ALKYL NITRILES

Nitrile	F.p., °C.	B.p., °C.	Nitrile	F.p., °C.	B.p., °C.
Aceto-	− 44 (m.p.)	81.5	Undecano-	...	260.8
Propio-	−103 (m.p.)	98	Lauro-	4.02	276.7
Butyro-	...	116	Tridecano-	...	292.8
Valero-	...	141	Myristo-	19.25	306.9
Capro-	...	164.8	Pentadecano-	...	322.1
Heptano-	...	186.9	Palmito-	31.40	334.3
Caprylo-	...	206.8	Margaro-	33.5 (m.p.)	346.7
Nonano-	...	225.9	Stearo-	40.88	357.4
Capri-	−14.46	244.1			

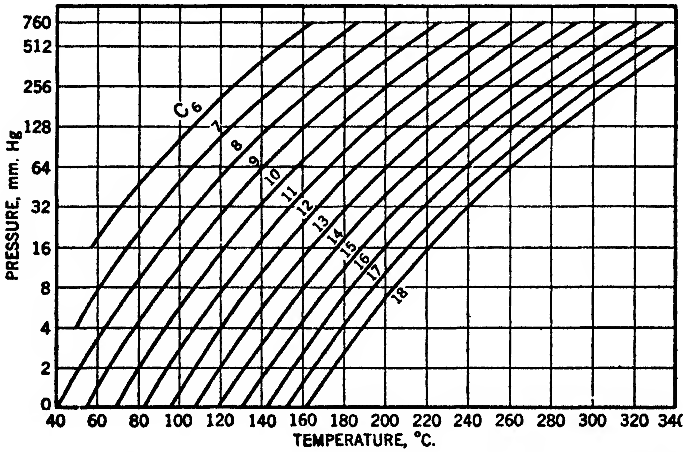

Fig. 76. Vapor pressure curves of the normal alkyl nitriles.[30]

duced in Table 136 and Figure 76. From Figure 76 it is evident that the vapor pressure curves for all the *n*-alkyl nitriles are similar in shape and that the temperature increment decreases from member to member as the series is ascended. A plot of the logarithm of the pressures against the reciprocals of the absolute temperatures shows that the boiling points of all members of the series lie on a smooth curve.

The solubilities of the even-numbered alkyl nitriles from C_{10} to C_{18} in sixteen different solvents over the entire range of useful temperatures of the solvent have been determined by Hoerr, Binkerd, Pool, and Ralston.[31] The solvents used were benzene, cyclohexane, tetrachloromethane, trichloromethane, ethyl ether, glacial acetic acid, ethyl acetate, butyl acetate, acetone, 2-butanone, methanol, ethanol (95%), isopropanol, *n*-butanol, nitroethane, and acetonitrile. It was established that a marked

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[31] C. W. Hoerr, E. F. Binkerd, W. O. Pool, and A. W. Ralston, *J. Org. Chem.*, 9, 68–80 (1944).

TABLE 136

BOILING POINTS OF NORMAL ALKYL NITRILES[a]

Number of C atoms	Boiling points, in degrees Centigrade at the following pressures (mm.)										
	1	2	4	8	16	32	64	128	256	512	760
6	. . .	. . .	. . .	44.7	57.0	71.6	87.8	106.1	126.4	149.9	164.8
7	. . .	. . .	48.5	61.1	74.7	89.9	106.8	125.8	147.1	171.3	186.9
8	41.1	52.0	64.0	77.3	91.6	107.3	124.7	143.9	166.1	191.2	206.8
9	55.0	66.1	79.0	92.4	107.1	123.3	141.2	160.2	183.5	209.3	225.9
10	69.6	81.1	93.7	107.6	122.3	138.8	157.2	177.8	201.0	227.4	244.1
11	82.9	94.8	107.8	121.8	137.1	154.1	172.7	193.5	216.7	243.7	260.8
12	95.8	107.3	120.1	134.4	150.1	167.4	186.7	208.1	232.4	259.4	276.7
13	107.6	119.8	133.2	148.1	164.2	181.7	201.3	222.9	247.2	275.5	292.8
14	118.9	131.6	145.4	160.4	177.1	194.8	214.7	237.1	261.7	298.3	306.9
15	130.5	143.6	157.6	172.7	189.2	207.2	227.4	250.2	275.4	304.3	322.1
16	142.3	155.0	168.6	183.9	200.5	218.8	239.2	262.2	287.4	316.2	334.3
17	152.3	164.9	179.1	194.8	211.9	230.4	251.3	274.0	299.6	328.2	346.7
18	161.3	174.6	189.0	204.5	221.7	240.8	261.4	284.6	311.4	339.8	357.4

[a] A. W. Ralston, W. M. Selby, and W. O. Pool, *Ind. Eng. Chem.*, 33, 682–683 (1941).

correlation existed between the solubility of the nitrile and the polarity of the solvent. In general the solubilities decreased with increased polarity of the solvent, and in any given solvent the solubility of the nitriles decreased with increasing molecular weight of the nitriles. Complete solubility data both in tabular and graphic form are given by the authors in their publication.

(*b*) *Preparation of Nitriles*

A number of methods both laboratory and industrial are available for the preparation of alkyl nitriles, several of which employ the corresponding aliphatic acids. One of the oldest of these methods comprises the dehydration of the ammonium salt of the fatty acid. This reaction is generally accomplished by distillation of the ammonium salt in the presence of a dehydrating agent such as phosphorus pentoxide. The same result can be accomplished by dehydrating the corresponding amide with phosphorus pentachloride or thionyl chloride. The formation of an amide probably occurs as an intermediate in the dehydration of the ammonium salt. It is known that distillation of palmitamide and stearamide at 760 mm. pressure yields the corresponding nitriles:

$$RCOONH_4 \xrightarrow{P_2O_5} RCN + H_2O$$

$$RCONH_2 \xrightarrow{heat} RCN + H_2O$$

The nitriles can be readily prepared by passing a mixture of fatty acid and ammonia over aluminum oxide heated to 400°C. Under these conditions all of the reactions involved in the formation of the ammonium salt from the free acid, and the subsequent dehydration steps, occur simultaneously or consecutively. According to Ralston and co-workers[22,25] these reactions may be carried out without the use of dehydrating agents or catalysts if the water which is formed is continuously removed and establishment of equilibrium prevented. However, the general procedure followed by Ralston and co-workers in the preparation of pure alkyl nitriles of the even acids consists of passing the corresponding acid over aluminum oxide in the presence of ammonia at 400°C., removing any unreacted acid, drying over potassium carbonate, and fractionally distilling *in vacuo* through a packed column. Alternative methods include treatment with solid potassium hydroxide to remove fatty acids and moisture, and distillation over phosphorus pentoxide.

In the commercial production of the higher aliphatic nitriles, fatty acids, obtained in the process of refining oils, and ammonia are heated to 675°F. by means of Dowtherm vapor in a contacting tower wherein partial reaction occurs to form nitriles and water. The mixture is then passed through a final catalyst chamber where the reaction is completed. The excess ammonia and water vapor are removed by passage through a water-cooled condenser and water separator and the nitrile or mixture of nitriles is withdrawn and the excess ammonia recycled to the original reactor.

Another method of producing alkyl nitriles consists in heating sodium or potassium cyanide with alkyl halides in dilute alcoholic solution, or by heating the alkali cyanides with solid alkali alkyl sulfates. Both of these methods tend to yield small amounts of the unpleasant smelling isonitriles:

$$KCN + RI \longrightarrow RCN + KI$$

$$KCN + ROSO_2OK \longrightarrow RCN + K_2SO_4$$

These by-products may be removed by shaking or heating the nitrile with dilute hydrochloric acid which hydrolyzes the isonitriles to amines and formic acid. When it is desired to prepare the odd-numbered alkyl nitriles, the reaction with potassium cyanide is generally preferable. By starting with the next lower even-numbered acid the desired odd-numbered nitrile can be obtained by the following sequence of reactions, namely, esterification of the acid, reduction of the ester to the alcohol, conversion of the alcohol to the iodide, and reaction of the iodide with potassium cyanide to form the nitrile.

Alkyl nitriles may also be prepared from primary amines by treatment with bromine and potassium hydroxide and from aldoximes by dehydration with acetic anhydride or thionyl chloride. The lower aliphatic nitriles can be prepared from primary alcohols (*n*-butanol and ethanol) and ammonia by reaction in the presence of reduced silver, or reduced copper, or preferably, a mixture of the two deposited on a partially dehydrated amorphous oxide of aluminum, thorium, or other rare earth metal. The oxide acts as a dehydrating agent and the copper or silver as the reducing agent.

(*c*) *Reactions of Nitriles*

The *n*-alkyl nitriles are among the most reactive aliphatic compounds known and consequently may serve as intermediates in the preparation of a variety of useful products including pharmaceuticals, dye intermediates, insecticides, solvents, and lacquers. A recent compilation[32] based on the technical literature contains forty reactions of the *n*-alkyl nitriles. Although these reactions are based primarily on experimental observations of the behavior of the lower molecular weight nitriles they are reproduced here to indicate the possibilities which exist in applying these same reactions with longer chain nitriles. Since most of these reactions are well known, only a few of them will be discussed here.

[32] Harshaw Chemical Co., Cleveland, Ohio.

REACTIONS OF NORMAL ALKYL NITRILES

(*1*) Acid to diamide:

$$RCN + R'COOH \longrightarrow RCONHCOR'$$

(*2*) Alcohol to ester:

$$RCN + R'OH + HCl \xrightarrow{H_2O} RCOOR' + NH_4Cl$$

(*3*) Alcohol to ester and ether:

$$RCN + 3R'OH \xrightarrow{BF_3} RC(OR')_3 \longrightarrow RCOOR' + R'OR'$$

(*4*) Alcohol to imino ether:

$$RCN + R'OH + (HCl) \longrightarrow RC(NH)OR'$$

(*5*) Alkyl carbonate to α-cyano ester:

$$RCH_2CN + (R'O)_2CO \xrightarrow{NaOR} RCH(CN)COOR' + R'OH$$

(*6*) Alkyl iodide to higher nitrile:

$$RCH_2CN + R'I \xrightarrow{NaNH_2} RR'CHCN \xrightarrow{R'I} RR'_2CCN$$

(*7*) Amine to alkylamidine:

$$RCN + R'NH_2 \longrightarrow RC(NH)NHR$$

(*8*) Ammonia to amidine:

$$RCN + NH_3 \longrightarrow RC(NH)NH_2$$

(*9*) Bromine to bromonitrile:

$$RCH_2CN + Br_2 \xrightarrow{S} RCHBrCN + HBr$$

(*10*) Chlorine to chloronitrile:

$$CH_3CN + 3Cl_2 \longrightarrow CCl_3CN + 3\,HCl$$

(*11*) Ester to β-ketonitrile:

$$RCH_2CN + R'COOC_2H_5 \xrightarrow{NaOC_2H_5} RCH(R'CO)CN$$

(*12*) Grignard reagent to ketone:

$$RCN + R'MgX \longrightarrow RR'C{=}NMgX \longrightarrow RR'C{=}O$$

(*13*) Hydrogen to aldimine to aldehyde:

$$RCN + H_2 \longrightarrow RCH{=}NH \xrightarrow{H_2O} RCHO + NH_3$$

(*14*) Hydrogen to amine to alcohol:

$$RCN + H_2 \longrightarrow RCH_2NH_2 \xrightarrow{HNO_2} RCH_2OH$$

(*15*) Hydrogen chloride to imino chloride:

$$RCN + HCl \longrightarrow RCCl(NH)$$

(*16*) Hydrogen sulfide to thioamide:

$$RCN + H_2S \longrightarrow RCS{\cdot}NH_2$$

(*17*) Hydrolysis to amide:

$$RCN + H_2O \xrightarrow{ZnO} RCONH_2$$

(*18*) Hydrolysis to acid:

$$RCN + 2\,H_2O + HCl \longrightarrow RCOOH + NH_4Cl$$

(*19*) Hydroxylamine to amidoxime:

$$RCN + NH_2OH \longrightarrow RC(NOH)NH_2$$

(*20*) Phenol to imino ether:

$$RCN + C_6H_5OH \longrightarrow RC(NH)OC_6H_5$$

(*21*) Sodium to iminonitrile:

$$2\,RCH_2CN \xrightarrow{Na} RC(NH)CHRCN$$

(*22*) Alcohol to cyanoethyl ether:

$$CH_2{=}CHCN + C_2H_5OH \xrightarrow{NaOR} C_2H_5OCH_2CH_2CN$$

(*23*) Aldehyde to cyanoethylaldehyde:

$$CH_2{=}CHCN + C_2H_5CHRCHO \longrightarrow C_2H_5CR(CH_2CH_2CN)CHO$$

REACTIONS OF NORMAL ALKYL NITRILES (*continued*)

(*24*) Amine to alkylaminonitrile:

$$CH_2{=}CHCN + RNH_2 \longrightarrow RNHCH_2CH_2CN$$

(*25*) Benzenediazonium chloride to phenylchloronitrile:

$$CH_2{=}CHCN + C_6H_5N_2Cl \longrightarrow C_6H_5CH_2CHClCN$$

(*26*) Bromine to dibromonitrile:

$$CH_2{=}CHCN + Br_2 \longrightarrow CH_2BrCHBrCN$$

(*27*) Chlorine to chloronitrile:

$$2\,CH_2{=}CHCN + 2\,Cl_2 \xrightarrow{\text{low temp.}} CH_2ClCCl_2CN + CH_2ClCH_2CN$$

$$CH_2{=}CHCN + Cl_2 \xrightarrow{230\text{–}450^\circ} CH_2{=}CClCN + HCl$$

(*28*) Chlorine water to chloro- and chlorohydroxynitriles:

$$2\,CH_2{=}CHCN + Cl_2 + H_2O \longrightarrow CH_2ClCHClCN + CH_2OHCHClCN$$

(*29*) Chloroform to chloronitrile:

$$CH_2{=}CHCN + CHCl_3 \longrightarrow (CCl_3CH_2CH_2CN)$$

(*30*) Glycol to glycol dicyanoethyl ether:

$$2\,CH_2{=}CHCN + (CH_2OH)_2 \longrightarrow (CH_2OCH_2CH_2CN)_2$$

(*31*) Hydration to dicyano ether:

$$2\,CH_2{=}CHCN + H_2O \xrightarrow{\text{alkali}} (CH_2CH_2CN)_2O$$

(*32*) Hydrogen to saturated nitrile:

$$CH_2{=}CHCN + 2\,H \xrightarrow{\text{Raney Ni}} CH_3CH_2CN$$

(*33*) Hydrogen chloride to chloronitrile:

$$CH_2{=}CHCN + HCl \longrightarrow CH_2ClCH_2CN$$

(*34*) Hydrogen sulfide to cyanoethyl sulfide:

$$2\,CH_2{=}CHCN + H_2S \longrightarrow S(CH_2CH_2CN)_2$$

(*35*) Ketone to tricyanoethyl methyl alkyl ketone:

$$3\,CH_2{=}CHCN + RCOCH_3 \xrightarrow{\text{NaOH}} RCOC(CH_2CH_2CN)_3$$

(*36*) Mesityl oxide to dicyanoethyl alkenyl ketone:

$$2\,CH_2{=}CHCN + (CH_3)_2C{=}CHCOCH_3 \xrightarrow{\text{alkali}} CH_2{=}C(CH_3)C(CH_2CH_2CN)_2COCH_3$$

(*37*) Phenol to phenoxynitrile:

$$CH_2{=}CHCN + C_6H_5OH \longrightarrow C_6H_5OCH_2CH_2CN$$

(*38*) Phenylacetonitrile to dicyanoethyl phenylacetonitrile:

$$2\,CH_2{=}CHCN + C_6H_5CH_2CN \longrightarrow C_6H_5C(CH_2CH_2CN)_2CN$$

(*39*) Pyrrole to *N*-cyanoethylpyrrole:

$$CH_2{=}CHCN + C_4H_5N \xrightarrow{\text{alkali}} C_4H_4NCH_2CH_2CN$$

(*40*) Resorcinol to cyanoethylresorcinol:

$$CH_2{=}CHCN + C_6H_4(OH)_2 \xrightarrow[\text{HCl}]{ZnCl_2} C_6H_3(OH)_2CH_2CH_2CN$$

The alkyl nitriles can be converted to the corresponding acids or amides by hydrolysis under different conditions. Amides are formed under conditions of mild hydrolysis such as heating with water at 180°C., or treating the nitrile with hydrogen peroxide and a base at 40°C., or by dissolving it in concentrated sulfuric acid and diluting the solution with water. Under conditions of alkaline hydrolysis (saponification), alkyl nitriles are first hydrated and then split to form the alkali soap and ammonia:

$$RCN + H_2O + NaOH \longrightarrow RCOONa + NH_3$$

Strong acid hydrolysis accomplishes a similar splitting, but with the higher molecular weight nitriles the splitting becomes increasingly difficult owing to the stability of the intermediate amide which is formed.

The nitriles enter into polymerization (condensation) reactions to give dimers and trimers when treated with metallic sodium or sodium amide. The reaction is useful in preparation of β-keto acids which are formed on hydrolysis of the dimeric nitriles.

Ralston, Harwood, and Pool[25] subjected nitriles to a process of cracking which comprises passage of the vapors of these substances through tubes packed with catalysts heated to 450–600°C., or heating the nitriles in a closed vessel to 420°. Both methods give the same type of "cracked fractions" but the latter method gives larger yields. The products of cracking were found by Ralston *et al.* to consist of mixtures of lower molecular nitriles and saturated and unsaturated hydrocarbons.

Two of the most important reactions of the nitriles are those with Grignard reagents to produce ketones and their reduction to the corresponding amines. The latter reaction is discussed under the preparation of amines.

6. Aliphatic Amines

The aliphatic amines are derivatives of ammonia in which one or more of the hydrogen atoms is replaced by an alkyl radical. Depending on the number of hydrogen atoms which are replaced, they are designated primary (RNH_2), secondary ($RR'NH$), and tertiary ($RR'R''N$) amines, respectively. According to Franklin,[33] the primary and secondary amines may be considered as the alcohols, and the tertiary amines as the ethers of the ammonia system.

The amines, like ammonia, are basic substances, but they ionize to a greater extent than the latter, and are, therefore, stronger bases. The alkaline reaction of the amines in aqueous solution and their salt-forming characteristics are due to the formation of unstable hydrates, *e. g.*, methyl amine forms methylammonium hydroxide which dissociates to give hydroxyl ions:

$$CH_3NH_2 + HOH \longrightarrow [CH_3NH_3OH] \rightleftharpoons CH_3NH_3^+ + OH^-$$

The salts of amines with mineral acids are analogous to ammonium salts and are formed both in aqueous solution and under anhydrous conditions,

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[33] E. C. Franklin, *The Nitrogen System of Compounds.* Reinhold, New York, 1935.

e. g., by passing hydrogen chloride gas into an ethereal solution of the amine. They are crystalline compounds and are more soluble in organic liquids than the ammonium salts. Both ammonia and the amines add certain alkyl halides to form alkyl ammonium salts. The highest degree of alkyl halide addition corresponds to a quaternary ammonium compound, R_4NX. The corresponding free bases are as follows: RNH_3OH, R_2NH_2OH, R_3NHOH, and R_4NOH. These substituted ammonia hydroxides are stronger bases than ammonium hydroxide. The secondary amines are stronger bases than either the primary or tertiary amines.[34] While these generalizations hold for the lower alkyl amines (methyl, ethyl, etc.), the properties undergo a gradual change as the aliphatic chain increases in molecular weight and structural configuration. For example, the solubility of the alkyl amines in water decreases rapidly with increasing length of the carbon chain. Although ethylamine is miscible with water in all proportions, hexylamine is soluble to the extent of only about 1% and dodecylamine less than 0.2%. The aliphatic amines and their salts are not only of interest because of their industrial applications but because the source of the alkyl radicals in these compounds is the fatty acids. The hydrocarbon chains of the aliphatic amines represent the positive portions of the molecules in contrast to the soaps, sulfonic acids, etc., in which the alkyl radicals represent the negative portions. This shift in the "ionic" relations markedly affects the adsorptive properties of the amines and amine salts.[35] As "cationic" substances they are useful as flotation, water treatment, and textile finishing agents.[36,37]

They are strongly adsorbed on glass, pigments, silicates, clays, limes, and metals, and thus serve to modify the surface properties of these substances. The amines possess bactericidal[37] and insecticidal[38] properties, as well as other properties which make them adaptable to a variety of uses.

McCorkle[39] has recently patented a process whereby relatively pure long chain unsaturated hydrocarbons can be continuously produced from primary amines. According to the claims of this patent, primary aliphatic amines having eight or more carbon atoms can be broken down by heat to yield unsaturated hydrocarbons whose chain length corresponds to that of the alkyl group of the amine, *i. e.*, dodecylamine hydrochloride can be made to yield dodecene, octadecenylamine phosphate will yield octadecadiene, etc. The reaction depends on heating the salts of the primary aliphatic amines with nonoxidizing inorganic acids and especially with phosphoric acid.

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[34] N. F. Hall and M. R. Sprinkle, *J. Am. Chem. Soc.*, **54**, 3469–3485 (1932).
[35] A. W. Ralston, *Oil & Soap*, **19**, 212–213 (1942).
[36] A. W. Ralston, *Oil & Soap*, **17**, 89–91 (1940).
[37] A. W. Ralston, *Chem. Eng. News*, **21**, 3–6 (1943).
[38] A. W. Ralston, J. P. Barrett, and E. W. Hopkins, *Oil & Soap*, **18**, 11–13 (1941).
[39] M. R. McCorkle (to Armour and Co.), U. S. Pat. 2,355,314 (Aug. 8, 1944).

In a continuous process phosphoric acid is heated to 300–400°C. under reduced pressure and the primary aliphatic amine is slowly added. Alkylamine phosphate is formed and decomposes to form the corresponding olefin. The reaction is presumed to occur through the momentary formation of amine phosphate followed by its thermal decomposition to produce the olefin and ammonium metaphosphate. The olefin distills and the phosphate decomposes to form metaphosphoric acid and ammonia which latter also distills from the reaction mixture. This process provides a means of obtaining long chain olefins from fatty acids by reaction of the latter with ammonia to form amides, conversion of the amides to amines, and ultimately the amines to the corresponding olefins.

(a) *Properties of Amines*

Although the physical constants (melting points, boiling points, densities, refractive indices, solubilities, etc.) of many individual amines have been determined and recorded in the literature, the only systematic investigations of these properties are those of Ralston and co-workers. The melting and boiling points for the first six members of the homologous series of *n*-alkyl primary amines, and the boiling points for the entire series from methyl- to octadecylamine have been determined and are collected in

TABLE 137

MELTING AND BOILING POINTS OF PRIMARY, SECONDARY, AND TERTIARY ALKYL AMINES

Amine	Primary, R_1NH_2		Secondary, R_2NH		Tertiary, R_3N	
	M.p., °C.	B.p., °C.	M.p., °C.	B.p., °C.	M.p., °C.	B.p., °C.
Methyl	−92.5	−6.5	−96	7.4	−124	3.5
Ethyl	−80.6	19	−50 (−39)	56	−114.8	89.5
Propyl	−83.0	48.7	−39.6	110.7 (98)	− 93.5	156.0
Butyl	−50.5	77.8	...	160	...	214
Amyl	−55.0	104	...	202 745 mm.	...	...
Hexyl	−19.0	132.7	...	...	...	...
Heptyl	−23.0	156.9	...	...	...	...
Octyl	...	179.6	14.6α 26.7β	297	− 34.6	...
Nonyl	...	202.2	...	...	...	...
Decyl	17[a]	220.5	...	...	27	265
Undecyl	16.5[a]	241.6	...	...	...	...
Dodecyl	28.3[a]	259.1	46.9α 51.8β	...	15.7	...
Tridecyl	27[a]	275.7	56.5	...	...	...
Tetradecyl	38.2	291.2	60.6	...	...	...
Pentadecyl	...	307.6	63.3	...	...	...
Hexadecyl	46.8[a]	322.5	...	...	...	...
Heptadecyl	...	335.9	...	...	...	...
Octadecyl	53.0[a]	348.8	72.3	...	54	...

[a] Freezing point.

Table 137. Ralston, Selby, Pool, and Potts[40] determined the boiling points of the *n*-alkyl primary amines over a wide range of pressures (1 to 760 mm.) and constructed the corresponding vapor pressure–temperature curve for each member of the series. These data are reproduced in Table 138 and Figure 77.

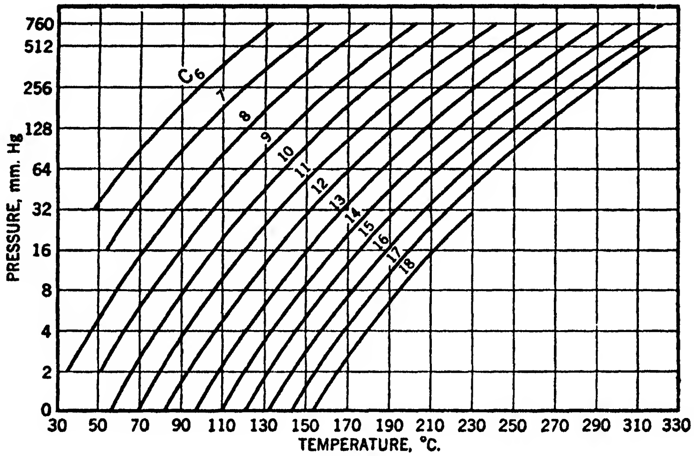

Fig. 77. Vapor pressure curves of normal primary aliphatic amines.[40]

Ralston[36] reported data with reference to the solubility of octyl- and decylamines, and dodecylamine and tetradecylamine acetates in water at various temperatures. Harwood, Ralston, and Selby[41] determined the solubilities of the primary alkyl amine hydrochlorides corresponding to C_{10} to C_{18} in 95% ethanol, and the solubilities of the corresponding acetates in 95% ethanol and anhydrous benzene. When the temperature–solubility data were plotted there was obtained a family of curves which, in the case of the hydrochlorides and acetates in 95% ethanol, exhibited pairing similar to that observed in the case of the corresponding fatty acids. The amine hydrochloride having an even number of carbon atoms is paired with the next higher member having an odd number of carbon atoms. The pairing in the case of the acetates is peculiar. Heptadecylamine acetate is less soluble than hexadecylamine acetate, while pentadecylamine acetate is more soluble than tetradecylamine acetate, and tridecylamine acetate is more soluble than dodecylamine acetate. The even- and odd-numbered carbon compounds may be considered as forming two

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[40] A. W. Ralston, W. M. Selby, W. O. Pool, and R. H. Potts, *Ind. Eng. Chem.*, **32**, 1093–1094 (1940).

[41] H. J. Harwood, A. W. Ralston, and W. M. Selby, *J. Am. Chem. Soc.*, **63**, 1916–1920 (1941).

TABLE 138

BOILING POINTS OF NORMAL ALKYL PRIMARY AMINES[a]

Number of C atoms	Boiling points, in degrees Centigrade, at the following pressures (mm.)											
	1	2	4	8	16	32	64	128	256	512	760	Calcd.
6	...	...	...	...	...	47.7	62.5	79.1	98.1	119.4	132.7	130.8
7	...	...	...	...	53.8	67.3	81.8	99.8	119.7	143.4	156.9	155.0
8	...	35.2	46.6	58.9	72.1	86.6	102.8	121.1	141.5	164.9	179.6	177.6
9	...	51.5	62.9	75.6	89.4	104.8	122.2	141.2	162.8	187.3	202.2	198.9
10	56.3	66.9	78.4	91.2	105.6	121.4	138.8	158.3	180.2	204.9	220.5	219.0
11	69.0	80.3	91.9	105.1	120.0	136.7	155.3	175.7	198.4	224.9	241.6	238.1
12	81.4	93.5	106.3	120.5	135.2	152.3	171.2	191.8	214.9	242.1	259.1	256.4
13	97.0	108.0	120.8	134.9	150.6	167.8	186.7	207.4	230.9	258.2	275.7	273.8
14	109.2	120.9	133.6	147.8	163.4	181.4	201.1	222.9	246.6	274.2	291.2	290.5
15	120.5	132.3	145.5	160.1	176.3	194.6	214.5	236.9	261.7	289.7	307.6	306.6
16	131.8	143.9	157.6	172.7	189.4	207.9	228.2	250.7	275.8	304.6	322.5	322.0
17	143.2	155.0	168.6	183.9	200.6	219.3	239.7	262.3	288.1	317.6	335.9	337.0
18	153.2	166.1	180.0	195.5	212.3	232.0	...	...	...	...	348.8[b]	351.4

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[a] A. W. Ralston, W. M. Selby, W. O. Pool, and R. H. Potts, *Ind. Eng. Chem.*, 32, 1093–1094 (1940).

[b] To avoid thermal decomposition, this boiling point was determined on a fresh sample as rapidly as possible.

distinct solubility series. The interval between the solubility curves of the even series is less than that between the odd series which results in the apparent order noted. Octadecylamine and hexadecylamine acetates gave two solubility curves in 95% ethanol thus indicating the existence of polymorphism in these compounds. The curves for the solubilities of the amine acetates in anhydrous benzene gave the same order as the corresponding curves for these salts in 95% ethanol. Ralston and co-workers[42] also determined the solubilities of the primary alkyl amines of the series C_{10} to C_{18} over the useful temperature range of fourteen organic solvents. The data are given in the original publication in the form of tables and curves.

Published physical constants for the homologous series of secondary and tertiary alkyl amines are less numerous than for the primary amines. The available melting and boiling data have already been given in Table 137. The values in this table for the melting and boiling points of the secondary and tertiary amines from C_8 to C_{18} are from the publications of Ralston and co-workers[43,44] who also determined the solubilities of the same amines over the useful temperature range of fourteen organic solvents.

Although the data in Table 137 are incomplete with regard to the secondary and tertiary amines, it is apparent that the secondary amines have the highest, and the tertiary amines the lowest melting points of the three classes of amines. On the other hand, the boiling points appear to increase in the order of the increasing number of alkyl groups in the amine.

(*b*) *Preparation of Amines*

The primary amines were first prepared by Wurtz[45] by the hydrolysis of alkyl isocyanates, but the method is of limited applicability. A more general method was discovered by Hofmann[46] in 1849 whereby ammonia may be directly alkylated by means of an alkyl halide. A mixture of primary, secondary, tertiary, and quaternary amines are formed when an alkylating agent such as an alkyl halide, alkyl nitrate, or dialkyl sulfate reacts with an aqueous or alcoholic solution of ammonia and subsequent addition of alkali:

$$RX + NH_3 \longrightarrow RNH_2{\cdot}HX \xrightarrow{NaOH} RNH_2 + NaX + H_2O$$

The process of alkylation of ammonia is simple, but it is of limited application owing to the difficulty of controlling the degree of alkylation

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[42] A. W. Ralston, C. W. Hoerr, W. O. Pool, and H. J. Harwood, *J. Org. Chem.*, **9**, 102–112 (1944).

[43] C. W. Hoerr, H. J. Harwood, and A. W. Ralston, *J. Org. Chem.*, **9**, 201–210 (1944).

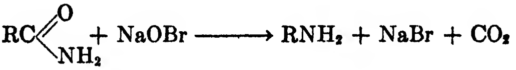
[44] A. W. Ralston, C. W. Hoerr, and P. L. DuBrow, *J. Org. Chem.*, **9**, 259–266 (1944).

[45] A. Wurtz, *Compt. rend.*, **28**, 223–227 (1849), **29**, 203–207 (1849).

[46] A. W. Hofmann, *Ann.*, **74**, 117–177 (1850).

short of the formation of the quaternary compound and because of the further difficulty of separating the mixture of alkylated ammonias which are formed. Some degree of control of the reaction may be obtained by the use of an inorganic iodide as catalyst or the use of polyalcohols as solvents. Where the differences in physical properties, *e. g.*, boiling points of the mono-, di-, and trialkyl amines are sufficiently great to permit separation of the mixture into its components, the method is especially valuable. This is the case with the ethylamines which are commercially prepared in this manner and the individual amines separated by fractional distillation. With the higher homologs such separation is not possible.

The primary amines can, however, be obtained in excellent yields and uncontaminated by secondary amines or other by-products by another method discovered by Hofmann[47] in 1881. This method consists in the treatment of an amide with sodium hypochlorite or hypobromite which results in the elimination of the carbonyl group of the amide as carbon dioxide:



$$RC\begin{smallmatrix}\nearrow O\\ \searrow NH_2\end{smallmatrix} + NaOBr \longrightarrow RNH_2 + NaBr + CO_2$$

The reaction proceeds through a series of intermediate products, one of which is the isocyanate which is hydrolyzed by alkali to form the alkyl amine as was shown by Wurtz to occur in the original preparation of methyl- and ethylamines. The reaction proceeds smoothly and efficiently for all of the lower amides. With increasing molecular weight the yields decrease, but they can be improved by a modified procedure which employs bromine and sodium methoxide in methanol as solvent.

The Curtius[48] reaction consisting of treatment of the hydrazide with nitrous acid to form the azide, thermally decomposing the azide to form the isocyanate, and hydrolysis of the isocyanate to the amine has already been mentioned.

Many types of catalytic reactions are known to produce amines. For example, the lower alcohols when heated to 300°C. in the presence of ammonia and alumina, the blue oxide of tungsten, and silica gel produce amines. However, the reaction does not stop at the primary amine but produces mixtures of all three amines. A similar reaction occurs when ethanol is heated with ammonia and zinc chloride in an autoclave at 300°C. for 8 hours. Aldoximes, $RCH{=}NOH$, can be dehydrated by heating to 350–370°C. in the presence of aluminum or thorium oxides to give the corresponding nitriles which can, in turn, be reduced by nickel and hydrogen to form the amine.[49,50] However, the oxime can be directly reduced

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[47] A. W. Hofmann, *Ber.*, **15**, 407–416 (1882).
[48] T. Curtius, *J. prakt. Chem.*, **50**, 275–295 (1894).
[49] A. Mailhe and F. de Godon, *Bull. soc. chim.*, **23**, 18–20 (1918).
[50] A. Maihle, *Compt. rend.*, **166**, 121–123 (1918).

electrolytically, or with sodium amalgam and acetic acid, aluminum amalgam, or hydrogen and a catalyst. The reduction of nitriles, oximes, amides, and nitroparaffins, constitutes the most important process of obtaining primary amines. The first three of these nitrogenous compounds may be readily prepared from fatty acids while the nitroparaffins are preferably prepared from petroleum hydrocarbons.

Reduction of Normal Alkyl Nitriles.—The reduction of alkyl nitriles, either by chemical reducing agents or by catalytic hydrogenation, involves the addition of two pairs of hydrogen atoms to the triple bond, for example:

$$RC{\equiv}N + 4\,H \longrightarrow RCH_2NH_2$$

The required nitriles can be obtained by dehydration of the ammonium salts of fatty acids as already mentioned, or by reduction of fatty acid esters to alcohols and conversion of the alcohols to nitriles by way of the alkyl halides. The reduction can be accomplished by treatment of the nitrile with zinc and hydrochloric acid,[51,52] magnesium–copper couple and Devarda's alloy in aqueous solution,[53] or with sodium and alcohol,[54–56] reagents which merely serve to produce atomic hydrogen.

The yield of primary amine, and the amount and nature of the side reaction products, varies with the hydrogenation medium. Reduction with zinc and sulfuric acid proceeds so slowly that with some nitriles appreciable losses occur through hydrolysis. Ammonia and secondary amines are produced when sodium and alcohol are used. With slightly diluted alcohol, yields of 90% to 95% of primary amines have been reported. If an anhydrous medium is employed (sodium and anhydrous ether), nitriles undergo polymerization, for example:

$$2\,RCH_2CN \xrightarrow{\text{Na, anhydrous ether}} RCH(CN)C({=}NH)CH_2R$$

Catalytic hydrogenation of nitriles with molecular hydrogen provides the best method of obtaining amines both on a laboratory and an industrial scale. Hydrogenation is readily accomplished with Raney nickel or nickel on kieselguhr as a catalyst at relatively low temperatures. Both primary and secondary amines are produced but conditions may be controlled to produce a high yield of the primary amine.

The formation of secondary amines during hydrogenation is assumed to occur as the result of loss of ammonia from two moles of primary amine:

$$2\,RNH_2 \longrightarrow R_2NH + NH_3$$

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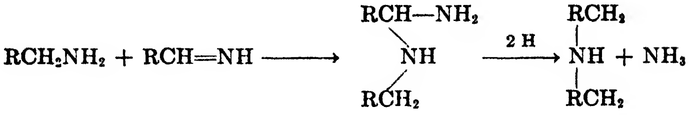
[51] O. Mendius, *Ann.*, **121**, 129–153 (1862).
[52] A. Siersch, *Ann.*, **144**, 137–145 (1867).
[53] H. Brunner and A. Rapin, *Schweiz. Wochschr.*, **46**, 455–457 (1908).
[54] A. Ladenburg, *Ber.*, **19**, 780–783 (1886).
[55] F. Krafft and F. Tritschler, *Ber.*, **33**, 3580–3585 (1900).
[56] *J.* N. Rakshit, *J. Am. Chem. Soc.*, **35**, 444–447 (1913).

followed by hydrogenative fission or hydrogenolysis:



$$RCH_2NH_2 + RCH{=}NH \longrightarrow \begin{matrix} RCH{-}NH_2 \\ \diagdown \\ NH \\ \diagup \\ RCH_2 \end{matrix} \xrightarrow{2\,H} \begin{matrix} RCH_2 \\ | \\ NH \\ | \\ RCH_2 \end{matrix} + NH_3$$

According to Adkins,[57] the formation of secondary amines may be repressed by carrying out the hydrogenation as rapidly as possible in the presence of a high ratio of catalyst and at a temperature and pressure sufficiently high to complete the reaction in one to two hours. When Adams' platinum catalyst is used, formation of secondary amines can be suppressed by carrying out the hydrogenation in acetic anhydride. This method is not feasible with a nickel catalyst as it would be attacked by the anhydride.

Ralston and co-workers prepared all of the *n*-alkyl amines from C_6 to C_{18} by hydrogenation of the corresponding nitriles. The crude amines were fractionally distilled to remove any unchanged nitrile and secondary amine. Details of the hydrogenation procedure are not given but presumably were similar to those described by Young and Christensen[58] who patented the hydrogenation of nitriles in the presence of an aqueous solution of ammonia, caustic soda, or other alkali capable of maintaining free hydroxyl ions in the hydrogenation medium.

The secondary amines (dioctyl, didodecyl, ditridecyl, ditetradecyl, dipentadecyl, and dioctadecyl) investigated by Hoerr, Harwood, and Ralston[43] were prepared from the corresponding primary amines by heating them for five to six hours at 200°C. in the presence of Raney nickel catalyst. Purification was accomplished by fractional distillation *in vacuo* or by repeated crystallization from ethanol–benzene mixtures in an atmosphere of nitrogen. The tertiary amines (trioctyl, tridodecyl, and trioctadecyl) investigated by Ralston, Hoerr, and DuBrow[44] were prepared by heating the corresponding secondary amines with the appropriate alkyl iodides for about three hours at 160–170°C. at atmospheric pressure. Purification was accomplished by repeated crystallizations from 95% ethanol containing benzene.

Young[59] patented a process for producing secondary and tertiary amines by catalytic hydrogenation of nitriles under conditions which provide for the continuous removal of the by-product ammonia, formed when two primary amines react to yield a secondary amine or when a primary amine

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[57] H. Adkins, *Reactions of Hydrogen with Organic Compounds over Copper-Chromium Oxide and Nickel Catalysts*. Univ. Wisconsin Press, Madison, 1937.

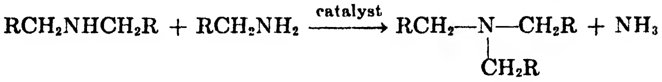
[58] H. P. Young, Jr., and C. W. Christensen (to Armour and Co.), U. S. Pat. 2,287,219 (June 23, 1942).

[59] H. P. Young, Jr. (to Armour and Co.), U. S. Pat. 2,355,356 (Aug. 8, 1944).

and a secondary amine yield a tertiary amine as indicated by the following reactions:

$$RC{\equiv}N + 2\,H_2 \xrightarrow{\text{catalyst}} RCH_2NH_2$$

$$2\,RCH_2NH_2 \xrightarrow{\text{catalyst}} RCH_2{-}NH{-}CH_2R + NH_3$$



$$RCH_2NHCH_2R + RCH_2NH_2 \xrightarrow{\text{catalyst}} RCH_2{-}\underset{\displaystyle CH_2R}{\underset{|}{N}}{-}CH_2R + NH_3$$

The reaction is carried out at a temperature of 150° to 200°C. under pressure in a special vessel which provides for valving the ammonia and a portion of the hydrogen in such manner that adequate hydrogen is available for reduction and the concentration of ammonia is sufficiently low so as not to interfere with the formation of the desired amines.

Preparation of Unsaturated Amines.—Monounsaturated amines may be prepared from the corresponding monoethenoid fatty acids by the procedure described by Krafft and Tritschler.[55] Undecenoic, oleic, elaidic, and brassidic acids were converted to the corresponding chlorides by treatment with phosphorus pentachloride. The chlorides were then treated with ammonia in ethanol to form the amides, and the amides dehydrated to form nitriles. The nitriles were reduced with sodium and alcohol to give the corresponding amines. The steps involved may be illustrated in the case of undecenoic acid as follows:

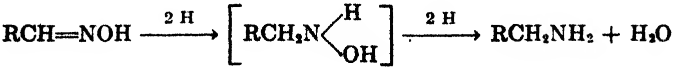
$$CH_2{=}CH(CH_2)_8COOH \xrightarrow{PCl_5} CH_2{=}CH(CH_2)_8COCl \xrightarrow[\text{ethanol}]{NH_3}$$

$$CH_2{=}CH(CH_2)_8CONH_2 \xrightarrow{\text{heat}} CH_2{=}CH(CH_2)_8CN \xrightarrow[\text{ethanol}]{Na}$$

$$CH_2{=}CH(CH_2)_8CH_2NH_2$$

The reduction of the nitrile to amine is conducted as follows: Three parts of unsaturated nitrile are dissolved in thirty parts of absolute ethanol and the solution cooled to the temperature of ice. Four parts of metallic sodium are added gradually to the cold solution. After all the sodium has been added, the mixture is warmed to complete the reduction and the warm solution is poured into ice water. The free amine is separated by extraction with ether, and the ethereal solution is dried over potash or barium hydroxide and then distilled.

Reduction of Oximes and Amides to Amines.—The oximes, obtained by condensation of hydroxylamine with aldehydes or ketones, can also be reduced to primary amines, presumably by addition of hydrogen at the double bond and reduction of the hydroxyl group:



$$RCH{=}NOH \xrightarrow{2\,H} \left[RCH_2N\begin{matrix}\diagup H\\ \diagdown OH\end{matrix}\right] \xrightarrow{2\,H} RCH_2NH_2 + H_2O$$

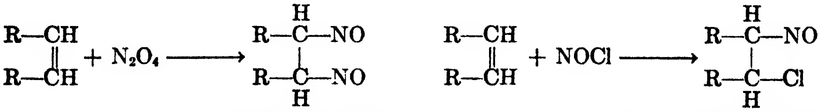
The reduction can be accomplished by means of sodium and ethanol, sodium amalgam and dilute acetic acid, or hydrogenation over kieselguhr-supported nickel catalyst. Yields of 60% to 75% of *n*-heptylamine can be obtained by reduction of *n*-heptaldoxime with sodium and ethanol compared with 60% to 65% by hydrogenation with a catalyst. Secondary amines are formed in either case.

Amides may be hydrogenated without prior conversion to the nitrile, but since they are less reactive, chemical reduction is ineffective and catalytic reduction requires the use of high temperatures and pressures (200 to 300 atmospheres). The yields are relatively low and a considerable amount of secondary amine is formed. Thus, lauramide when hydrogenated with copper–chromium at 250°C. in dioxane produces about equal percentages of laurylamine and dilaurylamine.

7. Nitrogen Addition at the Double Bond

Many attempts have been made to introduce nitrogen at the double bond of unsaturated fatty acids but few of them have been successful, or if successful, the products obtained have been of academic interest only. Three reagents, namely nitrogen trioxide (N_2O_3), nitrogen tetroxide (N_2O_4), and nitrosyl chloride (NOCl), have been extensively investigated with respect to the addition of nitrogen to the double bond of unsaturated compounds and of these only the latter two have been investigated to any extent with respect to the reaction with the higher unsaturated fatty acids.

Certain unsaturated hydrocarbons, especially those of higher molecular weight, form blue or greenish blue addition products with nitrogen tetroxide and nitrosyl chloride according to the following equations:



$$\begin{array}{l}\text{R—CH}\\ \quad\;\|\\ \text{R—CH}\end{array} + N_2O_4 \longrightarrow \begin{array}{c}\text{H}\\ \text{R—C—NO}\\ |\\ \text{R—C—NO}\\ \text{H}\end{array} \qquad \begin{array}{l}\text{R—CH}\\ \quad\;\|\\ \text{R—CH}\end{array} + \text{NOCl} \longrightarrow \begin{array}{c}\text{H}\\ \text{R—C—NO}\\ |\\ \text{R—C—Cl}\\ \text{H}\end{array}$$

Alkylene nitrosate   Alkylene nitrosochloride

These compounds readily polymerize to form dimers which are colorless products but on solution or melting revert to monomeric blue or greenish blue forms.

(*a*) *Reaction of Nitrogen Tetroxide with Unsaturated Fatty Acids*

Egoroff[60] investigated the reaction of nitrogen tetroxide ($2\ NO_2 \rightleftharpoons N_2O_4$) with a series of unsaturated acids of the formula $C_nH_{2n-2}O_2$, including acrylic, methylacrylic, crotonic, isocrotonic, allylacetic ($\Delta^{4,5}$-pentenoic),

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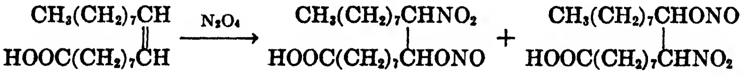
[60] I. W. Egoroff (I. V. Egorov), *J. Russ. Phys.-Chem. Soc.*, **35**, 358–375, 466–482, 482–488, 716, 965–973 (1903).

propylideneacetic ($\Delta^{2,3}$-pentenoic), etc., and concluded that these acids added NO_2 to form mono and dinitro compounds. The investigation was subsequently extended to oleic and elaidic acids.[61] It had been shown previously by Varrentrapp,[62] and by Meyer[63] that nitrous acid produced addition products with oleic acid or isomerized it to elaidic acid depending on the reaction conditions. Lidoff[64] also had shown that nitrogen tetroxide in the cold converted oleic acid to elaidic acid, but at 80–85°C. it formed addition products. Egoroff, on the other hand, found that nitrogen tetroxide formed addition products with oleic acid even in ice-cold petroleum naphtha. The isomerization of oleic to elaidic acid resulted only when a specified minimum amount of nitrogen tetroxide reacted with oleic acid while above this amount addition reactions occurred. In ice-cold petroleum naphtha, oleic acid reacted with nitrogen tetroxide to form the nitrous acid ester of nitrohydroxystearic acid (m.p. 85–87°C.):

$$CH_3(CH_2)_7CHNO_2CHOH(CH_2)_7CO_2NO_2$$

If, indeed, a reaction of this type occurred at all, it would be expected to produce a mixture of the 9-hydroxy-10-nitro and 9-nitro-10-hydroxy esters. The compound was stated to possess a normal molecular weight and to produce nitroacetylstearic acid (yellow oil) on acetylation, and aminohydroxystearic acid (m.p. 143–44°C.) on subsequent reduction with zinc and hydrochloric acid. If the original addition occurred to form positional isomers, then these subsequent reaction products would likewise consist of isomeric mixtures.

In a later work, Jegorow[65] assumed that oleic and other monounsaturated acids reacted with nitrogen tetroxide to form isomeric nitro nitrites as indicated by the following scheme in which the reaction between oleic acid and nitrogen tetroxide is illustrated:



$$\begin{array}{c}CH_3(CH_2)_7CH\\ \|\\ HOOC(CH_2)_7CH\end{array} \xrightarrow{N_2O_4} \begin{array}{c}CH_3(CH_2)_7CHNO_2\\ |\\ HOOC(CH_2)_7CHONO\end{array} + \begin{array}{c}CH_3(CH_2)_7CHONO\\ |\\ HOOC(CH_2)_7CHNO_2\end{array}$$

When heated with water at 160–70°C., fission occurred with the formation of nonanoic (pelargonic) acid, nitrononane, azelaic acid, and nitrononanoic acid. When heated with concentrated hydrochloric acid at 130–140°C., nonanoic and azelaic acids and hydroxylamine were obtained. The identities of the nitro derivatives were established by reduction to the corresponding amino derivatives. Undecenoic acid, when treated with nitrogen tetroxide and similarly hydrolyzed, gave sebacic and formic acids; erucic gave nonanoic and undecanedioic acids.

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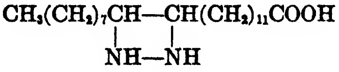
[61] I. W. Egoroff, *J. Russ. Phys.-Chem. Soc.*, **35**, 973–997 (1903).
[62] F. Varrentrapp, *Ann.*, **35**, 196–215 (1840).
[63] H. Meyer, *Ann.*, **35**, 174–188 (1840).
[64] A. Lidoff, *J. Russ. Phys.-Chem. Soc.*, **27**, 177–182 (1895); **24**, 515–524, 524–526 (1892).
[65] J. Jegorow, *J. prakt. Chem.*, **86**, 521–539 (1912).

Bauer and Bähr[66] succeeded in introducing nitrogen at the position previously occupied by the double bond of erucic acid by an indirect method. Erucic acid was converted to oxidoerucic acid (m.p. 67.5°C.) by oxidation with perbenzoic acid. To a saturated solution of oxidoerucic acid in hot benzene, there was slowly added an excess of hydrazine hydrate and the mixture heated for five hours to 130–135°C. in a bomb. The product of this reaction melted at 94.5°C. and was almost insoluble in cold petroleum naphtha and ethyl ether and only slightly soluble in alcohol, but soluble in acetone and benzene. It could not be acetylated or benzylated and the results of analysis corresponded to the formula:



$$\mathrm{CH_3(CH_2)_7}\underset{\mathrm{NH}}{\underset{|}{\mathrm{CH}}}\!-\!\!-\!\underset{\mathrm{NH}}{\underset{|}{\mathrm{CH}}}\mathrm{(CH_2)_{11}COOH}$$

Heterocyclic systems such as the one postulated by Bauer and Bähr are but little known and the structure assigned to the hydrazine reaction product of oxidoerucic acid requires further substantiation.

(*b*) *Reaction of Nitrosyl Chloride with Unsaturated Fatty Acids*

Nitrosyl chloride was first prepared by Bunge[67] and its reactions with olefins and terpenes investigated by Tilden and co-workers,[68–70] Tönnies,[71] Thiele,[72] Angeli,[73] and others. It apparently possesses some specificity of activity with respect to double-bond addition. For example, it does not add to crotonic and cinnamic acids[70] or to an allyl group, $—CH_2CH:CH_2$, but does add to the isomeric propenyl group, $—CH:CH·CH_3$.[73] Tilden and Forster[70] observed that oleic, elaidic, and erucic acids when dissolved in chloroform and treated with gaseous nitrosyl chloride formed blue-colored solutions from which waxy crystals precipitated on standing. The nature of these products was not determined but the acids apparently reacted to form a mixture of positionally isomeric nitroso chlorides, *e. g.*, 9-chloro-10-nitroso- and 9-nitroso-10-chloro-oleic acid.

Kaufmann and Röver[74] applied this reagent to the quantitative estimation of the unsaturation of fatty acids and oils. They investigated the reaction of nitrosyl chloride with tiglic, oleic, and erucic acids, methyl linoleate, mixtures of linoleic and linolenic acids, olive, sesame, rapeseed, sunflower, soybean, linseed, and perilla oils. They failed to observe any

[66] K. H. Bauer and O. Bähr, *J. prakt. Chem.*, **122**, 201–213 (1929).

[67] N. Bunge, *Ber.*, **4**, 289 (1871).

[68] W. A. Tilden (W. A. Filden!), *Ber.*, **8**, 549 (1875); W. A. Tilden and W. A. Shenstone, *Ber.*, **10**, 908–909 (1877).

[69] W. A. Tilden and J. J. Sudborough, *J. Chem. Soc.*, **63**, 479–484 (1893).

[70] W. A. Tilden and M. O. Forster, *J. Chem. Soc.*, **65**, 324–335 (1894).

[71] P. Tönnies, *Ber.*, **12**, 169–170 (1879).

[72] J. Thiele, *Ber.*, **27**, 454–456 (1894).

[73] A. Angeli, *Ber.*, **24**, 3994–3996 (1891).

[74] H. P. Kaufmann and P. Röver, *Fette u. Seifen*, **47**, 103–108 (1940).

selective addition of nitrosyl chloride but developed an empirical method of determing the so-called nitrosyl value.

The determination is carried out by weighing a 0.12 to 0.20 g. sample of fat or fatty acid in the same manner as in making an iodine value determination. The flask containing the weighed sample is cooled in ice water and 25 ml. of nitrosyl chloride in dry carbon tetrachloride or a mixture of 20% tetrachloride and 80% acetic acid containing 1% of acetic anhydride is added. The normality of the nitrosyl chloride solution should be approximately 0.1 to 0.2, but the exact value need not be known. The stopper is replaced and sealed with paraffin and the flask allowed to stand 72 hours in an ice chest. Water is then added to hydrolyze the excess nitrosyl chloride, according to the equation:

$$NOCl + H_2O \longrightarrow HNO_2 + HCl$$

The mixture is transferred to a separatory funnel, the aqueous phase removed and the carbon tetrachloride washed twice with water. Hydrochloric acid in the combined aqueous solutions is determined by titration with ammonium thiocyanate (method of Volhard) or by titration with silver nitrate solution (method of Fajans). A blank is run on the reagent and the nitrosyl value calculated by means of the equation:

$$\text{NO.V.} = \frac{2.538(a - b)}{e}$$

where NO.V. is the nitrosyl value, a the titration value for the reagent blank, b the titration value of the unknown, and e the weight of the sample. The nitrosyl value calculated in this manner is equal to the iodine value.

Beckham and Crowder[75] obtained a broad patent on the action of nitrosyl chloride with organic compounds containing at least one nonaromatic C═C linkage (mono-olefins) which comprises reacting the compound with NOCl in a reaction mixture containing 0.5 to 1.0 mole of sodium carbonate or other normal alkali-metal carbonate for each mole of mono-olefin. The mixture of olefin and sodium carbonate is maintained between 0° and 25°C. and NOCl led into it until 1.25 to 3.0 moles have been reacted per mole of mono-olefin. Among the olefins cited is oleic acid and a large number of its derivatives. The nitrosyl chloride reaction products are claimed to have particular utility as intermediates in the manufacture of sulfonates by reaction with alkali metal or ammonium sulfites,[76] as well as for preparing phosphonates, arsonates, etc.

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[75] L. J. Beckham and J. A. Crowder (to Solway Process Co.), U. S. Pat. 2,371,418 (March 13, 1945).

[76] L. J. Beckham (to Solway Process Co.), U. S. Pat. 2,265,993 (Dec. 16, 1941).

CHAPTER XIX

SULFUR DERIVATIVES OF THE FATTY ACIDS

Only two classes of sulfur-containing derivatives of fatty acids have been investigated to any appreciable extent. These are the thio acids and esters and the sulfated and sulfonated acids. The latter are of some importance industrially while the former are, as yet, only of theoretical interest.

1. Thio Acids and Esters

The thio acids and esters corresponding to the normal fatty acids have not been extensively investigated probably because of their disagreeable odor and lack of any marked characteristic properties of the few known members of the series. Detailed knowledge of the properties of the higher aliphatic thio acids is still lacking and that pertaining to the esters consists primarily of the work of Ralston, Segebrecht, and Bauer.[1]

The introduction of one sulfur atom into the carboxyl group of the aliphatic acids might be expected to produce two different products corresponding to a *thiolic* acid, RCOSH, and a *thionic* acid, RCSOH. Actually, no aliphatic acid is known corresponding to the formula for a thionic acid. The lower members of the thiolic acid series may be prepared by treating fatty acids with a sulfide of phosphorus or by reacting acid halides with sodium hydrosulfide, NaSH. The corresponding esters of thio acids may be prepared by esterification of a fatty acid with a mercaptan or thio alcohol, or by reaction of an acid halide with a mercaptan or with lead mercaptide.

The low molecular weight thio acids are colorless liquids or low melting solids with an unpleasant odor. They form alkali salts which are soluble in water and salts of heavy metals which are insoluble in this medium. When heated with water the latter decompose with the formation of metallic sulfides. The higher aliphatic thio acids do not appear to have been prepared. However, a number of alkyl esters of thio acids have been prepared and some of their properties determined. Although they may be prepared by any one of the methods mentioned above, the reaction of acid chlorides and thio alcohols is preferable.

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[1] A. W. Ralston, E. W. Segebrecht, and S. T. Bauer, *J. Org. Chem.*, **4**, 502–505 (1939).

The methyl, ethyl, propyl, isobutyl, and isoamyl thio esters of acetic and propionic acids have been prepared and described by Faber and Reid,[2] who also prepared the methyl, ethyl, *n*-propyl, and *n*-butyl thio esters of lauric, myristic, palmitic, and stearic acids and the *n*-propyl thio ester of oleic acid. All of the above-mentioned higher thio acid esters have also been prepared by Ralston, Segebrecht, and Bauer[1] who synthesized these compounds by reaction of the acid chlorides with the corresponding mercaptans. The properties of the higher aliphatic thio acid esters as determined by Ralston *et al.* are recorded in Table 139.

TABLE 139

PROPERTIES OF ESTERS OF ALIPHATIC THIO ACIDS[a]

Thio acid ester	M.p. or b.p., °C	Refractive indices		Density 60°	Molecular refraction	
		n^{25}_D	n^{60}_D		Obs.	Calcd.
Methyl thiolaurate	112–115[b]	1.4642	1.4496	0.8734	70.84	70.22
Ethyl thiolaurate	115–117[b]	1.4626	1.4478	0.8645	75.66	74.83
n-Propyl thiolaurate	126–128[b]	1.4628	1.4478	0.8610	80.32	79.45
n-Butyl thiolaurate	133–135[b]	1.4640	1.4493	0.8595	85.08	84.07
Methyl thiomyristate	34–35	....	1.4507	0.8668	80.23	79.45
Ethyl thiomyristate	134–136[b]	1.4632	1.4488	0.8609	84.86	84.07
n-Propyl thiomyristate	148–150[b]	1.4627	1.4485	0.8568	89.61	88.69
n-Butyl thiomyristate	149–151[b]	1.4642	1.4501	0.8570	94.26	93.31
Methyl thiopalmitate	44–45	....	1.4521	0.8644	89.44	88.69
Ethyl thiopalmitate	172–175[b]	1.4648	1.4513	0.8547	94.74	93.31
n-Propyl thiopalmitate	27–28	1.4642	1.4507	0.8559	98.90	97.92
n-Butyl thiopalmitate	29–30	1.4646	1.4505	0.8579	103.02	102.54
Methyl thiostearate	50–51	....	1.4526	0.8624	98.51	97.92
Ethyl thiostearate	38–39	....	1.4514	0.8550	103.56	102.54
n-Propyl thiostearate	34–35.5	....	1.4509	0.8508	108.41	107.16
n-Butyl thiostearate	31–32	....	1.4529	0.8534	112.89	111.78
n-Propyl thiooleate	175–178[b]	1.4713	1.4577	0.8643	107.46	106.69

[a] A. W. Ralston, E. W. Segebrecht, and S. T. Bauer, *J. Org. Chem.*, 4, 502–505 (1939). [b] At 1 mm. pressure of mercury.

The products were found to be relatively stable and could be distilled under diminished pressure without decomposition. The densities of the ethyl, *n*-propyl, and *n*-butyl thio esters at 60°C. are, in each case, greater than those of the corresponding acids. Thio acids cannot be produced by hydrolysis of the esters since reaction occurs to regenerate the mercaptan and the aliphatic fatty acid:

$$\text{RCOSR}' + \text{HOH} \longrightarrow \text{RCOOH} + \text{R}'\text{SH}$$

2. Fatty Acid Sulfates and Sulfonates

The sulfates and sulfonates comprise two groups of sulfur derivatives of fatty acids which may be defined chemically and prepared by specific methods. They are, however, often confused in nomenclature and, in the

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[2] E. M. Faber and E. E. Reid, *J. Am. Chem. Soc.*, 39, 1930–1938 (1917).

case of commercial products, are not always definite chemical entities. Although sulfated and sulfonated oils and fatty acids prepared by the direct action of sulfuric acid, oleum, sulfur trioxide, and chlorosulfonic acid have been known for about a century, the chemistry of these reactions has, as yet, not been completely clarified. Once the object of considerable research[3–5] from the standpoint of elucidating the reaction mechanisms and structures of the reaction products, little attention is now devoted to these aspects, and in recent years publications on the subject have more often been in the form of patents rather than reports of research.

(a) *Sulfation Reactions*

Frémy[6] appears to have been the first to investigate the reaction of sulfuric acid on triolein and he established the fact that hydrolysis of the glyceride occurred simultaneously with alteration of the oleic acid. Subsequently, it was shown that the extent of the hydrolysis varied with the reaction conditions but generally it progressed to the stage of forming di- and monoglycerides.[7–10]

The nature of the reaction occurring at the double bond of monounsaturated acids such as oleic, or in the case of hydroxy monoethenoid acids such as ricinoleic acid, as well as in glyceride oils containing these acids, remained obscure for many years. It is now generally assumed that when an unsaturated hydroxy acid, such as ricinoleic acid, is treated with sulfuric acid at low temperatures (35°C. or below), two reactions occur, the first of which consists in esterification of the hydroxyl group as shown in the following equation:

$$CH_3(CH_2)_5CHOHCH_2CH{:}CH(CH_2)_7COOH + H_2SO_4 \longrightarrow$$

$$CH_3(CH_2)_5CH(O{\cdot}SO_3H)CH_2CH{:}CH(CH_2)_7COOH + H_2O$$

The hydrogen of the introduced sulfate group is replaceable by alkali metals, and compounds of this type, therefore, form alkali salts containing the group $—CH(OSO_3Na)CH_2CH{:}CH—$. Turkey-red oil, made by treating castor oil with sulfuric acid, forms salts in this manner which are

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[3] D. Burton and G. F. Robertshaw, *Sulphated Oils and Allied Products*, Chem. Pub. Co., New York, 1940, pp. 21–35. See F. H. Kroch and K. Tomlinson, *J. Intern. Soc. Leather Trades' Chem.*, 30, 316–323 (1946); D. Burton and L. F. Byrne, *ibid.*, 30, 306–315 (1946).

[4] H. K. Dean, *Utilization of Fats.* Chem. Pub. Co., New York, 1938.

[5] F. Ullmann, *Enzykolopädie der technischen Chemie.* 2nd ed. rev., Vol. IX, Urban & Schwarzenberg, Berlin, 1932, pp. 800–807.

[6] E. Frémy, *Ann.*, 19, 296–300 (1836); 20, 50–69 (1836); *Ann. chim. phys.*, 65, 113–149 (1837).

[7] A. Müller-Jacobs, *Dinglers Polytech. J.*, 229, 544–546 (1878); 251, 499–506, 547–552 (1884); 254, 302–312 (1884).

[8] L. Liechti and W. Suida, *Ber.*, 16, 2453–2458 (1883); *Dinglers Polytech. J.*, 254, 350–352 (1884).

[9] H. Schmid, *Dinglers Polytech. J.*, 250, 543–548 (1883); 254, 346–350 (1884).

[10] A. Grün and O. Corelli, *Z. angew. Chem.*, 25, 665–670, 947 (1912).

referred to as "Turkey-red oil soaps." The characteristic emulsifying and surface-active properties of these "soaps" are presumed to be due to the presence of the alkali sulfate substituent.

It was first assumed by Müller-Jacobs[7] that the radical —HSO_3 added to the double bond of oleic acid, and by Sabanejeff[11] that a product was formed corresponding to:

$$CH_3(CH_2)_7CHOHCH(HSO_3)(CH_2)_7COOH$$

This kind of compound would constitute a true sulfonic acid[12] not readily susceptible to hydrolysis, whereas the compound produced by the reaction of sulfuric acid on oleic acid readily underwent hydrolysis to form hydroxy acids. Saytzeff[13] therefore concluded that the reaction of sulfuric acid at the double bond likewise led to the formation of a monosulfuric acid ester or a hydrogen sulfate addition product. This conclusion was subsequently verified by Benedikt and Ulzer[14] and by Geitel.[15]

$$CH_3(CH_2)_7CH{:}CH(CH_2)_7COOH + H_2SO_4 \longrightarrow CH_3(CH_2)_7CH_2CH(O{\cdot}SO_3H)(CH_2)_7COOH$$

When this sulfo derivative reacts with water, hydrolysis occurs with the formation of the corresponding hydroxy acid:

$$CH_3(CH_2)_7CH_2CH(O{\cdot}SO_3H)(CH_2)_7COOH + H_2O \longrightarrow CH_3(CH_2)_7CH_2CHOH(CH_2)_7COOH + H_2SO_4$$

Therefore, it is presumed in the case of ricinoleic acid that both the hydroxy group and the double bond react with sulfuric acid to form sulfates rather than sulfonates. However, reaction probably occurs more readily at the hydroxyl group than at the double bond and the end product, therefore, probably consists of a mixture of mono- and polysulfates whose relative proportions depend on the reaction conditions.

Various oils and fatty acids are subjected to the action of sulfuric acid to form products similar to those illustrated by oleic and ricinoleic acids. These products were first applied in mordant dyeing of textiles but are now used in a variety of textile operations. So-called "sulfonated" or red oil prepared by the action of sulfuric acid on olive oil first appears to have been used in mordant dyeing by Runge.[16–18] The first use of Turkey-red oil prepared from castor oil is attributed to Walter Crum (1875) of Scot-

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[11] A. Sabanejeff, *J. Russ. Phys.-Chem. Soc.*, **18**, 35–49, 87–98 (1886).

[12] K. H. Bauer and G. Kutscher, *Chem. Umschau Fette Öle Wachse Harze*, **32**, 57–64 (1925).

[13] M., C., and A. Saytzeff, *J. prakt. Chem.*, **35**, 369–390 (1887); *J. Russ. Phys.-Chem. Soc.*, **18**, 328–348 (1886).

[14] R. Benedikt and F. Ulzer, *Monatsh.*, **8**, 208–217 (1887).

[15] A. C. Geitel, *J. prakt. Chem.*, **37**, 53–90 (1888).

[16] F. F. Runge, *Farbenchemie.* 3 vols., Mittler, Berlin, 1834–1850.

[17] J. Dépierre, *Traité de la teinture et de l'impression des matières colorantes artificielles.* Vol. II, Baudry, Paris, 1891–1905, p. 210.

[18] E. Lauber, *Dinglers Polytech. J.*, **247**, 469–471 (1883).

land.[5] In addition to olive and castor oils, fish, sperm, linseed, soybean, and rapeseed oils are now sulfated or sulfonated for use as textile assistants, leather-filling agents, cutting oils, etc.

(b) *Hydrolysis of Sulfated Fats and Fatty Acids*

Sulfation of fatty oils by means of sulfuric acid is generally accompanied by hydrolysis of the glyceride and of the sulfate, which reactions are in turn followed by others involving estolide and lactide formation as well as some dimerization. The di- and monoglycerides formed by hydrolysis are, in whole or in part, esterified with sulfuric acid to form heteroglycerides containing both fatty acid and inorganic radicals.

Unsaturated fatty acids behave in much the same manner as was observed by Price and Griffith[19] in the course of an investigation on the alkaline hydrolysis of sulfated oleic acid. In fact tetrameric compounds were isolated from sulfated oleic acid which were assumed to have been formed by interesterification between the carboxyl and hydroxyl groups of the sulfated acid. These estolides are not readily hydrolyzed by mineral acids but, on alkaline hydrolysis, apparently regenerate monomeric hydroxy acids. In fact Price and Griffith[19] patented a process comprising sulfation with sulfuric acid or oleum followed by alkaline hydrolysis as a means of obtaining high yields (70–75%) of hydroxy acids compared to yields of 50% or less normally obtained by acid hydrolysis.

Hydroxyl groups have been detected in unsaturated fatty acids subjected to sulfation reactions at positions considerably removed from the double bond. Whether they are formed by direct hydroxylation at these remote positions, or by sulfation followed by hydrolysis, or by migration of the hydroxyl group during hydrolysis has not yet been established. For example, Shukoff and Schestakoff[20] found that heating the higher monoethenoid acids with concentrated sulfuric acid produced hydroxy acids which were subsequently dehydrated to form lactones. 9-Hydroxy- and 10-hydroxystearic acids were assumed to produce γ-stearolactone as the result of migration of the hydroxyl group to the fourth carbon atom. Oleic and elaidic acids were presumed to undergo hydroxylation at the double bond, followed by migration of the hydroxyl group, and lactonization to produce γ-stearolactone. Erucic acid and $\Delta^{10,11}$-undecenoic acid were presumed to form γ-behenolactone and γ-undecanolactone, respectively. Only the γ-behenolactone was obtained in crystalline form (m.p. 63.5°C.), which on oxidation with chromic acid produced γ- or 4-ketobehenic acid (m.p. 103°C.). The γ-undecanolactone, on treatment with acid or alkali, gave γ- or 4-hydroxybehenic acid (m.p. 34°C.). The oily reaction products

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[19] D. Price and R. Griffith (to National Oil Products Co.), U. S. Pat. 2,367,050 (Jan. 9, 1945).

[20] A. A. Shukoff and P. J. Schestakoff, *J. Russ. Phys.-Chem. Soc.*, **40**, 830–839 (1908).

were apparently not homogeneous and the conclusions concerning their structures can therefore not be considered as settled.

Schaeffer and co-workers[21] subjected oleic acid to sulfation at 10°C. with a 3:1 molar ratio of sulfuric acid (95.5%) and hydrolyzed the resulting product with alcoholic potassium hydroxide. The hydrolyzate was reacidified and esterified with methanol and fractionally distilled to separate the methyl monohydroxystearate fraction. The distilled fraction was oxidized with nitric acid with ammonium vanadate as catalyst and the oxidation products separated by steam distillation. Esters of dibasic acids having more than ten carbon atoms were found in the water-insoluble portion. The dimethyl ester of 14-tetradecanedicarboxylic acid (m.p. 49.5–50.3°C.) was isolated and identified. Esters of monobasic acids longer than decanoic were stated to be present but were not specifically identified.

It is evident that the so-called "sulfonated" oils and acids of commerce consist of various mixtures of sulfated oil, sulfated acids, sulfuric acid esters, hydroxy acids, estolides, lactides, and di- or higher polymeric substances, depending on the nature of the raw material and the conditions of "sulfonation" (sulfation). However, under certain conditions of sulfonation to be mentioned later, these products may also contain some true sulfonated acids or oils.

Sulfated Alcohols.—In addition to the sulfates prepared by treatment of fatty acids and oils with sulfuric acid, other surface-acting compounds containing sulfate radicals are known. About 1930, a group of detergents (Gardinol, Dreft, Drene, etc.), consisting of sulfates of long chain alcohols prepared by catalytic hydrogenation of fats or fatty acids, were placed on the market. They may be represented as being prepared according to the following scheme:

$$\mathrm{RCOOH} \xrightarrow{H_2} \mathrm{RCH_2OH} \xrightarrow{O(SO_2ONa)_2} \mathrm{RCH_2OSO_2ONa}$$

They may also be produced from mono- and diglycerides in which one of the hydroxyl groups is esterified with sulfuric acid or sodium pyrosulfate, $Na_2S_2O_7$. Syntex M, sodium glyceryl monolaurate sulfate, is typical of this class of commercial product.

(c) *Sulfonation Reactions*

True sulfonic acids, in which carbon-to-sulfur bonding occurs, may be prepared by a variety of methods but particularly by carrying out the sulfonation in a relatively anhydrous medium. Oleum, sulfur trioxide, and chlorosulfonic acid are generally employed in treating unsaturated acids or oils containing these acids for the production of true sulfonated products.

When fuming sulfuric acid (oleum) is used in place of sulfuric acid, sul-

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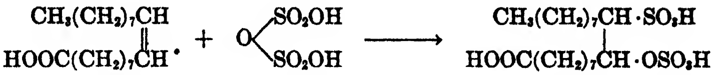
[21] B. B. Schaeffer, E. T. Roe, J. A. Dixon, and W. C. Ault, *J. Am. Chem. Soc.*, **66**, 1924–1925 (1944).

fonation probably occurs according to the following reaction, illustrated with oleic acid:



$$\begin{array}{l} CH_3(CH_2)_7CH \\ \quad\quad\quad\quad\; \| \\ HOOC(CH_2)_7CH \end{array} + O\begin{array}{l} SO_2OH \\ SO_2OH \end{array} \longrightarrow \begin{array}{l} CH_3(CH_2)_7CH\cdot SO_3H \\ \quad\quad\quad\quad\; | \\ HOOC(CH_2)_7CH\cdot OSO_3H \end{array}$$

The resulting product therefore contains a sulfate and a sulfonic acid group. The former, on hydrolysis with water, is converted to a hydroxy group while the latter is unaffected. The final product will, therefore, be a hydroxysulfonic acid:

$$CH_3(CH_2)_7CH(SO_3H)CHOH(CH_2)_7COOH$$

If the reaction with sulfuric acid is carried out in the presence of an organic acid anhydride or chloride, sulfonation is claimed to occur at a carbon atom adjacent to the double bond.[22] Thus, methyl oleate when treated with acetyl chloride and sulfonated at 0°C. with sulfuric acid is claimed to produce among other products a true sulfonic acid in accordance with the following equation:

$$CH_3(CH_2)_7CH:CHCH_2(CH_2)_6COOR \xrightarrow[H_2SO_4]{CH_3COCl} CH_3(CH_2)_7CH:CHCH(SO_3H)(CH_2)_6COOH$$

Another representative of the class of true sulfonates derived from fatty acids, but which contains the carbon-sulfur bond in the ester portion of the molecule, is sodium β-oleylethane sulfonate (Igepon A). This product is prepared by esterifying oleic acid with isethionic acid and treating the sulfonic acid with alkali:

$$CH_3(CH_2)_7CH:CH(CH_2)_7COOH + HOCH_2CH_2SO_3H \longrightarrow$$
$$CH_3(CH_2)_7CH:CH(CH_2)_7COOCH_2CH_2SO_3Na$$

A similar product (Igepon T) results when oleic acid is treated with taurine, $NH_2CH_2CH_2SO_3H$. Reaction occurs between the hydroxyl group of the acid and the amino hydrogen with the formation of a substituted amide, $CH_3(CH_2)_7CH:CH(CH_2)_7CONHCH_2CH_2SO_3Na$.

The number of sulfated and sulfonated derivatives of the fatty acids is now considerable and their industrial production is limited more by economic than chemical considerations. Reference should be made to special texts, particularly those of Burton and Robertshaw[3] and Dean,[4] for detailed information concerning various sulfating and sulfonating agents and reactions for producing the various products of this type.

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[22] H. Bertsch (to H. Th. Böhme Akt.), U. S. Pat. 1,923,608 (Aug. 22, 1933).

E. SYNTHESIS OF FATTY ACIDS

CHAPTER XX

IN VITRO SYNTHESIS OF FATTY ACIDS

1. Introduction

The earliest systematic synthesis of normal fatty acids dates from about the 1870's although various methods were known and applied prior to this time in the preparation of individual fatty acids. A number of methods are now available for accomplishing the synthesis of practically all of the normal fatty acids and several methods are available which are especially applicable to the synthesis of unsaturated fatty acids. Most of the methods involve the use of compounds such as alcohols, aldehydes, nitriles, or other acids of the approximate molecular weight of the required acid and converting these by oxidation, hydrolysis, or condensation to the corresponding acid. In some cases the acids may be produced by oxidative degradation of compounds of high molecular weight as, for example, the air oxidation of paraffins obtained synthetically by the Fischer-Tropsch process or by distillation of coal.

While most of the known methods are generally applicable to the synthesis of low molecular weight fatty acids, they may produce very low yields or fail entirely when applied to the synthesis of long chain acids. None of the methods can therefore be considered as standard or generally applicable in every case wherever the need arises for some particular synthetic acid. However, some effort has been made to include a number of general and special methods for the preparation of pure acids in *Organic Syntheses*.[1,2] The number of acids included therein is now fairly extensive and includes both normal and substituted acids such as amino-, arseno-, bromo-, chloro-, dichloro-, hydroxy-, methyl-, and phenyl-substituted acids. Some of the methods involve the preparation of the required acids from natural sources rather than synthesis from simpler molecules.

Although these methods are not generally applicable to the preparation of all members of a given homologous series, it is oftentimes possible to extend their applicability by minor modifications. Directions for the preparation of alkylhalides and halohydrins, as well as higher alcohols, which are often required as intermediates in various fat and fatty acid syntheses are also

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[1] H. Gilman, *Organic Syntheses*. Collective Vol. I, Wiley, New York, 1932.

[2] A. H. Blatt, *Organic Syntheses*. Collective Vol. II, Wiley, New York, 1943.

included in this collection of methods. Among the intermediates to be found therein are allyl alcohol and bromide, *n*-butyl and isobutyl bromides and chlorides, *n*-butanoyl chloride, ethyl, *n*-octyl and *n*-dodecyl bromides, glycerol-α,α'-dichloro- and dibromohydrin, glycerol-α-monochlorohydrin, *n*-heptyl alcohol, methyl-*n*-hexylcarbinol, *n*-hexadecyl iodide, lauryl alcohol, oleyl alcohol, etc.

Among the earliest syntheses of the saturated acids are those of Lieben and Rossi[3] and of Lieben and Janecek[4] who prepared all of the normal acids from acetic to heptanoic. Starting with methyl alcohol, they applied the reactions shown in the accompanying equations and repeated them in sequence until the chain was lengthened to seven carbon atoms;

$$CH_3OH \longrightarrow CH_3I \longrightarrow CH_3CN \longrightarrow CH_3COOH \longrightarrow CH_3CHO \longrightarrow$$
$$CH_3CH_2OH \longrightarrow CH_3CH_2I \longrightarrow CH_3CH_2CN \longrightarrow CH_3CH_2COOH, \text{ etc.}$$

Higher fatty acids have also been prepared by a modification or extension of this method. For example, Francis, Piper, and Malkin[5] prepared a number of the higher fatty acids by reducing the ethyl ester of the parent acid with hydrogen under pressure and at a high temperature, and then halogenating the alcohol and reacting it with hydrogen cyanide followed by saponification. The sequence of reactions used were as follows:

$$\underset{\text{Ethyl stearate}}{C_{17}H_{35}COOC_2H_5} \xrightarrow{H_2} C_{17}H_{35}CH_2OH \xrightarrow{HI} C_{17}H_{35}CH_2I \xrightarrow{HCN}$$
$$C_{17}H_{35}CH_2CN \xrightarrow{H_2O} \underset{\text{Nonadecanoic acid}}{C_{17}H_{35}CH_2COOH}$$

Margaric acid was prepared from palmitic acid and the C_{19}, C_{20}, and C_{21} acids were prepared from stearic acid by repetitions of this method. Erucic acid was first reduced to behenic acid, esterified, reduced to the corresponding alcohol, and from it the C_{23} and C_{26} acids were prepared by the abovementioned sequence of reactions.

Levene and Taylor[6] employed a method similar to that used by Francis *et al.*, except that the ethyl ester was reduced with metallic sodium in alcohol solution. Oleic acid was reduced to stearic acid, and erucic to behenic or *n*-docosanoic acid, which formed the materials for increasing the chain length by way of the nitriles. The series of odd- and even-numbered acids from stearic to hexacosanoic were prepared in this manner.

Hofmann[7] devised a second method of synthesis based on the conversion

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[3] A. Lieben and A. Rossi, *Ann.*, **159**, 58–69, 70–79 (1871).

[4] A. Lieben and G. Janecek, *Ann.*, **187**, 126–149 (1877).

[5] F. Francis, S. H. Piper, and T. Malkin, *Proc. Roy. Soc. London*, **A128**, 214–252 (1930).

[6] P. A. Levene and F. A. Taylor, *J. Biol. Chem.*, **59**, 905–921 (1924).

[7] A. W. Hofmann, *Ber.*, **14**, 2725–2736 (1881); **15**, 407–416, 752–762, 762–775 (1882); **17**, 1406–1412 (1884); **18**, 2734–2741 (1885). See E. Lutz, *ibid.*, **19**, 1433–1441 (1886).

of the amide of a fatty acid to an acid containing one less carbon atom than the original amide. According to this method, the amides are treated with bromine and caustic potash and the carbonyl group is split off in the form of carbon dioxide with the formation of a primary amine containing one less carbon atom. The amine is then transformed into the corresponding nitrile. Hydrolysis of the nitrile produces the corresponding acid which can again be converted into an amide and the process repeated according to the following scheme:

$$\underset{\text{Stearic acid}}{C_{16}H_{33}CH_2COOH} \longrightarrow C_{16}H_{33}CH_2CONH_2 \longrightarrow C_{16}H_{33}CH_2NH_2 \longrightarrow$$
$$C_{16}H_{33}CN \longrightarrow \underset{\text{Margaric acid}}{C_{16}H_{33}COOH}$$

By the use of these reactions, Krafft[8] and others converted stearic acid to margaric acid and the latter to palmitic acid, and by further reactions of the same type to nonanoic (pelargonic) acid. It may be said, therefore, that all of the odd- and even-numbered carbon acids from acetic to palmitic have been synthesized by means of these two series of reactions starting with either methyl alcohol or naturally occurring stearic acid.

One of the oldest methods of producing fatty acids of shorter chain length than the original acid, which was also used by Krafft, involves the pyrolysis of the barium salts of the higher acids in the presence of barium acetate. This reaction produces an alkyl methyl ketone which, on oxidation, yields the next lower homologous acid:

$$\underset{\text{Barium stearate}}{Ba(C_{17}H_{35}COO)_2} \xrightarrow[\text{distill}]{Ba(CH_3COO)_2} \underset{\text{Methyl stearone}}{2\ C_{17}H_{35}COCH_3} \xrightarrow{CrO_3} \underset{\text{Margaric acid}}{2\ C_{16}H_{33}COOH}$$

Margaric acid by the same reaction yields palmitic acid.

The synthesis of the lower members of the aliphatic acid series can be readily effected by means of the Grignard[9] reaction. When carbon dioxide is passed into an ethereal solution of organomagnesium halides, RMgI or RMgBr, an organomagnesium compound of the formula $RCOO \cdot MgX$ is precipitated which, on decomposition by ice and dilute sulfuric acid, yields the corresponding acid. Grignard prepared acetic, isovaleric, and isohexanoic acids by this means. The synthesis of acetic acid from methyl iodide may be represented by the following equations:

$$CH_3I \xrightarrow{+Mg} CH_3MgI \xrightarrow{+CO_2} CH_3COOMgI \xrightarrow{+HOH} CH_3COOH + MgOHI$$

Although applicable to the preparation of the lower members of the aliphatic acid series, the Grignard reaction has not been extensively used to

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[8] F. Krafft, *Ber.*, 12, 1664–1668, 1668–1673 (1879).

[9] V. Grignard, *Ann. Univ. Lyon* [N.S. 1], *Sciences, médecine*, No. 6, 1–116 (1901). See *Sur les combinaisons organomagnésiennes mixtes et leur application à des synthèses d'acides, d'alcools et d'hydrocarbures*, Gauthier-Villars, Paris; Rey, Lyon. 1901, p. 118.

TABLE 140

PROPERTIES OF ALIPHATIC ACIDS AND DERIVATIVES PREPARED BY THE MALONIC ESTER SYNTHESIS BY BLEYBERG AND ULRICH[a]

Number of C atoms	Acid			Anhydride			Ethyl ester melting point, °C.	Alcohol melting point, °C.	Iodide melting point, °C.
	Melting point, °C.	Density, d^{100}	Refractive index, n_D^{100}	Melting point, °C.	Density, d^{100}	Refractive index, n_D^{100}			
20	76.1–76.3	0.8240	1.4250	77.5–77.7	0.8225	1.4301	...	...	...
22	80.3–80.7	0.8221	1.4270	81.7–81.9	0.8206	1.4320	48.0–48.5	70.0–70.5	47.5–48.0
24	84.5–84.9	0.8207	1.4287	86.0–86.3	0.8196	1.4329	54.5–55.0	75.2–75.5	53.4–53.8
26	87.7–87.9	0.8198	1.4301	89.3–89.5	0.8188	1.4337	59.5–59.8	79.3–79.6	58.2–58.5
28	90.3–90.5	0.8191	1.4313	92.7–92.9	0.8183	1.4345	64.8–65.0	82.9–83.1	62.8–63.2
30	91.9–92.1	...	1.4323	94.6–94.7	...	1.4352	...	...	...

[a] W. Bleyberg and H. Ulrich, *Ber.*, 64, 2504–2513 (1931).

prepare the higher fatty acids because the chain length can only be extended one carbon atom at a time and the necessary Grignard compounds of the higher alkyl halides are not easily prepared.

2. Malonic Ester Synthesis

The malonic ester synthesis[10–12] constitutes a classical method for increasing the chain length of lower members of the aliphatic series. Like acetoacetic ester, the ester of malonic acid, $ROOC \cdot CH_2 \cdot COOR$, possesses two methylene hydrogen atoms which are readily replaceable by sodium. When the sodium compound is treated with an alkyl or other organic halide, the metal is replaced by the alkyl residue. On heating to a high temperature, the substituted malonic ester loses a molecule of carbon dioxide with the formation of a monobasic acid.

This method has been used frequently to prepare the lower members of the aliphatic acid series and Bleyberg and Ulrich[13] applied it also to the preparation of the even-numbered carbon acids from C_{20} to C_{30} and to the preparation of the corresponding anhydrides, ethyl esters, alcohols, and iodides. The method of preparation of the higher acids from the next lower homolog by this method is illustrated by the following equation:

$$RCOOH + C_2H_5OH \longrightarrow RCOOC_2H_5 \xrightarrow{Na} RCH_2OH \xrightarrow{HI} RCH_2I$$

$$\xrightarrow[\text{malonic ester}]{\text{sodium}} RCH_2CH(CO_2Et)_2 \xrightarrow{\text{hydrolysis}} RCH_2CH(COOH)_2 \xrightarrow{\text{heat}} RCH_2CH_2COOH$$

The various intermediates, fatty acids, and derivatives prepared by Bleyberg and Ulrich by application of the malonic ester synthesis are given in Table 140.

3. Acetoacetic Ester Synthesis

The acetoacetic ester synthesis is one of great utility in building up organic compounds and it is especially useful in the synthesis of the higher aliphatic acids. An example of the practical utility of this synthesis is represented by its application to the commercial production of caproic acid. At the time that caproic acid was first required in considerable quantity for the production of hexylresorcinol, butyl alcohol was commercially available and provided a means of obtaining caproic acid by way of the acetoacetic ester synthesis.[14]

The synthesis carried out with acetyl acetate and butyl bromide is:

$$2\,CH_3COOC_2H_5 + Na + \underset{\text{(trace)}}{NaOC_2H_5} \longrightarrow CH_3C(ONa){:}CHCOOC_2H_5 + C_2H_5OH$$

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[10] M. Conrad and C. A. Bischoff, *Ann.*, 204, 121–127 (1880).
[11] W. A. Noyes, *J. Am. Chem. Soc.*, 18, 1105–1106 (1896).
[12] C. Daimler, *Ber.*, 20, 203–204 (1887); *Ann.*, 249, 173–181 (1888).
[13] W. Bleyberg and H. Ulrich, *Ber.*, 64, 2504–2513 (1931).
[14] N. L. Drake and R. W. Riemenschneider, *J. Am. Chem. Soc.*, 52, 5005–5008 (1930).

The sodium ethylate produces an aldol condensation between the α-hydrogen of one molecule of the ester and the carbonyl group of another. The resulting product loses a molecule of alcohol, enolizes, and forms the sodio derivative. The sodio derivative on treatment with absolute alcohol and *n*-butyl bromide forms ethyl-*n*-butyl acetoacetate as follows:

$$CH_3C(ONa){:}CHCOOC_2H_5 + C_4H_9Br \longrightarrow CH_3COCH(C_4H_9)COOC_2H_5 + NaBr$$

On heating the ethyl-*n*-butyl acetoacetate with alcoholic potash, there is obtained the potassium salts of acetic acid and *n*-butylacetic or caproic acid from which the free acid is produced by acidification:

$$CH_3COCH(C_4H_9)COOC_2H_5 + 2\,KOH \longrightarrow CH_3COOK + C_4H_9CH_2COOK + C_2H_5OH$$

When *n*-amyl alcohol became commercially available, the production of caproic acid by way of the acetoacetic ester method was abandoned in favor of the simpler method of converting the alcohol to the acid via the iodide and cyanide (nitrile) according to the method used by Lieben and coworkers[3,4] to which reference has already been made. However, the method still retains its utility and merit as a laboratory method for the preparation of various types of long chain aliphatic compounds, including all of the normal aliphatic acids.

The self-condensation of esters having hydrogen on the α-carbon atom may be effected readily to produce keto esters which in turn can be hydrolyzed to form ketones. This self-condensation amounts to an acylation of the ester by another molecule of the same ester as indicated in the following equations:

$$RCH_2COOC_2H_5 + HCHRCOOC_2H_5 \longrightarrow RCH_2COCHRCOOC_2H_5 + C_2H_5OH$$
$$R_2CHCOOC_2H_5 + HCR_2COOC_2H_5 \longrightarrow R_2CHCOCR_2COOC_2H_5 + C_2H_5OH$$

In the case of some esters the condensation reaction is reversible and certain β-keto esters, especially those having one or two substituents on the α-carbon atom, are cleaved by alcoholic sodium hydroxide to form esters. For example, α-propionyl propionate is formed by the self-condensation of ethyl propionate in the presence of sodium ethoxide, but when treated with alcoholic sodium ethoxide it reverts to ethyl propionate. The reversibility of the reaction may be represented as follows:

$$2\,RCH_2COOC_2H_5 + NaOC_2H_5 \rightleftharpoons RCH_2C(ONa){:}C(R)COOC_2H_5 + 2\,C_2H_5OH$$

McElvain[15] avoided this back reaction in the case of the preparation of ethyl-α-propionyl propionate and ethyl-α-butyryl butyrate by periodic distillations of portions of the alkyl ester which had been used in considerable excess at the start of the reaction.

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[15] S. M. McElvain, *J. Am. Chem. Soc.*, **51**, 3124–3130 (1929).

The self-condensation of the acetoacetic ester type has been used to prepare a fairly extensive series of aliphatic β-keto esters of the type RCH_2CO-$CH(R)COOC_2H_5$. Briese and McElvain[16] prepared the β-keto esters of all of the aliphatic acids from *n*-valeric to myristic by the forced self-condensation of the corresponding ethyl esters in the presence of sodium ethoxide. The yields and boiling or melting points of these β-keto esters are shown in Table 141 above.

TABLE 141

CONDITIONS AND TIME REQUIRED FOR FORMATION OF β-KETO ESTERS[a]

Ethyl ester used	Reaction temperature, °C.	Reaction pressure, mm.	Time for completion, hrs.	Keto ester	
				Yield, %	B.p.$^{5\text{ mm.}}$ or m.p. in °C.
Valerate	89–90	120–130	7–8	77	109–110
Caproate	90–95	75–80	7–8	80	132–133
Heptanoate	90–95	60–65	7	78	147–148
Caprylate	90–95	20–25	5	84	173–175
Nonanoate	100–105	15–20	4–5	74	195–200
Caprate	105–110	15–20	4	74	220–225
Laurate	120–125	15–20	4	79	28–29 (m.p.)
Myristate	125–130	15–20	4	84	37–38 (m.p.)

[a] R. R. Briese and S. M. McElvain, *J. Am. Chem. Soc.*, 55, 1697–1700 (1933).

Each of the keto esters shown in Table 141 was converted by hydrolysis to the corresponding ketone by refluxing the ester for three or four hours with a 5% solution of potassium hydroxide in 90% alcohol. In the cases of valerone and caprone, the alcohol was removed by distillation and the residue diluted with water. The higher ketones crystallized from the reaction mixture on cooling. The hydrolysis proceeds smoothly and readily to give the ketones in good yield. The properties and yields of the ketones prepared by hydrolysis of the keto esters in Table 141 are shown in Table 142 above.

TABLE 142

PROPERTIES AND YIELD OF KETONES OBTAINED BY HYDROLYSIS OF THE CORRESPONDING KETO ESTERS[a]

Ketone	Melting point, °C.	Yield, %	Ketone	Melting point, °C.	Yield, %
Valerone	[b]	72	Nonanone	52–53	93
Caprone	14–15	81	Capraone	58–59	95
Heptanone	30–31	82	Laurone	68–69	98
Caprylone	41–42	93	Myristone	78–79	97

[a] R. R. Briese and S. M. McElvain, *J. Am. Chem. Soc.*, 55, 1697–1700 (1933).
[b] B.p. 88°C. at 22 mm. Hg.

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[16] R. R. Briese and S. M. McElvain, *J. Am. Chem. Soc.*, 55, 1697–1700 (1933). See S. M. McElvain, *ibid.*, 51, 3124–3130 (1929); A. C. Cope and S. M. McElvain, *ibid.*, 54, 4319–4325 (1932).

4. Robinson-Robinson Synthesis

The Robinson and Robinson[17] synthesis, developed originally for the preparation of the higher aliphatic keto acids, has in the course of its various modifications become of first importance as a means of obtaining many of the long chain aliphatic acids. As originally applied, it represented a modification of the malonic ester synthesis and later of the acetoacetic ester synthesis. The value and success of the method depends on the observation by Robinson and Robinson that, when two acyl groups occur in a long chain acylacetic ester, a stepwise hydrolysis can be carried out in such a manner that the stronger acid is preferentially removed.

It was known that oleic acid could be prepared from 10-ketostearic acid by its reduction to hydroxystearic acid followed by conversion to iodostearic acid and dehalogenation with caustic potash, hence a means of producing keto acids for conversion to the corresponding unsaturated acids was desired. The synthesis developed by the Robinsons made it possible to prepare any keto acid of the formula $R(CH_2)_mCO(CH_2)_nCOOH$. It was found that this synthesis could also be accomplished by the condensation of ethyl sodio-*n*-alkyl malonate and a carbethoxy alkyl chloride, or preferably by the use of ethyl sodio-2-acetyl alkylate and a carbethoxy alkyl chloride.

When ethyl sodio-2-acetyl nonanoate and 9-carbethoxynonanoyl chloride were brought into reaction in ethereal solution, the ester, $CH_3(CH_2)_6 \cdot CAc(COOEt)CO(CH_2)_8COOEt$, was produced. When cautiously hydrolyzed, first with cold dilute alkali, then with boiling dilute sulfuric acid, and finally with boiling aqueous sodium hydroxide, the sparingly soluble, crystalline sodium salt of 10-ketostearic acid was obtained, and this was converted by the methods given above to oleic acid unaccompanied by either elaidic or stearic acid.

6-Ketostearic and 4-ketopalmitic acids were synthesized by the same method, using ethyl sodio-2-acetyl *n*-tridecanoate and 5-carbethoxyvaleroyl chloride in the first case and ethyl sodio-2-acetyl *n*-tridecanoate and 3-carbomethoxypropionoyl chloride in the second case.

The method described above, although successful, gave only moderately satisfactory yields because a varying but always considerable amount of dibasic acid, $COOH(CH_2)_nCOOH$, was formed in the course of the synthesis. The method was improved by G. M. Robinson[18] by using as starting materials ethyl acetoacetate and the ω-bromo ester, $Br(CH_2)_nCOOEt$. The keto acid obtained on hydrolysis of the reaction product was subsequently reduced to the normal acid by the Clemmensen[19] method. The improved

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[17] G. M. Robinson and R. Robinson, *J. Chem. Soc.*, **127**, 175–180 (1925); **1926**, 2204–2209; *Ann. Repts. Progress Chem.*, **22**, 80 (1926).

[18] G. M. Robinson, *J. Chem. Soc.*, **1930**, 745–751.

[19] E. Clemmensen, *Ber.*, **46**, 1837–1843 (1913); **47**, 51–63, 681–687 (1914). See H. R. Le Sueur and J. C. Withers, *J. Chem. Soc.*. **107**, 736–739 (1915).

synthesis may be illustrated by the following equations:

(*1*) $CH_3COCHNaCOOEt + Br(CH_2)_{10}COOEt \longrightarrow$

(*2*) $CH_3COCH(COOEt)(CH_2)_{10}COOEt \xrightarrow[CH_3(CH_2)_nCOCl]{Na}$

(*3*) $CH_3(CH_2)_nCO \cdot C \cdot (COOEt)(CO \cdot CH_3)(CH_2)_{10}COOEt \longrightarrow$

$$CH_3(CH_2)_nCOCH_2(CH_2)_{10}COOH$$

Ethyl α-acetyl brassylate (*2*) is obtained in good yield from the readily available 11-bromoundecanoic ester. The complex (*3*) resulting from the condensation of the sodio derivative of (*2*) with an acid chloride, when submitted to a graded hydrolysis, yields the desired long chain keto acid accompanied by varying amounts of 13-ketotetradecanoic acid. These higher keto acids are readily reduced by the Clemmensen method, and thereby twelve carbon atoms are added at a time to the original acid.

By means of this method, stearic acid yields *n*-triacontanoic acid[20] and undecanoic and lauric acids yield tricosanoic and tetracosanoic acids, respectively.[21] Starting with behenoyl chloride, Francis *et al.*[22] synthesized tetratriacontanoic acid and then hexatetracontanoic acid ($C_{46}H_{92}O_2$) by the Robinson-Robinson method. A somewhat similar method was used by Perkins and Cruz[23] for synthesizing *dl*-chaulmoogric acid. In this case, acetoacetic ester was condensed with ω-cyanoundecanoyl chloride and then with $\Delta^{2,3}$-chlorocyclopentene and the resulting ketochaulmoogric acid was reduced with hydrazine and sodium ethylate to *dl*-chaulmoogric acid.

The compilation in Table 143 of the keto, normal, and unsaturated acids prepared by means of the original and modified Robinson-Robinson syntheses testifies to the value and utility of these methods of obtaining a variety of long chain aliphatic acids and corresponding derivatives. All of the keto acids listed in this table can be reduced to the corresponding hydroxy acids or oximated to produce the corresponding oximes.

5. Arndt-Eistert Synthesis

The Arndt-Eistert synthesis has been used in preparing the next higher homologs of the more readily available lower acids. It is applicable to both aliphatic and aromatic acids, but appears to have been used primarily for the synthesis of cycloalkyl, aromatic, and heterocyclic acids rather than for long chain normal aliphatic acids. The synthesis involves three steps, namely, the preparation of the acid chloride, formation of a diazo ketone,

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[20] G. M. Robinson, *J. Chem. Soc.*, **1934**, 1543–1545.

[21] R. Ashton, R. Robinson, and J. C. Smith, *J. Chem. Soc.*, **1936**, 283–285.

[22] F. Francis, A. M. King, and J. A. V. Willis, *J. Chem. Soc.*, **1937**, 999–1004.

[23] G. A. Perkins and A. O. Cruz, *J. Am. Chem. Soc.*, **49**, 1070–1077 (1927).

TABLE 143

KETO, SATURATED, AND UNSATURATED ACIDS AND DERIVATIVES PREPARED BY THE ROBINSON-ROBINSON SYNTHESIS

Number of C atoms	Acid or derivative	M.p., °C.
	Saturated keto acid or ester	
10	β-Benzoylpropionic	116
13	10-Ketotridecanoic	63
14	4-Ketomyristic	87
16	Ethyl 13-ketomyristate	28–29
16	4-Ketopalmitic	91–92
16	5-Ketopalmitic	88
16	7-Ketopalmitic	78
16	8-Ketopalmitic	77–78
16	4,13-Diketopalmitic	101
18	6-Ketostearic	87
18	9-Ketostearic	83
18	10-Ketostearic	83 (80.14)[a]
19	10-Ketononadecanoic	86–87
21	13-Keto-15-phenylpentadecanoic	72–74
21	15-Phenylpentadecanoic	60–61
22	10-Ketobehenic	94
23	Tricosanoic	78.86 (78.85)[a]
24	13-Ketotetracosanoic	95
24	Tetracosanoic	84 (83.5)[a]
28	13-Keto-22-phenylbehenic	81
28	22-Phenylbehenic	81
30	Ethyl 22-phenylbehenate	53
30	13-Keto-*n*-triacontanoic	104
30	*n*-Triacontanoic	93.5–94
32	Ethyl triacontanoate	70.5
34	Tetratriacontanoic	98.2
42	13-Keto-*n*-dotetracontanoic	110
46	Hexatetracontanoic	107.1
	Unsaturated acids	
14	4-Keto-Δ^{13}-tetradecenoic	79.5
18	Oleic	13[a], 16[a]
18	*dl*-λ-Ketochaulmoogric	76
18	*dl*-Chaulmoogric	68.5
21	*trans*-4-Keto-Δ^{12}-heneicosenoic	82.5
	Lactones	
14	γ-*n*-Decylbutyrolactone	30–31
14	γ-Δ^{9}-Decenylbutyrolactone	26–27
16	δ-Undecylvalerolactone	29.5–30
21	γ-Δ^{8}-Heptadecenylbutyrolactone	42
	Unclassified	
16	8-Ketopalmito amide	58
30	*n*-Triacontanol	86.5
30	*n*-Triacontanyl iodide	68.5
32	*n*-Triacontanyl acetate	69

[a] Freezing points.

and rearrangement of the ketone with loss of nitrogen. The synthesis which is described in detail by Bachmann and Struve[24] may be illustrated

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[24] W. E. Bachmann and W. S. Struve, in *Organic Reactions*. R. Adams, ed Vol. I, Wiley, New York, 1942, pp. 38-62.

as follows:

$$(1)\qquad \mathrm{RCOOH + SOCl_2 \longrightarrow RCOCl + HCl + SO_2}$$

$$(2)\qquad \mathrm{RCOCl + 2\,CH_2N_2 \longrightarrow RCOCHN_2 + CH_3Cl + N_2}$$

$$(3)\qquad \mathrm{RCOCHN_2 + HOH \xrightarrow{Ag} RCH_2COOH + N_2}$$

The acid chloride is prepared by treatment of the acid with $SOCl_2$ or other halogenating agent which is then converted to the diazo ketone by treatment with diazomethane, thus introducing an additional carbon atom in the molecule. Rearrangement of the ketone to the acid with loss of nitrogen occurs when the ketone is treated with water in the presence of colloidal silver or other catalyst.

6. Synthesis of Fatty Acids from Aldehydes and Aldehyde Esters

When the aldehyde is available the corresponding fatty acid may be obtained by simple oxidation. In many cases the aldehyde is less readily available than the corresponding acid, consequently only the lower members of the aliphatic acids have, as a general rule, been prepared by direct oxidation of an aldehyde or by aldol condensation followed by oxidation. For example, it is possible by condensation of acetaldehyde to produce crotonaldehyde, $CH_3CH{:}CHCHO$. Crotonaldehyde can be reduced by zinc-copper couple to normal butyl alcohol which on oxidation produces butyric acid.

Kuhn, Grundmann, and Trischmann[25] demonstrated the fact that crotonaldehyde solutions underwent condensation in the presence of piperidine acetate to form: octatrienal, $CH_3(CH{:}CH)_3CHO$; dodecapentaenal, $CH_3(CH{:}CHCHO)_5$; and hexadecaheptaenal, $CH_3(CH{:}CH)_7CHO$. Since the last-mentioned polyene aldehyde contains sixteen carbon atoms it can be reduced to cetyl alcohol and the alcohol can be oxidized to palmitic acid. On the other hand, the malonic acid condensation product of hexadecaheptaenal can be hydrogenated and distilled to produce stearic acid.

Fischer, Hultzsch, and Flaig[26] showed that dodecapentaenal, which contains twelve carbon atoms, can be reduced to lauraldehyde from which lauric acid is obtained by oxidation. The malonic acid condensation product of dodecapentaenal gives tetradecahexaenoic acid, $CH_3(CH{:}CH)_6$-COOH which can be reduced to give myristic acid.

Noller and Adams[27] have described a method for the preparation of both normal and hydroxy saturated fatty acids from aldehyde esters. The aldehyde esters are obtained by the ozonolysis of naturally occurring unsaturated acids by the method which has been described previously.

The synthesis of the saturated acids may be illustrated by the formation

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[25] R. Kuhn, C. Grundmann, and H. Trischmann, *Z. physiol. Chem.*, **248**, IV–V (1937).

[26] F. G. Fischer, K. Hultzsch, and W. Flaig, *Ber.*, **70**, 370–375 (1937).

[27] C. R. Noller with R. Adams, *J. Am. Chem. Soc.*, **48**, 1074–1080 (1926).

of tridecanoic acid from 8-aldomethyl octoate. *n*-Butylmagnesium bromide is condensed with 8-aldomethyl octoate to give 9-hydroxymethyl tridecanoate which is then treated with phosphorus tribromide to give the corresponding bromo ester. The bromo ester is heated with alcoholic potash to give a mixture of olefinic acids which are reduced in alcohol solution with platinum oxide–platinum black and hydrogen to tridecanoic acid. The various reactions may be illustrated as follows:

$$C_4H_9MgBr + CHO(CH_2)_7COOCH_3 \longrightarrow C_4H_9CHOH(CH_2)_7COOCH_3 \xrightarrow{PBr_3}$$

$$C_4H_9CHBr(CH_2)_7COOCH_3 \xrightarrow{KOH} \text{olefinic acids} \xrightarrow{H_2} CH_3(CH_2)_{11}COOH$$

7. Synthesis of Fatty Acids from Hydrocarbons

Large scale production of fatty acids by air oxidation of paraffins was developed in Germany during World War II and during the same period a method was developed for their production from olefins. Commercial production of fatty acids by the latter process was not achieved by the time hostilities ceased, although a plant with an estimated capacity of 10,000 tons annually of synthetic alcohols was erected and would have been in operation in a short time.

(*a*) *Synthesis from Paraffins*

The first-mentioned process, namely air oxidation of paraffins in the presence of permanganate catalysts, was operated on a large scale throughout the war, although there is some doubt that the claimed productions of 60,000 tons of fatty acids in 1940 and 100,000 tons in 1944 were actually achieved. The four plants, located at Magdeburg, Witten, Heydebreck, and Ludwigschafen-Oppau in Germany, probably had a combined maximum capacity of approximately 100,000 tons of fatty acids of various types and qualities.

Any saturated paraffin fraction of the appropriate molecular weight can be used in the air-oxidation process. These paraffin or Gatsch fractions having a mean molecular weight of 280–290 may be obtained by hydrogenation of coal or by the Fischer-Tropsch synthesis. Generally, only the fatty acids derived from oxidation of the Fischer-Tropsch *Gatsch* fraction, so-called Fischer *Gatsch*, has been used for the production of edible fats, but consumption has not exceeded five per cent of the production of fatty acids from this source. The remainder of the production has been used primarily in the manufacture of soaps.

Production of Paraffin Intermediates.—The Fischer-Tropsch process for the synthesis of hydrocarbons from water gas has developed gradually over a period of more than a quarter of a century. This development can be followed through a long series of articles published in *Brennstoff Chemie* from about 1923 on.

The Fischer-Tropsch process consists essentially of the reaction of carbon monoxide and hydrogen to form primarily straight chain hydrocarbons. About 1923, the process was operated by Badische Aniline Fabrik, using an iron catalyst and high pressure which resulted in the formation of a large amount of oxidized products. The iron catalyst was activated with potassium hydroxide and the reaction carried out at about 100 atmospheres pressure. This process is no longer used anywhere in Germany. New forms of iron catalysts, lower pressures, ranging from one to fifteen atmospheres, and temperatures about 230°C. are still used and under these conditions primarily saturated and unsaturated aliphatic hydrocarbons are produced. The newer Fischer-Tropsch process employs a cobalt–thoria–magnesia catalyst to hydrogenate carbon monoxide primarily to saturated paraffins. When the ratio of carbon monoxide to hydrogen is 1:1.2 (*i.e.*, water gas ratio) the reaction product consists of a mixture of saturated and olefinic hydrocarbons with less than 0.25% of oxidized products.

When the ratio of carbon monoxide to hydrogen is 1:2, only saturated hydrocarbons are produced or saturated hydrocarbons with a very low percentage of olefinic hydrocarbons. In 1938, the reaction was carried out at substantially atmospheric pressure and a temperature of 195–205°C. Another type of hydrogenation known as "middle pressure" hydrogenation conducted at about ten atmospheres pressure was operated extensively in the 1940's. The products of the normal Fischer-Tropsch process consist of saturated hydrocarbons ranging from methane to hydrocarbons of about 1000 molecular weight and melting point of 136°C.

The reaction is explained as being the result of formation of carbides[27a] at the points of activation on the surface of the catalyst. The carbides are linearly oriented and are hydrogenated to form straight chain compounds. The reaction and catalyst are very sensitive to changes in temperature and pressure. Increase in either of these factors first results in the formation of olefins and ultimately in oxidation products.

The mixture of hydrocarbons formed in the Fischer-Tropsch process are separated into five main fractions on leaving the reaction chamber. These fractions comprise: (*1*) the condensible gas fraction, principally propane and butane; (*2*) the gasoline fraction, pentane to octane, maximum boiling point of 160°C.; (*3*) Diesel oil fraction, b.p. 220–350°C., (*4*) Gatsch fraction, b.p. 320–450°C.; and (*5*) the solid paraffin wax fraction. These fractions are separated by an arrangement of air and indirect water condensers, wash oil and charcoal scrubbers, and other devices. A very high melting wax (m.p. about 136°C.) remains adsorbed on the catalyst and results in its ultimate inactivation.

The higher paraffins comprise from 10% to 50% of the polymerized water

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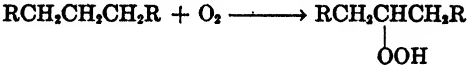
[27a] E. F. G. Herington, *Chemistry & Industry*, **1946**, 346–347.

gas depending on the manner of operation. Any of the paraffin fractions may be refractionated to produce fractions of the most desirable composition for specific applications and the higher fractions may be cracked to form olefins and lower molecular weight paraffins.

Oxidation of Fischer Gatsch Paraffins to Fatty Acids.—As previously stated, paraffin fractions of appropriate molecular weight from any source may be employed in the air-oxidation method of producing fatty acids but for use in edible fats only the Gatsch fraction from the Fischer-Tropsch process[28] can be used, as the nature of the raw material has a marked influence on the process and products of air oxidation.[29] For soapmaking purposes, the most desirable fraction contains hydrocarbons varying from $C_{18}H_{38}$ to $C_{28}H_{58}$ with an average molecular weight of 284.

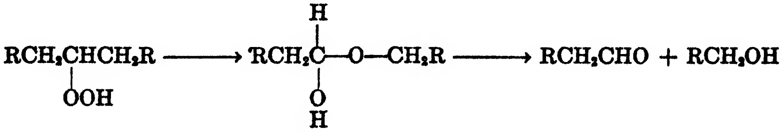
Experimental production of synthetic fatty acids by oxidation of paraffin hydrocarbons began about 1936 and reached full commercial production in 1939. The process has been described by Wittka,[30–32] Mannes,[33] Ohme,[34] Imhausen,[35] and others and is covered by numerous patents.[36]

The actual oxidation step is relatively simple and consists essentially of contacting air and paraffin in the presence of a suitable catalyst, generally $KMnO_4$ or a manganese soap such as manganese stearate. Although the exact mechanism by which oxidation occurs is unknown it is believed that O adds at various positions along the C chain to form hydroperoxides:



$$\mathrm{RCH_2CH_2CH_2R + O_2 \longrightarrow RCH_2\underset{\underset{OOH}{|}}{C}HCH_2R}$$

These hydroperoxides, being unstable, are converted successively to alcohols, aldehydes, and fatty acids presumably as follows:



$$\mathrm{RCH_2\underset{\underset{OOH}{|}}{C}HCH_2R \longrightarrow RCH_2\overset{\overset{H}{|}}{\underset{\underset{\underset{H}{O}}{|}}{C}}{-}O{-}CH_2R \longrightarrow RCH_2CHO + RCH_2OH}$$

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[28] F. Fischer and H. Pichler, *Ber.*, 72, 327–330 (1939).

[29] K. Blass, *Fette u. Seifen*, 51, 221–223 (1944).

[30] F. Wittka, *Gewinnung der höheren Fettsäuren durch Oxydation der Kohlenwasserstoffe.* Barth, Leipzig, 1940.

[31] F. Wittka, *Soap*, 16, No. 8, 28–32, 73; No. 9, 34–37, 73 (1940). See G. Wietzel, *Fette u. Seifen*, 46, 21–25 (1939); M. Aschenbrenner, *ibid.*, 46, 26–29 (1939); also F. Rofendahl, *Seifensieder-Ztg.*, 17, 68–70 (1944).

[32] F. Wittka, *Seifensieder-Ztg.*, 70, 50–51, 68–69 (1943).

[33] L. Mannes, *Die Chemie*, 57, 6–11 (1944).

[34] W. Ohme, *Oel u. Kohle*, 40, No. 5/6, 87–89 (1944).

[35] A. Imhausen, *Chem.-Ztg.*, 62, 213–215 (1938); *Kolloid-Z.*, 85, 234–246 (1938).

[36] Henkel & Cie G.m.b.H., French Pat. 832,546 (Sept. 28, 1938), 833,064 (Oct. 11, 1938); Märkischen Seifen-Industrie, French Pat. 818,796 (Oct. 4, 1937), German Pat. 722,591 (May 28, 1942); E. Keunecke (to I. G. Farbenindustrie A.-G.), U. S. Pat. 2,095,473 (Oct. 12, 1937), German Pat. 626,787 (March 10, 1936); I. G. Farbenindustrie A.-G., British Pat. 478,317 (Jan. 14, 1938); H. Pardun (to Noblee & Thörl G.m.b.H., German Pat. 723,528 (June 18, 1942).

$$2\,RCH_2CHO + O_2 \longrightarrow 2\,RCH_2COOH$$

Apparently other reactions also occur and the final reaction product consists of a complex mixture of unreacted paraffins, aldehydes, alcohols, ketones, fatty acids, hydroxy acids, esters, and other products. By separating and recycling the unreacted paraffins, about 80% of the original paraffin is ultimately recovered as fatty acids. The composition of the recovered fatty acids apparently varies considerably with the conditions of oxidation and subsequent fractionation. On a commercial scale four major fractions are generally produced which are claimed to be essentially as follows: C_4 to C_{10}, 12%; C_9 to C_{20}, 65%; C_{20} to C_{28}, 14%; residue, C_{28} and above, 9%. Somewhat different values have been reported by Wittka[31] as indicated by the data in Table 144 for a carefully fractionated sample of original mixed fatty acids.

TABLE 144

COMPOSITION OF FISCHER GATSCH PARAFFIN FRACTION AND DERIVED FATTY ACIDS[a]

Paraffin fraction		Derived fatty acids			
Number of carbon atoms	Per cent	Number of carbon atoms	Per cent	Number of carbon atoms	Per cent
19–22	27.4	7	7.25	14	8.75
22–25	31.0	8	4.25	15	9.00
25–27	23.7	9	5.70	16	6.70
27–28	11.7	10	7.40	17	6.25
Over 28	1.7	11	6.20	18	4.25
...	..	12	7.65	Over 18	18.20
...	..	13	8.30	...	..

[a] F. Wittka, *Soap*, 16, No. 8, 28–32, 73; No. 9, 34–37, 73 (1940).

Plant Process.—In actual practice, oxidation of the Fischer Gatsch fraction (b.p. 320–450°C.) is carried out as follows. The hot raw material is first centrifuged to remove any foreign solids after which it is charged into the oxidation towers. These are cylindrical vessels of ten to twelve tons' capacity made of aluminum, 1.8 to 2.3 meters in diameter and 10 meters high. The converter contains a mushroom-shaped false bottom perforated with about 1000 holes, one-sixteenth of an inch in diameter. The bottom of the converter contains an aluminum heating coil and about midway to the top, a cooling coil of the same material. The top of the converter is connected by means of a large vapor duct to a surface and then to a barometric condenser.

The catalyst, generally a 0.2% solution of potassium permanganate in water is prepared in 500-gallon tanks equipped with stirrers. In one variation of the oxidation process the paraffins may first be activated by mixing them with powdered potassium permanganate and heating to 150°C. for ten minutes. Where this step is omitted, the potassium permanganate solution is charged to the converter containing the paraffin and the mixture is heated to 110°C. to drive off the moisture. Air is then blown through the charge at the rate of about fifty cubic meters per hour per ton of charge. Since the reaction is exothermic, liberating approximately 500 calories per kilogram of paraffin, the charge must be cooled in order to maintain the preferred temperature of approximately 105°C. The aeration is continued for twenty hours after which time the reaction product will contain 33% to 35% of free fatty acids. By recycling the unreacted paraffin, the final over-all yield of fatty acids is about 80%.

Separation of the Fatty Acids.—The oxidate is washed with hot water to remove the water-soluble acids and catalyst, after which the residue is saponified at a temperature of 100°C. using direct steam. After standing about ten hours, the product separates into two layers consisting of about two-thirds soap and emulsified unsaponifiable materials and one-third unreacted paraffins. The latter are recycled to the converter. The other fraction is pumped continuously through an autoclave heated under pressure to 180°C. to break the emulsion and then to continuous separators. About one-third of the separated product at this stage is unreacted paraffin which is also returned to the converter.

The remaining oxidate is further freed of unsaponifiable matter by flash distillation. This is accomplished by heating the mixture under pressure to 320–380°C. in a gas-fired pipe still, adding steam and flashing into a baffled dephlegmating chamber at atmospheric pressure. The paraffin vapors pass to a condenser and are recycled to the converter. The soaps settle to the bottom of the chamber and are removed by means of a screw conveyor to solution tanks where they are dissolved in water and then acidulated. The separation of the unsaponifiable matter by solvent extraction described by Wittka,[31] Schrauth,[37] and others does not reduce the unsaponifiable matter below 4% compared to 1.2% by the flash distillation method.

The fatty acids recovered after acidulation are distilled in a series of four stills to produce the fractions previously alluded to, or other similar fractions depending on the conditions of distillation. When operated for the production of fatty acids for soap making, the vapor temperatures of the four stills are, respectively, 150–160°, 240°, 280–290°, and 320°C. The vacuum is varied correspondingly.

(b) *Synthesis from Olefins*

Fatty acids may be produced by synthesis from olefinic as well as paraffinic hydrocarbons. A process known as the Oxo process was developed in

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[37] W. Schrauth, *Chem.-Ztg.*, **63**, 274–278, 303–306 (1939); *Allgem. Oel- u. Fett-Ztg.*, **36**, 413–419 (1939).

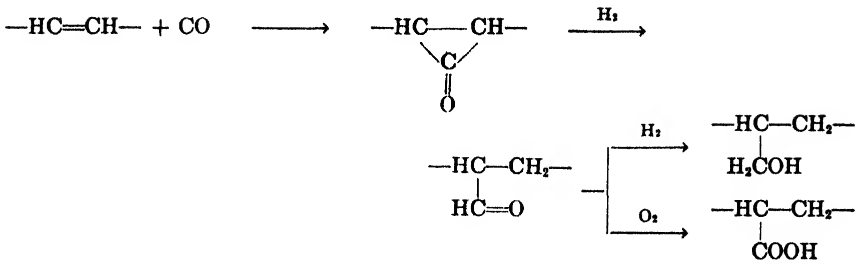
Germany for the production of fatty alcohols and acids from olefins and was operated on a pilot-plant scale (three tons per day) for several years, following which a plant of ten thousand tons annual capacity was erected. The plant was practically complete and ready for operation when hostilities ceased.

Production of Olefin Intermediates.—The necessary olefins may be produced either by cracking heavier paraffin fractions derived from the normal Fischer-Tropsch synthesis or by operating the Fischer-Tropsch process so as to produce a high ratio of olefins to paraffins. The Fischer-Tropsch process is normally operated to produce principally paraffinic hydrocarbons corresponding in composition to the five fractions previously mentioned—gas, gasoline, Diesel oil, Gatsch, and paraffin wax. The last-mentioned fraction is generally refractionated to produce a series of waxes for special uses. The fraction melting below 40°C. is added to the Gatsch fraction, thus producing a fraction containing paraffin hydrocarbons varying in composition from C_{20} to C_{40}.

In the Oxo process, this fraction (C_{20} to C_{40}) is cracked in a Dubbs cracking still at 400° to 450°C. to produce a mixture of 40% to 50% of olefins and the remainder, short chain saturated paraffins. Other paraffinic fractions, *e.g.*, the Diesel oil fraction, may also be cracked to produce olefins for use in producing short chain alcohols. However, the process is preferably operated to produce olefins having a chain length of C_{11} to C_{17} which are most desirable for producing alcohols for sulfonation.

The required olefins may however be produced directly from water gas by a modification of the Fischer-Tropsch process, thus avoiding the losses as well as the costs accompanying the cracking operation when paraffins are used. In the modified or cyclic Fischer-Tropsch process, water gas having a carbon monoxide to hydrogen ratio of 1.0 to 1.2–1.5 is continuously reacted and the products of reaction removed. The residual water gas is enriched with carbon monoxide to produce a ratio of carbon monoxide to hydrogen of 1.0 to 0.8 and further reacted in the same manner but with the formation of a higher ratio of olefins to paraffins. When operated in this manner the Fischer-Tropsch process produces about 50% of the desired olefins and renders unnecessary the cracking operation required with paraffins.

Conversion of Olefins to Alcohols and Acids.—Regardless of the source of the olefins, the subsequent steps in the synthesis are the same. The olefins are further reacted with water gas in the presence of the Fischer-Tropsch catalyst which results in the introduction of carbon monoxide at the double bond to form an unstable cyclic ketone which is subsequently reduced by the hydrogen to the corresponding aldehyde. The mixed aldehydes thus formed may then be further reduced to the corresponding alcohols or oxidized to acids. The reactions may be represented as follows:



$$-HC{=}CH- + CO \longrightarrow -HC\overset{}{-}CH-\ (\text{bridged by } C{=}O) \xrightarrow{H_2} -\underset{\displaystyle HC{=}O}{HC}-CH_2- \begin{cases} \xrightarrow{H_2} -\underset{\displaystyle H_2COH}{HC}-CH_2- \\ \xrightarrow{O_2} -\underset{\displaystyle COOH}{HC}-CH_2- \end{cases}$$

As illustrated in the accompanying equations, only primary alcohols are formed on reduction of the cyclic ketone, but since the double bond in the original olefin may be located anywhere along the hydrocarbon chain the final hydrogenation product will consist of a mixture of normal and iso alcohols.

The reaction between the olefins and water gas to produce aldehydes occurs in the presence of the same catalyst—90% cobalt, 7% thoria, and 3% magnesia deposited as carbonates on kieselguhr—as is employed in the original synthesis of the hydrocarbons. The subsequent reduction of the aldehydes to alcohols is carried out in the presence of Raney nickel catalyst. When it is desired to produce acids instead of alcohols the aldehydes are oxidized in the presence of sodium carbonate.

The C_{11} to C_{17} fractions of olefins derived either from cracked paraffins or by direct synthesis from water gas are reacted in vertical converters consisting of cylinders 400 mm. in diameter and 12 meters high. For purposes of heating and especially cooling the charge, since the reaction is highly exothermic, each converter is provided with a bundle of 30 tubes, 30 mm. I.D. and 38 mm. O.D., which extend three-fourths of the distance from the bottom of the chamber. Each converter is also provided with a reflux condenser to return any hydrocarbon or aldehyde which may be carried out by the gas.

A suspension of catalyst and liquid olefins, or of catalyst and Diesel oil if the reaction is to be carried out with gaseous olefins, is made by agitation in a mixing vessel and then pumped to a high pressure measuring tank from which it is charged to the converter to a depth of about three-fourths of its height or 720–840 liters, approximately 500–600 kg. of product.

Water gas, freed of impurities and especially of organic and inorganic sulfur to which the catalyst is extremely sensitive, is compressed to 200–300 atmospheres in a four-stage system of compressors and then reduced to 150 atmospheres at which pressure it is introduced into the bottom of the converter containing the reacting mass preheated to 150°C. The water gas is supplied for twenty to thirty minutes and the temperature maintained at 150–180°C. The relative amounts of aldehydes and ketones formed are primarily a function of the temperature of operation. The higher temperature, although favoring aldehyde production, reduces the final yield of these products owing to subsequent polymerization of aldehydes which is also favored by high temperature. For example, when operating with ethylene, temperatures as low as 85°C. can be used and under optimum conditions the reaction product is composed of 70% of propionaldehyde and 30% of diethyl ketone by weight.

The water gas, which originally has a composition corresponding to carbon dioxide and inserts 13%, carbon monoxide 38–39%, hydrogen 48–49%, is recycled through the converter after addition of fresh gas, usually in the ratio of 200 cubic meters per hour of exhaust gas and 40–50 cubic meters per hour of fresh gas. The final residual gas is exhausted and burned when the concentration of inert gases reaches approximately 30% and carbon monoxide and hydrogen, 15% to 20% and 40% to 50%, respectively. The catalyst may be reused 50 to 100 times depending on the type of olefins with which it is employed.

Since it is not possible to separate the various aldehydes and unreacted olefins by distillation because of the tendency for aldehydes to undergo polymerization under these conditions, the catalyst is removed and the reaction product is hydrogenated in the presence of Raney nickel catalyst to convert the aldehydes to alcohols and residual olefins to paraffins. The product from the second stage of the reaction is then fractionally distilled to separate the alcohols and paraffin hydrocarbons. The higher alcohols are subsequently sulfonated for the production of various detergent products and the paraffins are either used as such or returned to the Fischer-Tropsch plant.

8. Synthesis of Hydroxy and Keto Acids

(a) *Synthesis of α-Hydroxy Acids*

The α-hydroxy acids, RCHOHCOOH, may be prepared from aldehydes by way of the corresponding cyanohydrin, thus, α-hydroxybutyric acid may be produced from propionaldehyde by reaction of the latter with anhydrous liquid hydrogen cyanide and a basic catalyst, or preferably by reaction with sodium cyanide and sulfuric acid, to form propioncyanohydrin which on hydrolysis gives the desired hydroxy acid.

α-Hydroxy acids may also be produced by reacting aldehydes with sodium bisulfite and treating the bisulfite addition compound with sodium cyanide to form a cyanohydrin which can be hydrolyzed to the corresponding acid. The reaction may be illustrated as follows:

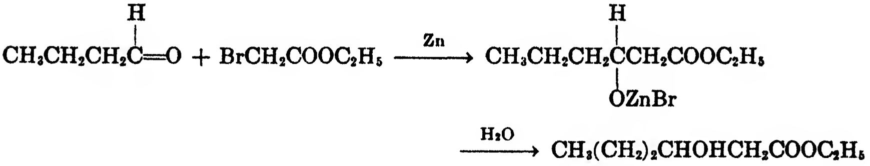
$$\mathrm{RCHO} \xrightarrow{\mathrm{NaHSO_3}} \mathrm{RCH(OH)SO_3Na} \xrightarrow{\mathrm{NaCN}} \mathrm{RCH(OH)CN} \xrightarrow{\text{hydrolysis}} \mathrm{RCH(OH)COOH}$$

The reaction is especially valuable in preparing α-hydroxy acids containing an aromatic ring, *e. g.*, mandelic acid.

α-Hydroxy acids are readily produced by reacting aliphatic acids with bromine and red phosphorus. When the free acid is used, the α-bromoacyl bromide is produced and is converted to the α-bromo acid by hydrolysis with water. Mendel and Coops[38] found that the long chain α-hydroxy acids could be readily prepared by reacting fatty acids, *e. g.*, palmitic acid, with bromine and red phosphorus at 80°C. for eight to ten hours to produce the α-bromo acid, esterifying the latter with methanol to form the α-bromo ester, acetylating with sodium acetate, and finally, by methanolysis, converting the acetyl methyl ester to the α-hydroxy ester from which the free acid is obtained by saponification in methanol solution.

(*b*) *Synthesis of β-Hydroxy Acids*

β-Hydroxy acids, $RCHOHCH_2COOH$, may likewise be prepared from the α-halogenated acids by means of the Reformatsky[39] reaction. The reaction is especially selective and is widely applicable to the production of β-hydroxy acids and their dehydration products. The synthesis involves the reaction of an α-bromo ester with zinc in the presence of an aldehyde or ketone. The action is presumed to proceed by way of an organozinc compound as illustrated in the following equations using butyraldehyde and α-bromoacetic ester to produce ethyl valerate:



$$CH_3CH_2CH_2\overset{H}{\overset{|}{C}}{=}O + BrCH_2COOC_2H_5 \xrightarrow{Zn} CH_3CH_2CH_2\underset{\underset{OZnBr}{|}}{\overset{\overset{H}{|}}{C}}CH_2COOC_2H_5$$

$$\xrightarrow{H_2O} CH_3(CH_2)_2CHOHCH_2COOC_2H_5$$

The Reformatsky reaction was applied by Adickes and Andresen[40] with minor variations to improve the yield, to the synthesis of a series of β-hydroxy acids ranging from β-hydroxyvaleric to β-hydroxylauric acid. Of this series (see Table 145), β-hydroxyheptanoic, β-hydroxycaprylic, β-hydroxyundecanoic, and β-hydroxylauric had not previously been described in the literature, and β-hydroxyvaleric, β-hydroxycaproic, β-hydroxynonanoic, and β-hydroxycapric had previously only been obtained as syrupy liquids. Of the β-hydroxy acids included in Table 145 all but three were prepared by Adickes and Andresen. The C_{14} acid was prepared by Thaler and Geist,[41] the C_{16} by Robinet,[42] and the C_{18} by Levene and Haller.[43]

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[38] H. Mendel and J. Coops, *Rec. trav. chim.*, **58**, 1133–1143 (1939).

[39] S. Reformatsky, *Ber.*, **20**, 1210–1211 (1887); **28**, 2842–2847 (1895). See J. A. Nieuwland and S. F. Daly, *J. Am. Chem. Soc.*, **53**, 1842–1846 (1931).

[40] F. Adickes and G. Andresen, *Ann.* **555**, 41–56 (1943).

[41] H. Thaler and G. Geist, *Biochem. Z.*, **302**, 369–383 (1939).

[42] M. Robinet, *Bull. soc. chim. Belg.*, **40**, 710–725 (1931).

[43] P. A. Levene and H. L. Haller, *J. Biol. Chem.*, **76**, 415–422 (1928).

TABLE 145

MELTING POINTS OF β-HYDROXY AND α-KETO ACIDS

Aliphatic chain	β-Hydroxy acid m.p., °C.	α-Keto acid m.p., °C.	Aliphatic chain	β-Hydroxy acid m.p., °C.	α-Keto acid m.p., °C.
C_3	Syrup	13.6	C_{11}	73-73.5	55
C_4	38	31-32	C_{12}	70-70.5	56.5-57
C_5	43-44	6-7	C_{13}	...	62-62.5
C_6	13	7-8	C_{14}	72-73	63.8
C_7	40-41	29-30	C_{15}	...	68-68.5
C_8	38-38.5	32-33	C_{16}	83-83.5	69
C_9	60	43-44	C_{18}	98	...
C_{10}	56-56.5	46-47			

(c) *Synthesis of ω-Hydroxy Acids*

A series of acids has been prepared in which the hydroxyl group is in each case attached to the terminal or ω-carbon atom. These acids are symmetrical with respect to the relative positions of the hydroxyl and carboxyl groups which are attached to opposite ends of the hydrocarbon chains. This series is of interest not only because it is relatively complete, but also because several of the acids have been found to occur in nature, particularly in the waxes of several species of juniper in which they are found both free and in the form of esters.

TABLE 146

ω-HYDROXY ACIDS PREPARED BY CHUIT AND HAUSSER[a]

Acid	Formula	M.p., °C.	Corresponding ω-bromo acid m.p., °C.
8-Hydroxycaprylic	$HO(CH_2)_7COOH$	58	38.5-39
9-Hydroxynonanoic	$HO(CH_2)_8COOH$	51-51.5	36
10-Hydroxycapric	$HO(CH_2)_9COOH$	75.5-76.5	42-42.5
11-Hydroxyundecanoic	$HO(CH_2)_{10}COOH$	70-70.5	51
12-Hydroxylauric[b]	$HO(CH_2)_{11}COOH$	84-85	52-52.2
13-Hydroxytridecanoic	$HO(CH_2)_{12}COOH$	79.5	59-59.2
14-Hydroxymyristic	$HO(CH_2)_{13}COOH$	91-91.5	61.8-62
15-Hydroxypentadecanoic[b]	$HO(CH_2)_{14}COOH$	84.8-85.2	65.2-65.5
16-Hydroxypalmitic[b]	$HO(CH_2)_{15}COOH$	95	70-70.5
17-Hydroxymargaric	$HO(CH_2)_{16}COOH$	87.5-88	70.5-71
18-Hydroxystearic	$HO(CH_2)_{17}COOH$	96.6-97.2	75.2-75.8
19-Hydroxynonadecanoic	$HO(CH_2)_{18}COOH$	91-91.5	73-74
20-Hydroxyarachidic	$HO(CH_2)_{19}COOH$	97.4-97.8	77-78
21-Hydroxyheneicosanoic	$HO(CH_2)_{20}COOH$	92.5-93	75-76

[a] P. Chuit and J. Hausser, *Helv. Chim. Acta*, 12, 463-492 (1929).
[b] Also reported from natural sources.

Chuit and Hausser[44] prepared a series of ω-hydroxy acids corresponding to the formula $HO(CH_2)_nCOOH$ by six different methods, among which

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[44] P. Chuit and J. Hausser, *Helv. Chim. Acta*, 12, 463-492 (1929). See P. Chuit, F. Boelsing, J. Hausser, and G. Malet, *ibid.*, 9, 1074-1093 (1926).

may be mentioned the reduction of the monoesters of dibasic acids with sodium and alcohol and the action of potassium cyanide or sodium malonic ester on the monobromohydrins of glycols and subsequent conversion to the hydroxy acids. The various acids of this series which have been prepared by Chuit and Hausser are given in Table 146. These investigators also prepared the methyl ethers, acetyl, and the ω-bromo acids corresponding to each of the hydroxy acids and for each series presented melting point data as a function of the number of carbon atoms in the chain.

(*d*) *Synthesis of α-Keto Acids*

Two methods are available for the preparation of α-keto acids, RCOCOOH, one of which employs the chloride of the next lower fatty acid to produce a keto nitrile. The acid chloride is reacted with silver cyanide to produce the nitrile which is then hydrolyzed to the corresponding keto acid as indicated in the following equations:

$$RCOCl + AgCN \longrightarrow RCOCN + AgCl$$

$$RCOCN + H_2O \longrightarrow RCOCOOH$$

The method is limited by the difficulty of saponifying the higher α-keto nitriles.[45]

The second method involves the use of the acetoacetic ester synthesis of the α-oxamic acid ester. This method is limited by the poor conversion of the oxamic ester to the keto ester. However, the related oxaloacetic ester synthesis applied by Adickes and Andresen[40] leads readily to the formation of α-keto esters. This synthesis is similar to the previously described malonic ester and acetoacetic ester syntheses. Oxaloacetic ester, like acetoacetic ester, reacts as an α-ketonic acid undergoing "acid" and "ketonic" hydrolysis. For the preparation of α-keto acids up to α-ketocapric acid, the method is carried out in the following way.

An alcohol-free suspension of sodium ethylate in ether (350 ml.) is prepared by reacting powdered metallic sodium (23 g.) with the calculated amount of absolute ethanol. To this solution there is added a solution of oxalodiethyl ester (87 g. or 0.5 mole). After two eight-hour periods of refluxing, the reaction mixture is poured into a mixture of ice and 50% sulfuric acid containing 60 g. of concentrated sulfuric acid. The ethereal solution of the oxalo-fatty acid diethyl ester is concentrated to 200 ml. and shaken with a solution of potassium carbonate (1:4) until the ether fails to give a reaction with alcoholic ferric chloride. The collected potassium carbonate extracts are washed once with ether, acidified with 20% sulfuric acid, and the ethereal solution separated, dried, and distilled, the last 100 ml. at 30°C. *in vacuo*. The crude α-oxalo fatty acid ester is diluted with

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[45] W. Tschelinzeff and W. Schmidt, *Ber.*, 62, 2210–2214 (1929).

water (1:4), two parts of concentrated hydrochloric acid added, and the mixture refluxed for six hours with rapid mechanical stirring to saponify and decarboxylate the ester. The solution is then neutralized with sodium hydroxide and the recovered α-keto acid purified by crystallization of the barium or calcium salt. For acids higher than capric the method requires modification to increase the yield by addition of a catalyst such as pyridine or piperidine.

The melting points of the α-keto acids prepared by Adickes and Andresen[40] together with several acids previously described by others are given in Table 145. All of the α-keto acids included in the table can be reduced to the corresponding α-hydroxy acids and in many instances this has been done.

The preparation of keto acids of various structures by the malonic ester and acetoacetic ester syntheses and by the Robinson-Robinson modifications of these syntheses has already been discussed. Keto acids may also be prepared by the action of alkyl magnesium and alkyl zinc chlorides on the monoalkyl ester chlorides of the dibasic acids. For example, acetyl zinc chloride and ethyl sebacoyl chloride (9-carbethoxynonanoyl chloride) react to form 10-ketostearic acid as follows:

$$CH_3(CH_2)_7ZnCl + ClCO(CH_2)_8COOEt \longrightarrow CH_3(CH_2)_7CO(CH_2)_8COOEt + ZnCl_2$$

This reaction will be referred to in connection with the synthesis of branched chain acids.

9. Synthesis of Alkyl- and Aryl-Substituted Acids

Both alkyl- and aryl-substituted aliphatic acids have been prepared synthetically and a number of the former have also been isolated from natural sources. Because of the need for branched chain acids of known constitution for comparison with similar acids isolated from natural sources, several methods have been developed for this purpose.

(a) *Alkyl-Substituted Acids*

Fordyce and Johnson[46] prepared two series of branched chain aliphatic acids corresponding to the general formulas:

$$\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!CH(CH_2)_nCOOH \quad \text{and} \quad \begin{matrix} C_2H_5 \\ CH_3 \end{matrix}\!\!>\!CH(CH_2)_nCOOH$$

by the action of isoalkyl magnesium halides on sebacoyl chloride, $ClOC(CH_2)_8COCl$, and 9-carbethoxynonanoyl chloride, $C_2H_5OOC(CH_2)_8COCl$. Alkylation results in the formation of a branched chain keto acid which on reduction by the Clemmensen method gives the corresponding branched

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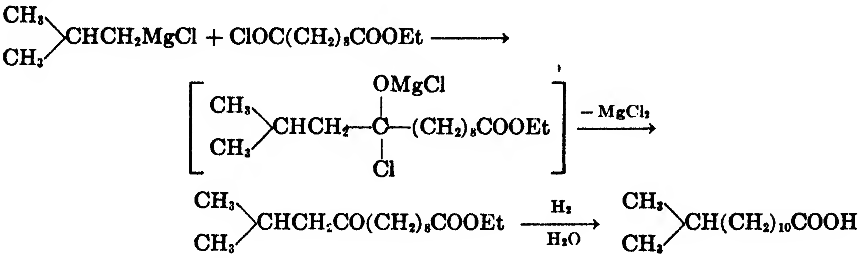
[46] C. R. Fordyce and J. R. Johnson, *J. Am. Chem. Soc.*, **55**, 3368–3372 (1933).

chain or iso acid. Thus, isobutyl magnesium chloride and 9-carbethoxynonanoyl chloride react to give 12-methyl-10-ketomyristate which on reduction and hydrolysis gives 12-methylmyristic (isomyristic) acid according to the following equations:



In the course of preparation of the above-mentioned series of branched chain acids, the corresponding keto acids from C_{14} to C_{18} were prepared and reduced to the corresponding alkyl-substituted acids (Table 147). The method is a general one and is especially useful owing to the extensive series of dibasic acids which are available but the yields are disappointingly low.

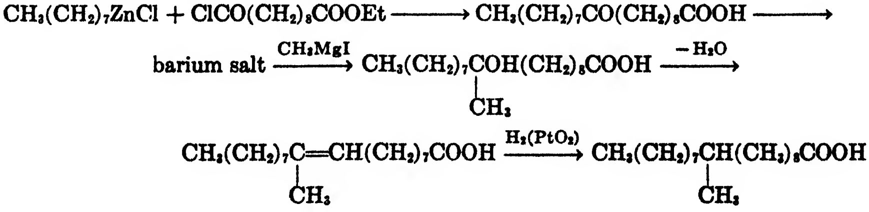
TABLE 147

SUBSTITUTED ACIDS SYNTHESIZED BY THE GRIGNARD REACTION[a]

Acid	M.p., °C.	Yield, %
10-Ketoisomyristic (12-methyl-10-ketotridecanoic)	54–55	43–47
Isomyristic (12-methyltridecanoic)	50.5–51	60–65
9-Ketoisomyristic	58.2–59.5	...
10-Ketopalmitic	75–75.8	28
10-Ketoisopalmitic (14-methyl-10-ketopentadecanoic)	68–69	24
Isopalmitic (14-methylpentadecanoic)	61.8–62.4	79
10-Ketostearic	82–82.8	12
10-Ketoisostearic (16-methyl-10-ketoheptadecanoic)	71.2–72	11
Isostearic (16-methylheptadecanoic)	67.6–68.2	76

[a] C. R. Fordyce and J. R. Johnson, *J. Am. Chem. Soc.*, **55**, 3368–3372 (1933).

Spielman[47] applied a modification of the method of Fordyce and Johnson to the synthesis of *dl*-10-methylstearic acid, m.p. 20–21°C., which was accomplished as indicated in the following equations:



$$CH_3(CH_2)_7ZnCl + ClCO(CH_2)_8COOEt \longrightarrow CH_3(CH_2)_7CO(CH_2)_8COOH \longrightarrow$$

$$\text{barium salt} \xrightarrow{CH_3MgI} CH_3(CH_2)_7\underset{\displaystyle CH_3}{\underset{|}{C}}OH(CH_2)_8COOH \xrightarrow{-H_2O}$$

$$CH_3(CH_2)_7\underset{\displaystyle CH_3}{\underset{|}{C}}{=}CH(CH_2)_7COOH \xrightarrow{H_2(PtO_2)} CH_3(CH_2)_7\underset{\displaystyle CH_3}{\underset{|}{C}}H(CH_2)_8COOH$$

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[47] M. A. Spielman, *J. Biol. Chem.* **106**, 87–96 (1934). See S. F. Velick and J. English, Jr., *ibid.*, **160**, 473–480 (1945).

The reaction of organometallic compounds with the acid chlorides of the half esters of dibasic acids is particularly useful in synthesizing long chain aliphatic compounds containing side chains, and as has been shown by Cason, the alkyl cadmium compounds are particularly useful for this purpose. Cason[48] prepared the ethyl ester of 10-keto-17-methyloctadecanoic acid by the reaction of diisononyl cadmium with ω-carbethoxynonanoyl chloride which was then converted by the Clemmensen reduction and hydrolysis to 17-methyloctadecanoic acid, m.p. 67.3–67.8°C.

(b) *Aryl-Substituted Acids*

Various syntheses of aryl-substituted aliphatic acids have been undertaken because of the value of these derivatives in physiological investigations of the theory of β-oxidation[49] and because of their possible industrial value.[50]

Eijkman[51] investigated the reaction between the lower members of the unsaturated fatty acid series, benzene (also, in some cases, toluene), and anhydrous aluminum chloride for the production of phenyl-substituted saturated acids. It was found that when the double bond occupied the position alpha to the carboxyl group, phenylation did not take place, which is in accord with the observation of Ponzio and Gastaldi[52] that similar acids containing a double bond at this position are relatively unreactive and add iodine from Hübl, Wijs, or Hanŭs solutions extremely slowly and never quantitatively.

When the double bond occupies a position farther removed from the carboxyl group, phenylation occurred but all of the products were found to be uncrystallizable oils. Nicolet and deMilt,[53] Schmidt,[54] and Fourneau[55] observed that phenylation of oleic acids under the same conditions likewise led to the formation of viscous oils. The reaction is very rapid and is completed in five minutes or less when equimolar mixtures of oleic acid and aluminum chloride are used in the presence of a large excess of benzene.

Harmon and Marvel[56] prepared a number of phenyl-substituted aliphatic acids from C_7 to C_{18} by methods which insured addition of the phenyl group at a specific carbon atom. These phenyl-substituted acids together with some of their properties are given in Table 148. The 9- and 10-phenylstearic acids prepared in this manner melted at 36.5–38° and 40–41.5°C.,

[48] J. Cason, *J. Am. Chem. Soc.*, **64**, 1106–1110 (1942).

[49] F. Knoop, *Beitr. chem. Physiol. Pathol.*, **6**, 150–162 (1904).

[50] A. J. Stirton and R. F. Peterson, *Ind. Eng. Chem.*, **31**, 856–858 (1939).

[51] J. F. Eijkman, *Chem. Weekblad*, **1**, 421–424 (1904); **2**, 229–231 (1905); **4**, 727–738 (1907); **5**, 655–666 (1908).

[52] G. Ponzio and C. Gastaldi, *Gazz. chim. ital.*, **42**, II, 92–95 (1912).

[53] B. H. Nicolet and C. M. deMilt, *J. Am. Chem. Soc.*, **49**, 1103–1106 (1927).

[54] E. G. Schmidt, *J. Am. Chem. Soc.*, **52**, 1172–1174 (1930).

[55] E. Fourneau and P. M. Baranger, *Bull. soc. chim.*, **49**, 1161–1172 (1931).

[56] J. Harmon and C. S. Marvel, *J. Am. Chem. Soc.*, **54**, 2515–2527 (1932).

respectively, and it was shown that the viscous oily preparations of previous workers consisted of an equimolar mixture of these two isomers.

TABLE 148

PROPERTIES OF SOME PHENYL-SUBSTITUTED FATTY ACIDS[a]

Acid	Boiling points		n_D^{20}	Sp.gr.$_{25}^{25}$
	°C.	mm.		
3-Phenylheptanoic	144–149	3	1.5049	1.0117
6-Phenyldecanoic	176–180	3	1.5000	0.9817
3-Phenylundecanoic	167–172	2.5	1.4960	0.9679
3-Phenyldodecanoic	165–171	0.3	1.4950	0.9623
8-Phenyldodecanoic	184–187	3	1.4970	0.9729
10-Phenyltetradecanoic	178–183	0.1	1.4936	0.9555
6-Phenylpentadecanoic	182–185	0.1	1.4924	0.9470
8-Phenylhexadecanoic	190–195	0.12	1.4912	0.9417
9-Phenyloctadecanoic	200–204	0.09	1.4891	0.9340
10-Phenyloctadecanoic	199–205	0.09	1.4894	0.9338

[a] J. Harmon and C. S. Marvel, *J. Am. Chem. Soc.*, **54**, 2515–2527 (1932).

Stirton and Peterson[50] prepared a series of aryl-substituted stearic acids from oleic acid by the use of the Friedel and Crafts reaction. These substituted acids included *p*-tolylstearic, *p*-chlorophenylstearic, *p*-bromophenylstearic, *p*-methoxyphenylstearic, *p*-phenoxyphenylstearic, and *p*-xenylstearic acids as well as ethyl tolyl stearate and methyl phenoxyphenyl stearate. All of the products consisted of viscous oils which could not be crystallized and probably consisted of mixtures of at least two isomers corresponding to additions at the ninth and tenth carbon atoms of oleic acid.

10. Synthesis of Unsaturated Acids

No general methods are available for the synthesis of unsaturated acids which are applicable for preparing an extensive homologous series of these compounds. Debromination of monobromo acids or dehydration of monohydroxy acids, except α- and ω-substituted acids, generally leads to mixtures of at least two positional isomers; consequently even specific short chain unsaturated acids are prepared by methods of limited applicability. With increasing chain length, synthesis of specific monounsaturated acids becomes increasingly difficult and the synthesis of polyunsaturated acids even more so.

(a) Synthesis of Oleic Acid and Isomers

A partial synthesis of $\Delta^{9,10}$-oleic acid was accomplished by Robinson and Robinson[57] by the method previously described for preparing keto acids. The ethyl ester of 2-acetyl nonanoate was prepared from *n*-heptyl iodide

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[57] G. M. Robinson and R. Robinson, *J. Chem. Soc.*, **127**, 175–180 (1925).

and acetoacetic ester, and its sodio derivative was condensed with 9-carbethoxynonanoyl chloride. The resulting ester was successively hydrolyzed with cold 5% alkali, boiling 5% sulfuric acid and then with boiling 5% aqueous sodium hydroxide to give 10-ketostearic acid (m.p. 83°C.). The 10-ketostearic acid was reduced by sodium in alcohol solution to 10-hydroxystearic acid (m.p. 84.5°C.).

Although apparently not experimentally carried out by Robinson and Robinson, they state that 10-ketostearic acid can be reduced to 10-hydroxystearic acid with sodium and alcohol which in turn can be converted to 10-iodostearic acid by treatment with phosphorus triiodide and water. The 10-iodostearic acid can be converted to oleic acid by the reaction of alcoholic potassium hydroxide which, according to Arnaud and Posternak,[58] leads to the formation of oleic and elaidic acids and some hydroxystearic acid. These reactions may be represented as follows:

$$CH_3(CH_2)_6I + CH_3COCHNaCOOC_2H_5 \longrightarrow CH_3(CH_2)_6CH(COCH_3)COOC_2H_5$$

$$CH_3(CH_2)_6CNa(COCH_3)COOC_2H_5 + ClCO(CH_2)_8COOC_2H_5 \longrightarrow$$

$$CH_3(CH_2)_6C(COCH_3)(COOC_2H_5)CO(CH_2)_8COOC_2H_5 \xrightarrow{\text{hydrolysis}}$$

$$CH_3(CH_2)_7CO(CH_2)_8COOH \xrightarrow[\text{alcohol}]{\text{sodium}} CH_3(CH_2)_7CHOH(CH_2)_8COOH \xrightarrow{PI_3}$$

$$CH_3(CH_2)_7CHI(CH_2)_8COOH \xrightarrow{\substack{\text{alcoholic} \\ \text{KOH}}} CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$$

If the halogen is attached at the tenth carbon atom as indicated by the accompanying equations it might be expected that dehalogenation might be accompanied by removal of a hydrogen from either of the adjacent carbon atoms, in which case a mixture of 9,10- and 10,11-oleic and elaidic acids would result.

Robinson and Robinson showed that 9,10-stearolic acid:

$$CH_3(CH_2)_7C{\equiv}C(CH_2)_7COOH$$

can be reduced by zinc dust and hydrochloric acid in the presence of titanous chloride and acetic acid to give oleic acid (f.p. 13°C.) which is identical with that isolated from olive oil. However, they were unable to reduce 10-ketostearic acid to stearolic acid and thus complete the synthesis.

Noller and Bannerot[59] effected the synthesis of an equilibrium mixture of $\Delta^{9,10}$-oleic and elaidic acids starting with 9-aldononyl chloride. The aldehyde on treatment with bromine, hydrogen bromide, and methyl alcohol gave 8,9-dibromo-9-methoxynonyl chloride. By means of the Grignard reaction, the latter compound was reacted with *n*-octyl bromide to give 8-bromo-9-methoxyheptadecyl chloride which on reduction with zinc in butanol solution gave $\Delta^{8,9}$-heptadecenyl chloride. The chloride was con-

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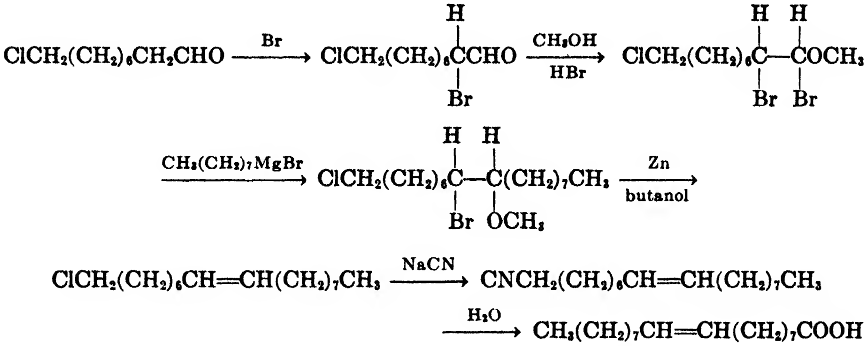
[58] A. Arnaud and S. Posternak, *Compt. rend.*, **150**, 1525–1528 (1910).

[59] C. R. Noller and R. A. Bannerot, *J. Am. Chem. Soc.*, **56**, 1563–1565 (1934).

verted to the corresponding nitrile and the latter hydrolyzed to give a mixture of $\Delta^{9,10}$-oleic and elaidic acids in the proportions of 37% to 63%, respectively. The reactions may be represented as follows:



$$ClCH_2(CH_2)_6CH_2CHO \xrightarrow{Br} ClCH_2(CH_2)_6\overset{H}{\underset{Br}{C}}CHO \xrightarrow[HBr]{CH_3OH} ClCH_2(CH_2)_6\overset{H}{\underset{Br}{C}}-\overset{H}{\underset{Br}{C}}OCH_3$$

$$\xrightarrow{CH_3(CH_2)_7MgBr} ClCH_2(CH_2)_6\overset{H}{\underset{Br}{C}}-\overset{H}{\underset{OCH_3}{C}}(CH_2)_7CH_3 \xrightarrow[butanol]{Zn}$$

$$ClCH_2(CH_2)_6CH{=}CH(CH_2)_7CH_3 \xrightarrow{NaCN} CNCH_2(CH_2)_6CH{=}CH(CH_2)_7CH_3$$

$$\xrightarrow{H_2O} CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$$

The synthetic oleic acid was characterized by its neutralization equivalent, iodine value, and preparation of the *p*-phenylphenacyl ester. The elaidic acid melted at 44°C. and was apparently identical with the acid prepared by elaidinization of natural oleic acid.

Strictly speaking, this is not a complete synthesis of oleic acid since the ω-chlorononylaldehyde was originally obtained from butyl oleate by reduction with sodium and alcohol to oleyl alcohol and treatment of the alcohol with thionyl chloride to give 9,10-octadecenyl chloride. Ozonolysis of the chloride resulted in fission at the double bond with the formation of ω-chlorononylaldehyde.

The fact that the final product of the synthesis consisted of a mixture of oleic and elaidic acids in the proportion of 37% to 63%, respectively, is interesting in view of the fact that Griffiths and Hilditch[60] found that catalytic elaidinization of oleic acid with oxides of nitrogen leads to an equilibrium mixture of 34% of oleic acid and 66% of elaidic acid. However, the formation of the two isomers must have occurred in a different manner in the synthesis than in the elaidinization reaction, possibly in the course of the reduction with zinc and butanol. However, some prior intermediate, for example the Grignard reaction product, may have been a mixture of isomers in the proportions which were observed in the end products of the synthesis.

The method of Noller and Bannerot,[59] which is essentially the same as that used by Dykstra, Lewis, and Boord[61] for the synthesis of olefins, was extended and improved by Baudart[62] who also synthesized oleic, elaidic,

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[60] H. N. Griffiths and T. P. Hilditch, *J. Chem. Soc.*, **1932**, 2315–2324; *J. Soc. Chem. Ind.*, **53**, 75–81T (1934).

[61] H. B. Dykstra, J. F. Lewis, and C. E. Boord, *J. Am. Chem. Soc.*, **52**, 3396–3404 (1930).

[62] P. Baudart, *Compt. rend.*, **217**, 399–400 (1943); **220**, 404–407 (1945).

undecenoic, dodecenoic and palmitoleic acids. Baudart condensed 1-methoxyhexyl-6-magnesium bromide with 1-ethoxy-1,2-dibromodecane and reduced the condensation product with zinc to give 1-methoxy-7-hexadecene which was treated with hydrobromic acid to give 1-bromo-7-hexadecene. The last-mentioned product was converted to the iodide and treated with sodium ethyl malonate in *n*-butanol. After saponification and decarboxylation a mixture of oleic (35%) and elaidic (65%) acids was obtained which was separated by means of the lead salt–alcohol method.

The reactions may be illustrated by the following scheme:

$$CH_3O(CH_2)_6MgBr + CHBr(OC_2H_5)CHBr(CH_2)_7CH_3 \longrightarrow$$

$$CH_3O(CH_2)_6CH(OC_2H_5)CHBr(CH_2)_7CH_3 \xrightarrow{Zn}$$

$$CH_3O(CH_2)_6CH{=}CH(CH_2)_7CH_3 \xrightarrow{HBr} Br(CH_2)_6CH{=}CH(CH_2)_7CH_3$$

$$\xrightarrow[\text{synthesis}]{\text{malonate}} HOOC(CH_2)_7CH{=}CH(CH_2)_7CH$$

With the use of other reactants the above synthesis can be applied to the preparation of other monounsaturated acids.

Kapp and Knoll[63] synthesized two positional isomers of ordinary oleic acid, namely, $\Delta^{16,17}$- and $\Delta^{17,18}$-oleic or octadecenoic acids. The synthesis was achieved by preparing the unsaturated keto acids by means of the acetoacetic ester method and reducing the keto acids by the Wolff-Kishner[64] method (see p. 385). $\Delta^{10,11}$-Undecenoic acid (m.p. 24.5°C.) was converted to $\Delta^{10,11}$-undecenoyl chloride by treatment with thionyl chloride and condensed with sodiodiethyl acetyl suberate to give α-acetyl-α-10,11-undecenoyl diethyl suberate. This product was hydrolyzed by the Robinson-Robinson stepwise procedure to give 8-keto-$\Delta^{17,18}$-octadecenoic acid which was reduced by the Wolff-Kishner method to $\Delta^{17,18}$-octadecenoic acid (m.p. 48–50°C.).

The various steps in the process may be represented by the following equations:

$$CH_3COCH_2COOC_2H_5 + NaOC_2H_5 + BrCH_2(CH_2)_4COOC_2H_5 \xrightarrow[\text{ethanol}]{\text{anhydrous}}$$

$$CH_3COCH[(CH_2)_5COOC_2H_5]COOC_2H_5 \xrightarrow[\text{ethyl ether}]{\text{Na, anhydrous}}$$

$$CH_3COCNa[(CH_2)_5COOC_2H_5]COOC_2H_5 + CH_2{=}CH(CH_2)_8COCl \longrightarrow$$

$$CH_2{=}CH(CH_2)_8COC(COCH_3)[(CH_2)_5COOC_2H_5]COOC_2H_5 \xrightarrow{\text{dil. aq. KOH}}$$

$$CH_2{=}CH(CH_2)_8COCH[(CH_2)_5COOC_2H_5]COOC_2H_5 \text{ (not isolated)} \longrightarrow$$

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[63] R. Kapp and A. Knoll, *J. Am. Chem. Soc.*, **65**, 2062–2064 (1943).
[64] L. Wolff, *Ann.*, **394**, 68–85, 86–108 (1912).

$$\xrightarrow{\text{dil. aq. } H_2SO_4} CH_2{=}CH(CH_2)_8CO(CH_2)_6COOC_2H_5 \xrightarrow[\text{acidification}]{\text{dil. aq. NaOH}}$$

$$CH_2{=}CH(CH_2)_8CO(CH_2)_6COOH \xrightarrow[\text{hydrazine HCl}]{\text{sodium ethoxide}} CH_2{=}CH(CH_2)_{15}COOH$$

Synthesis of $\Delta^{16,17}$-octadecenoic acid (m.p. 62.8–63.5°C.) was accomplished in the same manner using $\Delta^{9,10}$-undecenoyl chloride instead of $\Delta^{10,11}$-undecenoyl chloride.

It is worthy of note that these two oleic acids are solids of relatively high melting points compared to $\Delta^{9,10}$-oleic acid which would indicate that the melting points of the C_{18}-monoethenoid acids increase as the double bond is moved toward the terminal methyl group or that the products obtained were *trans*-isomers similar to elaidic acid. It is also noted that the reduction of the keto acid although apparently not involving the double bond gave a yield of 65% of unsaturated acid which is comparable to the equilibrium concentration of elaidic acid observed by Griffiths and Hilditch for the oleic-elaidic transformation. Since the Wolff-Kishner reduction of the keto acid is carried out at high temperatures and for protracted times in the presence of sodium, absolute alcohol, and hydrazine, it is not unlikely that isomerization occurred in this final step of the synthesis to give an equilibrium mixture of $\Delta^{17,18}$-oleic and elaidic acids.

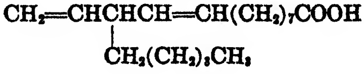
(*b*) *Synthesis of Linoleic Acid*

Using the same series of reactions as were used for the synthesis of oleic and elaidic acids, Noller and Girvin[65] attempted the synthesis of ordinary linoleic acid. In order to accomplish this synthesis, it was necessary to prepare 1-bromooctene-2 starting with acrolein and *n*-amyl magnesium bromide for use in preparing the required Grignard reagent. However, the method of preparation was such that a mixture of 1-bromooctene-2 and 3-bromooctene-1 was obtained in accordance with the following reactions:

$$CH_2{=}CHCHO + CH_3(CH_2)_4MgBr \longrightarrow CH_2{=}CHCHOH(CH_2)_4CH_3 \xrightarrow{PBr_3}$$

$$CH_2{=}CHCHBr(CH_2)_4CH_3 \rightleftharpoons BrCH_2CH{=}CH(CH_2)_4CH_3$$

Since the unsaturated bromo intermediate was a mixture of primary and secondary bromides, it is to be expected that the final product of the synthesis would contain, in addition to the desired $\Delta^{9,10,12,13}$-linoleic acid, another acid containing a branched chain at the eleventh carbon atom. This acid would be 11-*n*-amyl-9,12-tridecadienoic acid:



$$\begin{array}{l} CH_2{=}CH\underset{\displaystyle CH_2(CH_2)_3CH_3}{\underset{|}{C}}HCH{=}CH(CH_2)_7COOH \end{array}$$

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[65] C. R. Noller and M. D. Girvin, *J. Am. Chem. Soc.*, **59**, 606–608 (1937).

Neither the normal nor the branched chain acid was isolated in pure form but their presence in the final reaction mixture was demonstrated by indirect methods.

(c) *Synthesis of Unsaturated Hydroxy Acids*

Collaud[66] described the preparation of a series of unsaturated hydroxy acids, among them 16-hydroxy-$\Delta^{6,7}$-hexadecenoic acid and the saturated 6,16-dihydroxyhexadecanoic, and 6,7,16-trihydroxyhexadecanoic acids. For these preparations, undecylenic alcohol was converted by the method of Darzens and Meyer[67,68] to 11-chloroundecene-1, $CH_2{=}CH(CH_2)_8CH_2Cl$, from which the corresponding magnesium chloride was prepared and then treated with cyclohexanone to produce undecenylcyclohexanol.

The terminal methylene group of the alcohol was eliminated by ozonolysis and the hydroxy aldehyde which was formed was hydrogenated to give the diol which on dehydration produced the corresponding unsaturated alcohol. Ozonolysis and reduction resulted in the rupture of the cyclohexene ring and gave the corresponding hydroxyketo aldehyde which was reoxidized to the hydroxyketo acid, $HOOC(CH_2)_4CO(CH_2)_{10}OH$. Catalytic hydrogenation produced 6,16-dihydroxyhexadecanoic or 6,16-dihydroxypalmitic acid, melting at 111–112°C. Dehydration of the dihydroxy acid with phthalic anhydride gave a mixture of unsaturated acids from which 16-hydroxy-$\Delta^{6,7}$-hexadecenoic acid, m.p. 71–72°C. was separated. Upon oxidation with potassium permanganate, 6,7,16-trihydroxyhexadecanoic acid (m.p. 100–101°C.) was obtained.

Aleuritic acid, 8,9,16-trihydroxypalmitic acid,[69] which is isomeric with the 6,7,16-trihydroxypalmitic acid obtained by Collaud, was synthesized by Mitter, Sen-Gupta, and Bose.[70] The ethyl ester of ω-methoxy-$\Delta^{9,10}$-hexadecenoic acid, $CH_3O(CH_2)_6CH{:}CH(CH_2)_7COOEt$, which had been previously synthesized by Mitter and Mukherjee[71] was converted to 16-chloro-$\Delta^{9,10}$-hexadecenoic acid by treatment with fuming hydrochloric acid. The corresponding ethyl ester was acetylated with potassium acetate and the acetyl derivative oxidized with hydrogen peroxide to give 16-acetoxy-9,10-dihydroxypalmitic acid. Saponification with sodium hydroxide in ethanol gave 9,10,16-trihydroxypalmitic acid melting at 125°C. compared to 101° for the natural acid. The natural and synthetic products

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[66] C. Collaud, *Helv. Chim. Acta*, **25**, 965–977 (1942).

[67] G. Darzens and M. Meyer, *Compt. rend.*, **196**, 489–490 (1933).

[68] M. Meyer, *Compt. rend.*, **203**, 1074–1077 (1936).

[69] P. C. Mitter and P. C. Dutta, *J. Indian Chem. Soc.*, **16**, 673–676 (1939). P. C. Mitter and B. K. Bhattacharyya, *ibid.*, **19**, 69–75 (1942).

[70] P. C. Mitter, M. C. Sen-Gupta, and A. Bose, *J. Indian Chem. Soc.*, **21**, 295–296 1944).

[71] P. C. Mitter and S. Mukherjee, *J. Indian Chem. Soc.*, **19**, 303–307 (1942).

represent *cis*- and *trans*-compounds. The reactions by which the synthetic product was obtained may be represented as follows:

$$\mathrm{CH_3O(CH_2)_6CH{=}CH(CH_2)_7COOEt} \xrightarrow[\text{HCl}]{\text{fuming}} \mathrm{Cl(CH_2)_6CH{=}CH(CH_2)_7COOH}$$

$$\text{Ethyl ester} \xrightarrow[\text{acetate}]{\text{potassium}} \mathrm{CH_3COO(CH_2)_6CH{=}CH(CH_2)_7COOEt} \xrightarrow{\mathrm{H_2O_2}}$$

$$\mathrm{CH_3COO(CH_2)_6CHOHCHOH(CH_2)_7COOEt} \xrightarrow{\text{saponification}}$$

$$\mathrm{HO(CH_2)_6CHOHCHOH(CH_2)_7COOH}$$

CHAPTER XXI

BIOSYNTHESIS OF FATTY ACIDS

1. Introduction

Practically every organ of all plants and animals, no matter how far down the evolutionary scale, contains fatty acids in some form. Fatty acids, or derivatives thereof, have been isolated from bacteria, yeasts, algae and all species of higher plants and animals which have been investigated in this respect. The pollen of flowers, the seeds of plants, the spermatozoa and ova of animals are rich in fatty acids in the form of glycerides, phosphatides, and other lipids. The universal distribution of fatty acids or esters throughout the plant and animal kingdom, the intimate association of these materials with practically every cell, their storage in large quantities in special organs, and the specific nature of these substances in certain organisms and specialized organs, constitute ample proof of their biological importance. Fats appear to be of equal importance with the carbohydrates and proteins in the development and reproduction of all living organisms.

Compared with the carbohydrates and proteins, however, relatively little is known concerning the mode of synthesis and functions which fats perform in the living organism, whether plant or animal. In the case of animals, it is known that stored fats may serve as a source of energy which may be drawn on when the supply of available carbohydrates is inadequate or exhausted. This, however, is probably not the sole function or even the principal function of all fats even in animals, or in all organs of animals, since Mayer and Schaeffer[1] and Terroine[2] have observed that organs such as the kidney, lung, spleen, and heart of animals which have been starved to death contain the same amount of fat as the corresponding organs of normal animals. In the case of plants, no definite proof has been adduced that fats serve as a reserve material except possibly for reproductive organs such as the seeds of certain plants. Even in seeds the relative amount of fat present varies from a few per cent to more than half the weight of all other constituents combined.

Whether the fatty acids and fats are always synthesized at the site where they are found or are synthesized in some special organ and trans-

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[1] A. Mayer and G. Schaeffer, *J. physiol. path. gén.*, **15**, 534–548 (1913).
[2] É. F. Terroine, *Ann. sci. nat. Zool.*, **4**, 5–397 (1920).

ported throughout the living organism is not known with certainty. Perhaps both processes may occur in the same plant or animal.

Much of the experimental work directed toward an understanding of the synthesis of fatty acids has been carried out with animals since they can be fed specific diets and can be subjected to a certain amount of control which is not possible with plants except for the lower forms such as the bacteria, yeasts, molds, and other fungi. In the case of plants, analyses of various organs at different stages of growth furnish practically the only evidence with regard to fatty acid synthesis. Even here, many reported analyses are of little value because the supplemental data necessary for their interpretation are lacking.

One of the most common forms of this type of experiment is the determination of the percentage on a dry weight basis of fat or oil in seeds at different stages of maturity. Without a knowledge of the moisture content, total weight of the seed, and percentage of other constituents, little can be done to interpret these results in terms of mechanisms of synthesis. Considerable histological and anatomical data are also needed, especially with respect to the location of the oil, state of cell division and growth, and cell size at the time the analyses are made. The percentage of oil or fatty acids expressed on a dry weight basis obtained by analysis of a seed undergoing rapid cell division, and similar data obtained with seeds of the same plant but at a later stage of maturation when little cell division but considerable cell enlargement is occurring, may have entirely different significance with regard to the process and rate of fatty acid synthesis.

Although many analyses have been reported for the fatty acid composition of the blood of various species of animals, exceedingly few similar analyses have been reported for the cell saps of plants. Generally, it is assumed that the cell saps of plants are practically devoid of fats *per se*, but they may contain the precursors or intermediates of the higher fatty acids and glycerides. The cell saps of plants certainly are as variable in composition from species to species as are the fatty acids and fats found, for example, in the fruits and seeds of different species.

Not only is knowledge desired concerning the synthesis of the fatty acids but of all of their derivatives, the glycerides, phosphatides, wax esters, and of the analogous long chain substances, namely alcohols, ketones, hydrocarbons and other associated lipid materials.

Unfortunately there is no known plant or animal, however primitive, which contains a simple fat system consisting of but one or two fatty acids, or one or two simple esters, which might serve as a prototype in investigating any given hypothesis of synthesis. Some specialized organs may approach this condition but the plant or animal taken as a whole generally contains a complex group of lipid materials. The nearest approach to such experimental organisms are the few known bacteria, yeasts, molds, and other fungi which possess the ability to synthesize relatively large quantities of fatty acids when grown on artificial substrates. A few such organisms have been investigated to some extent, especially by Haehn and Kinttof,[3] Smedley-Maclean and Hoffert,[4] Barber,[5] Reichel and co-workers,[6,7] and others. Generally, the results of the experiments of this type which have been made in the past have left much to be desired since the quantitative composition of the fatty acids produced was not always determined. It is of obvious importance to know what acids are being produced, and their relative proportions, if light is to be shed on the nature of the synthetic process.

Numerous reviews and not a few books and monographs[8–12] have been devoted to the biochemistry of fatty acids and their derived and associated lipids and most of the known theories and experimental work on fat synthesis have been summarized therein. Even a cursory review of the literature leads to the impression that the greater amount of experimentation and speculation has in the past been concerned with the synthesis and metabolism of fats in animals rather than in plants. This is true despite the fact that animals are primarily dependent on plants for their supply of fats and for all but the simplest types of fatty acids.

2. Synthesis of Fatty Acids by Plants

Fundamental to the problem of fatty acid synthesis in plants are certain peculiarities, or what appear to be peculiarities perhaps for lack of adequate information, concerning the nature and distribution of fatty acids. For example, it is known that naturally occurring fatty acids generally contain only even-numbered carbon chains. Those acids occurring most frequently and in greatest quantity contain 12, 18, 24, 30, and 36 carbon atoms, *i. e.*, they are whole multiples of the hexose carbon chain. Furthermore, under normal conditions in the living plant relatively little free fatty acid is present and practically no free glycerol. The exceptions to the occurrence of free fatty acids in nature are two. In the early stages of development of certain oil-bearing seeds appreciable quantities of free fatty acids have been observed, whereas in later stages seeds from the same plant contain little or

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[3] H. Haehn and W. Kinttof, *Ber.*, **56**, 439–445 (1923); *Chem. Zelle Gewebe*, **12**, 115–156 (1925).

[4] I. Smedley-Maclean and D. Hoffert, *Biochem. J.*, **20**, 343–357 (1926).

[5] H. H. Barber, *Biochem. J.*, **23**, 1158–1164 (1929).

[6] L. Reichel and O. Schmid, *Z. angew. Chem.*, **51**, 190 (1938); *Biochem. Z.*, **300**, 274–283 (1939).

[7] L. Reichel and W. Reinmuth, *Biochem. Z.*, **299**, 359–362 (1938).

[8] W. R. Bloor, *Biochemistry of the Fatty Acids and Their Compounds, the Lipids.* Reinhold, New York, 1943.

[9] H. B. Bull, *The Biochemistry of the Lipids.* Wiley, New York, 1937.

[10] I. Smedley-Maclean, *The Metabolism of Fat.* Methuen, London, 1943.

[11] J. B. Leathes and H. S. Raper, *The Fats.* 2nd ed., Longmans, Green, London, 1925.

[12] H. Maclean and I. S. Maclean, *Lecithin and Allied Substances.* Longmans, Green, London, 1927

no free fatty acids. This was shown to be true by Ivanov[13] for rape, hemp, poppy, sunflower, and flax seeds. Similar results were found by Eyre and Fisher,[14] Eyre,[15] Barker,[16] and others. The variation in the free fatty acid content of linseed oil with growth is illustrated by the data in Table 149 which is condensed from the extensive data of Eyre[15] on two varieties of flax, *Linum usitatissimum* and *L. cibrosum.*

TABLE 149

VARIATION IN FREE FATTY ACID CONTENT OF LINSEED OIL WITH GROWTH, EXPRESSED AS PERCENTAGE OF OLEIC ACID

Days after flowering	*Linum cibrosum*	*Linum usitatissimum*
14	42.0	4.3
17	11.8	...
20	7.2	2.1
23	3.6	1.1
28	1.6	...
32	...	0.3
44	0.6	...
46	...	0.3
66	0.4	0.2
76	...	0.2
84	0.06	...

The other condition under which high free fatty acids are observed is the case of oil seeds which have undergone damage or deterioration either while still attached to the parent plant or after removal at maturity. As a result of adverse weather conditions, excessive rain, frost, etc., cottonseed, soybeans, and other oil seeds have been observed to develop a high content of free fatty acids while the plants are still in the field. Adverse storage conditions may result in an equally high content of free fatty acids in normal seed. It is now established, especially with cottonseed, that this type of free fatty acid formation is due to general autolysis of the cells, mixing of the cell contents, and hydrolysis of the fats by lipolysis.[17,18]

With these exceptions, free fatty acids are generally not encountered in either plants or animals to any appreciable extent. Therefore, any synthesis of fatty acids must be accompanied by a simultaneous synthesis of glycerol, and subsequent esterification. Another peculiarity is the apparently rare occurrence of mono- and diglycerides in nature. It might be expected that these glycerides occur also in the early stages of fat production in oil seeds but it is possible that no serious effort has ever been made to detect

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[13] S. Ivanov, *Botan. Centr. Beihefte*, 28, 159–191 (1912); *Ber. deut. botan. Ges.*, 29, 594–602 (1911).

[14] J. V. Eyre and E. A. Fisher, *J. Agr. Sci.*, 7, 120–134 (1915).

[15] J. V. Eyre, *Biochem. J.*, 25, 1902–1908 (1931).

[16] M. F. Barker, *J. Soc. Chem. Ind.*, 51, 218–222T (1932).

[17] M. L. Karon and A. M. Altschul, *Plant Physiol.*, 19, 310–325 (1944).

[18] A. M. Altschul, M. L. Karon, L. Kyame, and M. Caravella, *Oil & Soap*, 20, 258–262 (1943); L. Kyame and A. M. Altschul, *Plant Physiol.*, 21, 550–561 (1946).

them at the stage of growth where high free fatty acids have been observed. If, however, free fatty acids and mono- and diglycerides are generally absent in the living plant, then the rate of fatty acid formation must be nicely adjusted to three times the rate of glycerol formation.

(a) *Hexose Condensation Hypothesis*

With regard to chain length, the C_{18} acids (saturated, mono- and polyethenoid, hydroxy, and keto acids) taken as a group predominate in both plants and animals. Oleic acid, together with the diunsaturated linoleic acid, are represented in practically every plant or animal and quite often make up the bulk of the acids present. The C_{30} and C_{36} acids are found primarily in various natural waxes and especially the leaf-coat waxes. The C_{12} and C_{24} acids are found in the fats of certain species of plants and animals but generally to a lesser extent than C_{14} and C_{16} fatty acids. Although monounsaturated fatty acids, and to a lesser extent di-, tri- and highly unsaturated acids, corresponding to each saturated fatty acid are known to occur in nature, nevertheless, the C_{18} unsaturated acids predominate.

These observations seem to support the hypothesis that fatty acids are derived from hexose units by some method of condensation and terminal oxidation. If hexose molecules are condensed primarily to form fatty acids they must simultaneously either be reduced or be dehydrated to remove the hydroxyl groups. If simple reduction of the hydroxy groups occurred, the resulting acid would be saturated; if dehydration occurred by splitting out water between hydroxyl groups and adjacent hydrogen atoms, each molecule of water removed would result in the formation of a double bond. In order to account for the formation of unsaturated acids under the first assumption, the parent saturated acid must subsequently be dehydrogenated; and to account for the formation of saturated acids under the second assumption, the parent unsaturated acid must subsequently be hydrogenated. It has generally been assumed that saturated acids are formed first and subsequently are dehydrogenated to produce unsaturated acids. However, either dehydrogenation or hydrogenation could occur in the presence of the appropriate dehydrogenase-hydrogenase enzyme system.

No means of experimentally verifying either hypothesis are available at present. However, it was observed by Dollear, Krauczunas, and Markley[19] and later verified by Scholfield and Bull[20] that the ratio of saturated to unsaturated acids in soybean oil is relatively constant, regardless of the iodine number (102.9 to 151.4) of the oil. It was also observed that the percentage of linoleic and linolenic acids increased more or less regularly with increased iodine number of the oil, while the reverse was true with respect to the percentage of oleic acid. These observations might be explained on the as-

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[19] F. G. Dollear, P. Krauczunas, and K. S. Markley, *Oil & Soap*, 17, 120–121 (1940).
[20] C. R. Scholfield and W. C. Bull, *Oil & Soap*, 21, 87–89 (1944).

sumption that three hexose molecules condensed and underwent dehydration to form a highly unsaturated C_{18} acid which subsequently underwent a stepwise hydrogenation to form linolenic, linoleic, oleic, and stearic acids. The extent to which each acid would accumulate would depend on the relative rates and the equilibrium constants of the several hydrogenation reactions.

The foregoing hypothesis, however, does not account for the formation of the intermediate acids between C_{12}, C_{18}, C_{24}, C_{30}, and C_{36} and particularly for the relatively abundant C_{14} and C_{16} acids. Palmitic acid is considered by some to be the predominant saturated acid of nature.

At this point it seems pertinent to consider the meaning of the phrase "predominant acid of nature" which is frequently used but not always defined. It can mean that this acid is encountered in some specific organ or organism in more species than is any other acid or of all other acids in a given mixture, or it can mean the total natural production by weight or other measure is greater than that of any other acid. Still other meanings become evident on a few moments' reflection.

If the statement is intended to apply only to the number of species in which all the fatty acid components have been quantitatively determined, it is quite possible that the limited number of species thus far examined compared to the hundreds of thousands which exist may be misleading, especially since the bulk of these determinations has been confined to seed fats. If it applies to the relative percentage of a specific acid in a mixture of fats or fatty acids, the same argument applies and may be complicated further by the fact that the same acid may be passing from organism to organism, *e. g.*, from grass to animal to human or other sequence, with relatively little change. If it is applied to the total amount of a specific acid synthesized in nature it may be impossible of interpretation, *e. g.*, the babassu palm is counted by the billions in the jungles of the Amazon Valley and the amount of oil produced annually by these palms has been estimated to equal the entire world production of vegetable oils from all sources. Since this oil contains about 45% of lauric acid compared to 6% to 8% of palmitic acid, it requires a tremendous production on the part of nature elsewhere to overbalance this lauric acid with some other acid. An analogous example, however, exists in the case of the oil palm, ***Elaeis guineensis***, which grows in enormous numbers all over the world. This oil palm contains palmitic acid as the predominant saturated acid of the pericarp oil. Whether or not palmitic acid is the predominant acid, its frequency of occurrence and relatively large amounts in nature require explanation.

(*b*) *β-Oxidation and Resynthesis*

One hypothesis which has been advanced to explain the occurrence of palmitic and other "non-hexose multiple" acids in nature assumes that the original acid formed by hexose condensation undergoes β-oxidation (*cf.* pages 479–480) to form acids containing two less carbon atoms than the unoxidized acid. Thus, stearic acid by β-oxidation would give palmitic acid, palmitic acid would yield myristic acid, and myristic acid would yield lauric acid. However, lauric acid could also be formed directly by condensation of two hexose units and might therefore be assumed to occur in greater abundance and with higher frequency than palmitic acid; otherwise it must be assumed that the number of β-oxidations which can occur in sequence is limited. The condensation of two pentose and one glucose units to form palmitic acid is discounted as being no more likely than the condensation of three pentose units to form a C_{15} acid.[9]

Another theory which has been proposed to explain the presence in fats of acids which are nonmultiples of C_6, assumes that glucose is broken down into acetaldehyde[21,22] and the fatty acid synthesized by a stepwise series of aldol condensations.[23] The work of Raper[24] lends support to this theory with regard to the formation of short chain fatty acids. Smedley[25] and Smedley and Lubrzynska[26] proposed a similar synthesis by way of acetaldehyde derived from pyruvic acid. According to this synthesis, acetaldehyde condenses with pyruvic acid to form an unsaturated α-keto acid which loses carbon dioxide to form crotonaldehyde. The crotonaldehyde similarly condenses with pyruvic acid to give higher unsaturated aldehydes which are ultimately oxidized to acids of varying chain lengths and degrees of unsaturation. A modification of these two hypotheses was suggested by Smedley-Maclean and Hoffert[4] in which acetaldehyde was condensed to form a hexose and the latter directly condensed to form higher fatty acids.

Barber[5] investigated the production of fatty acids by a species of *Penicillium* which was grown on a series of substrates consisting of sucrose, glucose, xylose, and glycerol which contain, respectively, twelve, six, five, and three carbon atoms. Each of these substrates was utilized by the organism to produce palmitic, stearic, oleic, and linoleic acids both in the free state and combined with glycerol. Analytical data indicated that the organism produced the same fatty acids and glycerides in relatively similar proportions regardless of the nature of the substrate. These experiments do not appear to substantiate the theory that direct condensation represents the entire mechanism of synthesis. Either direct condensation is followed by oxidation or, according to Barber, all the substrates are first broken down to a common intermediate which is utilized in the subsequent synthesis of the fatty acids.

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[21] M. Nencki, *J. prakt. Chem.*, **17**, 105–124 (1878).

[22] F. Hoppe-Seyler, *Z. physiol. Chem.*, **3**, 351–361 (1879).

[23] A. Magnus-Levy, *Beitr. chem. Physiol. Path.*, **2**, 261–296 (1902); *Arch. Anat. Physiol., Physiol. Abt.*, **1902**, 365–369.

[24] H. S. Raper, *J. Chem. Soc.*, **91**, 1831–1838 (1907).

[25] I. Smedley, *J. Chem. Soc.*, **99**, 1627–1633 (1911).

[26] I. Smedley and E. Lubrzynska, *Biochem. J.*, **7**, 364–374 (1913).

(c) *Effect of Environment*

It has been observed by many workers that environment, especially climate, markedly influences the type of fatty acids which compose the glycerides of a specific fat or oil. For example, it is known that the fats of many plants indigenous to the tropics contain fatty acids of shorter chain length and a higher degree of saturation than do those from related plants of temperate climates. Also, it is in tropical species of plants that many of the abnormal types of fatty acids are found including hydroxy, keto, conjugated double bond, and cyclic acids. The high temperatures, high humidities, rich soils, etc., appear to have induced plants indigenous to these regions to develop a variety of acids which are generally not found in plants indigenous to temperate climates. The formation of hydroxy and keto acids may indicate the existence of more active oxidative mechanisms in tropical plants if these acids are formed by oxidation of saturated acids, or less active mechanisms if derived by reduction of condensed hexose sugars. Also the occurrence of conjugated acids in fats of tropical plants rather than the isolated double bond acids implies a different dehydrogenation or dehydration mechanism, depending on the nature of the precursor, than that which predominates in plants indigenous to temperate climates.

McNair[26a] has compiled and reviewed the data and literature on the synthesis of plant fats as related to evolutionary order and environment. The reader should consult this work for a more comprehensive discussion than is possible here.

Variation in Unsaturation.—The peculiar variation which has been observed in the unsaturation of the fatty acids synthesized by plants may ultimately provide a clue to the mechanism of synthesis. In fact, unsaturation is the easiest detectable characteristic of fatty acids and is susceptible to experimental alteration. For example, it is known from agronomic experiments that the iodine value of the oil from the same variety of oilseed will decrease or increase when grown in warmer or colder climates, respectively. It has been observed that a given variety of flax normally grown in the Northwest (the Dakotas and Minnesota) will produce seed containing oil as much as 20 units lower in iodine value when grown in the Southwest (Texas). If grown under irrigation, as for example in the Imperial Valley of California, the iodine number of the oil will be intermediate between the two.

It is also well established that the iodine value of the fatty acids or oil of many plants increases steadily during growth and maturation. The variation in iodine value with growth is illustrated by the results in Table 150,

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[26a] J. B. McNair, *Botan. Rev.*, **11**, 1–59 (1945). See J. B. McNair, *Am. J. Botany*, **16**, 832–841 (1929); **18**, 518–525 (1931); **21**, 427–452 (1934); *Field Museum Nat. History Botan. Ser.*, Pub. 276, 9 (No. 2), 47–68 (1930); *Bull. Torrey Botan. Club*, **62**, 515–532 (1935); *Science*, **94**, 422 (1941); *Lloydia*, **6**, 155–156 (1943).

TABLE 150

VARIATION IN OIL CONTENT AND IODINE VALUE OF LINSEED OIL WITH GROWTH AND MATURATION

Days after flowering	Oil content		Iodine value
	Per cent (dry wt.)	Per cent (original)	
10	2.45	0.46	114.1
15	27.85	8.47	124.7
20	35.98	16.67	129.8
25	37.15	22.38	164.9
29	36.56	20.62	171.9
35	36.84	22.38	180.1
39	36.42	23.35	183.0
44	36.14	25.39	188.0
51	36.55	30.70	191.9

which are condensed from the results of Barker.[27] Cartter and Hopper[28] have amassed a considerable amount of data illustrating the effect of soil, climate, and fertilizer treatment on the degree of unsaturation of soybean oil.

What is most important to this type of work and which is entirely lacking in practically all such reported data is a knowledge of the fatty acid composition of these oils. Without information concerning the changes in the specific acids which are responsible for the variation in iodine number, this type of data is of little value in formulating any theory concerning the nature of the synthetic process active in the plant. Only recently has such data become available, especially with respect to change in composition as a function of maturity.

Another significant fact pertaining to the synthesis of fatty acids is the relatively large amounts of unsaturated acids which are present in fish and other marine animals. Whether this tendency to produce predominantly unsaturated acids is associated with the more primitive organization of these animals or to the effect of environment, *i. e.*, relatively low and uniform temperatures compared to plants, or to the ingested food, is as yet a matter of speculation.

3. Synthesis of Fatty Acids by Animals

There is little enough evidence concerning the synthesis of fatty acids by plants, but that pertaining to animals is still less. Direct evidence that fats are synthesized by animals is difficult to obtain with the result that most investigators in this field have been concerned with the metabolic fate of ingested fatty acids rather than with the mechanisms of biosynthesis.

Although the bulk of the fats and fatty acids stored or metabolized by animals is derived directly or indirectly from plants, it appears that some

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[27] M. F. Barker, *J. Soc. Chem. Ind.*, 51, 218–222T (1932).

[28] J. L. Cartter and T. H. Hopper, *U. S. Dept. Agr. Tech. Bull.*, No. 787, 66 pp. (1942).

fats and fatty acids can be synthesized by animals from carbohydrates and possibly also from proteins.[29] However, the type of acids which can be synthesized by animals is extremely limited compared to plants. This limitation has been especially demonstrated by the work of Hilditch, Lea, and Pedelty[30] who have shown that pigs reared on specific diets produce primarily palmitic, oleic, and stearic acids. The inability of animals to synthesize linoleic, linolenic, and arachidonic acids has been demonstrated by Burr and co-workers[31–35] in connection with their studies on the deficiency disease which is induced when these acids are omitted from the diet.

Karrer and Koenig[36] found that none of the five unsaturated acids which were added successively to linoleic acid-free diets could be converted by animals to linoleic acid, as indicated by growth failure and the characteristic deficiency diseases which developed on these diets. Bernhard and Schoenheimer[37] and Bernhard, Steinhausen, and Bullet[38] have shown that mice and rats cannot synthesize linoleic or linolenic acid from carbohydrates even when given large doses of vitamin B_6. These experiments would appear to indicate that polyunsaturated acids cannot be synthesized by the animal from carbohydrates or by dehydrogenation of saturated or monounsaturated fatty acids.

Perhaps the greatest variety of fatty acids produced by animals is found in the milk fat of mammals. These acids are primarily short chain fatty acids, generally saturated but with small amounts of the corresponding monounsaturated acids and some octadecadienoic acids.[39] It has usually been assumed that the short chain acids found in animals resulted from β-oxidation of ingested longer chain acids. However, Klem[40] observed that when the triglycerides of deuteriumized lauric and myristic acids were fed to rats, the acid underwent an increase in chain length in the animal organism instead of a decrease. Deuteriumized lauric acid was converted to myristic acid and deuteriumized myristic to palmitic acid. The author interpreted these results to indicate that β-oxidation was a reversible process. Since the process of β-oxidation has itself never been proved, the re-

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[29] T. P. Hilditch, *The Chemical Constitution of Natural Fats.* Wiley, New York, 1941, pp. 271–289.

[30] T. P. Hilditch, C. H. Lea, and W. H. Pedelty, *Biochem. J.*, **33**, 493–504 (1939).

[31] G. O. Burr and M. M. Burr, *J. Biol. Chem.*, **82**, 345–367 (1929); **86**, 587–621 (1930).

[32] G. O. Burr, M. M. Burr, and W. R. Brown, *Proc. Soc. Exptl. Biol. Med.*, **28**, 905–907 (1931).

[33] G. O. Burr, M. M. Burr, and E. S. Miller, *J. Biol. Chem.*, **97**, 1–9 (1932).

[34] G. O. Burr and A. J. Beber, *J. Nutrition*, **14**, 553–566 (1937).

[35] G. O. Burr, J. B. Brown, J. P. Kass, and W. O. Lundberg, *Proc. Soc. Exptl. Biol. Med.*, **44**, 242–244 (1940).

[36] P. Karrer and H. Koenig, *Helv. Chim. Acta*, **26**, 219–226 (1943).

[37] K. Bernhard and R. Schoenheimer, *J. Biol. Chem.*, **133**, 707–712 (1940).

[38] K. Bernhard, H. Steinhausen, and F. Bullet, *Helv. Chim. Acta.*, **25**, 1313–1318 (1942).

[39] T. P. Hilditch and H. Jasperson, *J. Soc. Chem. Ind.*, **64**, 109–111 (1945).

[40] A. Klem, *Fette u. Seifen*, **51**, 184–188 (1944).

versibility of the mechanism is also questionable. It would appear more plausible to assume that some form of condensation occurs to increase the chain length of the ingested acids. However, it may be possible that more than one organ is capable of synthesizing or transforming fats, *e. g.*, that synthesis of fats may occur in the liver and short chain acids may be produced by degradation of long chain acids in specialized organs such as the mammary glands.

Another peculiarity of the distribution of fatty acids is the predominance —already remarked upon—of unsaturated acids in fish and other marine animals. However, the same types of fatty acids appear to be present in algae, plankton, and other primitive aquatic plants and animals which furnish the primary source of food of all fish and marine animals either directly or indirectly. It is not improbable then that fish and other marine animals are also incapable of synthesizing fatty acids or glycerides but derive these substances from external sources some of which may be metabolized directly and others stored *per se.*

If it is true that the wide variety of fatty acids found in fish and other marine animals is derived from marine plants, that most land animals cannot synthesize polyunsaturated acids as appears to be the case, and that the short chain acids found in milk fats are produced by degradation of longer chain acids, then the problem of fatty acid synthesis in animals is greatly simplified and leaves the problem of the synthesis of the varied and complicated acids in the domain of plants.

It is not unlikely that the synthesis of fatty acids and glycerides in the higher plants and in animals may occur by quite different mechanisms, and that these substances may serve entirely different purposes in different organisms, and in specific organs, thus rendering it impossible to explain their origin by a single mechanism.

F. ISOLATION AND IDENTIFICATION OF FATTY ACIDS

CHAPTER XXII

SEPARATION OF FATTY ACIDS

1. Introduction

The isolation and identification of the component acids comprising a natural fat or wax is generally a difficult process, especially if it is to be carried out in a quantitative rather than a qualitative manner. Fats and waxes are of all degrees of complexity and sometimes contain fatty acids of widely different properties, *e. g.*, they may comprise readily volatile and highly nonvolatile acids, or completely saturated and highly unsaturated acids. On the other hand, they may comprise a homologous series of acids differing only slightly from member to member in chemical and physical properties and thus affording no ready means of sharp separation or of preparing characteristic derivatives unequivocally differentiating them from neighboring members of the series.

Owing to the complexity of the mixture of acids present in natural fats and waxes, no single method is universally applicable to their separation. In some cases several methods, usually of different degrees of applicability, are available and a choice must be made between them especially since the separation may be conducted for one or another of several different purposes. For example, it may be desired to know as exactly as possible the quantitative composition of a fatty acid mixture or merely to identify qualitatively the presence of a specific acid in the mixture, or it may be desired to prepare a small quantity of a highly pure acid or a large quantity of a less pure acid. For each condition some method or combination of methods of separation is preferable to any other.

The present methods have been developed over a long period and although they are now more reliable than at any previous time they still leave much to be desired in the way of simplicity and accuracy. Some methods formerly in vogue have been superseded by others of greater accuracy but the search continues for simpler, more widely applicable and more reliable ones.

The available techniques may be divided into three general types involving separation by (*1*) *distillation,* (*2*) *solubility,* and (*3*) *adsorption* of fatty acids *per se,* or after conversion into esters, salts, or halogenated derivatives. It is sometimes feasible to effect a partial separation of the glycerides or wax esters by crystallization either with or without solvent or by molecular distillation, but generally little advantage is gained by such preliminary fractionation.

Similarly, a number of methods are available for characterizing a given fatty acid after it has been separated from its admixture with other acids. These methods involve: (*1*) determination of one or more physical properties such as melting point, boiling point, refractive index, etc.; (*2*) determination of one or more chemical properties such as absorption of iodine, thiocyanogen, hydrogen, etc.; or (*3*) preparation of a characteristic derivative, usually an ester, and determination of the properties of the derivative.

Regardless of the subsequent procedure to be followed in separating and identifying the component acids of a natural fat or wax, it will usually be desirable to saponify the product to produce a mixture of fatty acids, and in some cases to convert these to a mixture of monoesters; therefore reference will be made to these processes as preliminary to the actual separation and identification processes.

2. Saponification and Esterification

(*a*) *Saponification of Fats and Waxes*

Saponification of a fat or wax may be accomplished in a number of different ways and the precise manner in which it is accomplished depends to some extent on the nature of the original material and the object to be attained. Most fats as well as waxes are saponifiable by means of potassium and sodium hydroxides, alkali alcoholates, or some other base in methanol, ethanol, butanol, or other organic solvent. Fats may also be hydrolyzed with steam under pressure or by the action of a catalyst such as Twitchell reagent or some other aromatic sulfonic acid.

For purposes of quantitative identification, it is essential that all operations involved in the saponification and subsequent steps be conducted in such a manner that no alteration of the fatty acid occurs. The unsaturated fatty acids are especially prone to undergo alteration, *e. g.*, the highly unsaturated acids of fish oils tend to undergo isomerization and polymerization when heated too long or in the presence of concentrated alkali. It has been observed by various workers that heating unconjugated polyethenoid acids in the presence of alkalies results in the production of varying amounts of conjugation depending on conditions.[1-4] The conditions which favor the production of conjugation are long periods of heating,

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[1] W. J. Dann and T. Moore, *Biochem. J.*, **27**, 1166–1169 (1933).

[2] T. Moore, *Biochem. J.*, **31**, 138–154 (1937).

[3] J. H. Mitchell, Jr., H. R. Kraybill, and F. P. Zscheile, *Ind. Eng. Chem., Anal. Ed.*, **15**, 1–3 (1943).

[4] J. P. Kass and G. O. Burr, *J. Am. Chem. Soc.*, **61**, 3292–3294 (1939).

use of high boiling solvents (butanol, ethylene glycol monoethyl ether, diethylene glycol), and high concentrations of alkali.

On the other hand, the true waxes and some fats (wool fat, spermaceti, leaf fats) which contain waxy materials and some other esters, are not readily saponified under mild conditions and recourse must be had to more drastic methods to insure complete saponification.

In addition to polymerization and isomerization reactions, more or less oxidation may occur during saponification of glycerides of the highly unsaturated acids, especially if they contain conjugated double bonds; consequently, it is necessary to protect them against oxidation by passing a current of nitrogen or hydrogen through the reaction mixture.

Saponification of Fats.—For ordinary fats and oils, Hilditch[5] has observed that saponification is readily accomplished by refluxing for six hours, 100 parts of fat with 60 parts of potassium hydroxide and 500 parts of 95% to 100% ethanol. Sodium methylate has been frequently recommended[6–9] for use with difficultly saponifiable fats. Even for ordinary fats its use is advantageous as the saponification is decidedly more rapid. Steet[10] found that 0.5 *N* potassium hydroxide in ethylene glycol monoethyl ether gave instantaneous saponification at the boiling point of the solution and that complete saponification occurred even in wool fat and carnauba wax in fifteen minutes. Redemann and Lucas[11] found that potassium hydroxide in diethylene glycol resulted in complete saponification of many types of esters in three minutes.

Marcus[12] has described a so-called "cold saponification" process which was originally proposed for separating vitamins A and D in an essentially unaltered form from cod liver oil. Actually the "cold saponification" comprises a reaction of an oil with concentrated aqueous alkali which proceeds exothermally, provided a small amount (less than one per cent on the basis of the oil used) of ethanol is added. The exothermic reaction will not occur without the addition of the alcohol but once added, the reaction becomes vigorous and is complete in a short time. The process may be carried out by dissolving 260 g. of potassium hydroxide in 250 ml. of water. To this solution there is added with vigorous stirring a liter of the oil to be saponified. Ten milliliters of ethanol is then added, whereupon the exothermic reaction starts and is complete in a few minutes.

Another method of saponification which is intended to produce mini-

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[5] T. P. Hilditch, *The Chemical Constitution of Natural Fats.* Wiley, New York, 1941, pp. 367, 368.

[6] A. Kossel and K. Obermüller, *Z. physiol. Chem.*, **14**, 599–601 (1890).

[7] A. Kossel and M. Krüger, *Z. physiol. Chem.*, **15**, 321–330 (1891).

[8] K. Obermüller, *Z. physiol. Chem.*, **16**, 152–159 (1892).

[9] A. Beythien, *Pharm. Zentralhalle*, **38**, 850–852 (1897).

[10] W. R. Steet, *Analyst*, **61**, 687 (1936).

[11] C. E. Redemann and H. J. Lucas, *Ind. Eng. Chem., Anal. Ed.*, **9**, 521–522 (1937).

[12] J. K. Marcus, *J. Biol. Chem.*, **80**, 9–14 (1928).

mum alteration in the labile constituents has been described by Heilbron *et al.*[13] In this method, 500 g. of oil is heated with 1250 ml. of a 12% solution of alcoholic potassium hydroxide for one hour at 75°C. under an atmosphere of nitrogen.

Saponification of Waxes.—The saponification of waxes and particularly insect waxes, has been shown by Chibnall and co-workers[14] to be especially difficult and cannot be completely accomplished by the same methods used in saponifying ordinary fats and oils. Not only is the saponification extremely difficult, but the subsequent separation of the soaps and liberated alcohols is complicated by peculiar and unexpected solubility relationships. It was recognized for a long time that, in general, the solubility of the long chain fatty acids and alcohols in organic solvents decreased with increasing length of the carbon chain, but it was not recognized that the sodium and potassium soaps of fatty acids become increasingly soluble in organic solvents with increase in chain length.[15] The sodium and potassium soaps of the higher fatty acids, C_{26} to C_{36}, are soluble to an appreciable extent in boiling acetone and freely soluble in boiling benzene. On the other hand, the calcium salts are only slightly soluble in boiling alcohol and acetone, but are nearly insoluble in boiling benzene and are completely insoluble in boiling ethyl ether.

Chibnall and co-workers[14] developed a method for saponifying waxes which, although involved and tedious, leads to complete separation of the fatty acids and alcohols. The process involves the saponification of the wax in a benzene–alcohol solution of potassium hydroxide, followed by a second saponification with sodium ethoxide of the unsaponified portion of wax remaining after the first treatment.

The details of the method are best illustrated by the description given by the authors for its application to a specific wax, namely, coccerin wax, obtained from *Coccus cacti.* These are as follows:

> "The wax (62 g.) was dissolved in 1800 ml. of hot benzene, 1200 ml. of 10% alcoholic potash were added, and the mixture was boiled under reflux for 12 hours. At the end of that period 3 liters of 95% alcohol containing 160 g. of calcium chloride were added and the boiling continued for another 2½ hours. The mixture was then filtered hot, using a battery of hot water-jacketed conical filters. The residual calcium soaps were extracted three times successively with 3 liters of boiling alcohol and then with the same volume of boiling acetone. The filtrates were cooled, and the crude cocceryl alcohol which separated was collected. This

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[13] I. M. Heilbron, R. N. Heslop, R. A. Morton, E. T. Webster, J. L. Rea, and J. C. Drummond, *Biochem. J.*, **26**, 1178–1193 (1932).

[14] A. C. Chibnall, A. L. Latner, E. F. Williams, and C. A. Ayre, *Biochem. J.*, **28**, 313–325 (1934). See A. Pollard, A. C. Chibnall, and S. H. Piper, *ibid.*, **25**, 2111–2122 (1931); A. C. Chibnall, S. H. Piper, H. A. El Mangouri, E. F. Williams, and A. V. V. Iyengar, *ibid.*, **31**, 1981–1986 (1937); B. K. Blount, A. C. Chibnall, and H. A. El Mangouri, *ibid.*, **31**, 1375–1378 (1937).

[15] S. H. Piper, A. C. Chibnall, and E. F. Williams, *Biochem. J.*, **28**, 2175–2188 (1934).

material (41 g.) was treated five times successively with boiling acetone and filtered hot. The filtrates on cooling gave 24 g. of crude alcohol. The residue insoluble in the hot acetone (12 g.) contained calcium soaps, which in the previous stage must have been rendered soluble in hot alcohol by the excess of potash present, a little unsaponified wax and much unidentified material. The crude alcohol and residue were therefore collected, dissolved in 1200 ml. of hot benzene and boiled under reflux for 3½ hours with sodium ethoxide (20 g. of sodium in 480 ml. of alcohol). 30 g. of calcium chloride in 250 ml. of 95% alcohol were then added, and and the boiling was continued for 2 hours. The mixture was filtered hot, and the insoluble soaps were extracted three times successively with 1 litre of boiling 95% alcohol and finally with 1 litre of boiling acetone. The combined filtrates, on cooling, gave 26.5 g. of crude cocceryl alcohol, M.P. 99-100°. This was digested with 3½ litres of boiling acetone and filtered hot. The filtrate, on cooling, gave 15 g. of alcohol, M.P. 99.6-99.8°. The residue was treated three times, successively, in the same way, giving a further 4.7 g. of alcohol, M.P. 100.2-100.5°. The ultimate residue of soap weighed 0.8 g., and the acetone mother-liquors on evaporation gave 4 g. of crude alcohol which was neglected.

"The calcium soaps from the first saponification were boiled under reflux with 2 litres of glacial acetic acid until the solution was clear and the mixture poured into an excess of cold water. The precipitated acids were collected, the treatment with glacial acetic acid repeated, and the product crystallized from acetone. The material thus obtained (25.7 g.) was digested for some time with 3 litres of boiling acetone and filtered hot. On cooling, the filtrate gave 14.1 g. of fatty acid, M.P. 98.2-99°. Three further extractions of the residue gave in all 6.5 g. of fatty acid, M.P. 104-105°. The ultimate residue was neglected, as also were the 3 g. of crude acid recovered from the acetone mother-liquors on evaporation. The gross yield of acids recovered was 23.6 g. and of alcohol 23.7 g., showing a loss of 14.7 g."

Recovery of Fatty Acids from the Saponification Medium.—Following saponification of ordinary fats or oils, it is usually preferable to remove the unsaponifiable constituents from the fatty acid soaps unless they are present in very small amounts, *i. e.*, less than 0.5% on the basis of the original fat. This operation is difficult and tedious at best. Removal of the unsaponifiable material is ordinarily accomplished by partially removing the alcohol, diluting the residue with a large volume of water, and extracting the soap solution with ethyl ether or petroleum naphtha. It is general practice to remove about one-half of the alcohol by distillation before adding water to the mixture of soaps and unsaponifiable material. Reduction of the alcohol concentration beyond about half of the original volume is generally avoided because of the possibility of altering the unsaturated acids by prolonged heating in the presence of a constantly increasing concentration of alkali, and also because the presence of some alcohol tends to minimize the formation of emulsions during the subsequent extraction of the unsaponifiable matter.

There are several methods available which permit the removal of nearly all of the alcohol where this is desirable without much risk of affecting the unstable constituents. One such means is to add water to the distilling mixture to maintain the original alkali concentration relatively constant while the alcohol is being distilled. Another method is to employ distillation technique which permits the removal of the alcohol at a low temperature, *i. e.*, slightly above room temperature. This can be accomplished with a still similar to that described by Naumann[16] for preparing biological extracts.

In the usual procedure of removing approximately half of the alcohol, the residue is transferred to a separatory funnel, diluted with water, and the unsaponifiable matter extracted by shaking with an organic solvent, preferably ethyl ether or petroleum naphtha. Not uncommonly there are formed difficultly separable emulsions and oftentimes separation of the soaps and unsaponifiable matter is rather incomplete owing to the fact that neither the aqueous phase nor the organic liquid phase is homogeneous with respect to either solvent. The difficulties in this operation have led to the introduction of various modified procedures intended to simplify the separation or reduce the tedium. Hilditch,[5] for example, has described a continuous extractor for use in handling large volumes of soap solutions.

When using the cold saponification process, Marcus[12] found it expedient to extract the unsaponifiable matter with ethylene dichloride. The use of this solvent was found to overcome the formation of emulsions and had the advantage of separating below the lighter soap solution. Repeated extractions can be made without removing the soap solution from the separatory funnel as is the case when ethyl ether or petroleum naphtha is used.

After removal of the unsaponifiable matter, the fatty acids are liberated from the soaps by the addition of acid. The longer chain acids which are relatively insoluble can be separated from the aqueous medium by allowing them to stand, preferably below room temperature, until they rise to the surface. After separation of the fatty acids they should be washed to remove entrained mineral acids and then dried and weighed. All these operations should be carried out in the presence of an inert gas wherever appreciable quantities of unsaturated acids are present. If the original fat contains low molecular weight fatty acids which are more or less soluble in water, the wash waters and acidulated aqueous layer should be extracted with ether to recover these acids. These acids may be kept separate or added to the higher molecular weight acids as desired.

At this point the procedure for handling the acids may be varied considerably depending on the nature of the components, their relative amounts, and the objective to be achieved, *e. g.*, whether it is desired to

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[16] H. N. Naumann, *Biochem. J.*, **29**, 994–997 (1935).

determine quantitatively the relative proportions of the different acids present in the original mixture, or merely to obtain some one highly pure component. Generally, the mixture of acids will be too complex to render direct separation of the individual components possible by a single process, as for example, distillation. Therefore, it is necessary to separate the mixture into two or more gross fractions containing a smaller number of components of relatively similar nature. It may be desirable to separate (*1*) the readily volatile from less volatile acids, (*2*) saturated from unsaturated acids, (*3*) components of saturated fraction from each other, and (*4*) components of the unsaturated fraction from each other. It may be desirable to conduct these operations on the free acids, esters, salts, or halogen derivatives, if not at this stage, at some subsequent stage.

(*b*) *Preparation of Esters*

It may often be desirable to conduct the separation of a mixture of fatty acids by distillation or other treatment of the corresponding monoesters. The required monoesters may be prepared by direct esterification of monohydric alcohols and the mixed acids obtained by saponification and subsequent acidulation of a fat or oil, or by esterification of the individual fractions obtained by prior partial separation of metallic salts, bromo derivatives, or other means. The esters may also be prepared directly from the fat or oil by alcoholysis, thereby eliminating the prior saponification operation. Either methanol or ethanol may be used for preparation of the corresponding esters. Ethyl esters possess the advantage over the methyl esters of somewhat greater thermal stability, lower boiling point, and availability of more extensive characterizing data such as melting and transition points, crystal spacing, etc.

Methods of preparing monoesters by direct esterification and alcoholysis have been discussed in a previous chapter. As pointed out in Chapter X, there is no general agreement as to the best method of accomplishing the direct esterification of fatty acids. This operation depends to some extent on the nature and amount of acids to be esterified. For quantities up to a few hundred grams the procedure most generally followed comprises refluxing the mixed acids for three to six hours with two to four times their weight of methanol or ethanol containing two per cent by weight of sulfuric acid or 1% to 2% by weight of dry hydrochloric acid as catalyst.

The esterification mixture is then distilled at as low a temperature as possible, especially if it contains esters of highly unsaturated acids, to remove most of the alcohol. The residue is dissolved in ethyl ether and washed, first with water to remove the mineral acid catalyst, and then with dilute sodium carbonate solution to remove any unesterified fatty acids, and finally with water to remove any excess of sodium carbonate. When the esterification operation is conducted as part of a quantitative analysis, any unreacted fatty acids should be subjected to further esterification. Other conditions for conducting the esterification process and recovery of esters are described in Chapter X.

Preparation of esters by direct methanolysis or ethanolysis of ordinary fats and oils possesses many advantages over the method of saponification and re-esterification, especially when conducted under the conditions prescribed by Kurz.[17] The conversion of glycerides present in the more common fats and oils to methyl or ethyl esters occurs rapidly (two hours) even at room temperature and many times more rapidly at 50° to 60°C., merely by shaking a homogeneous solution of these substances in methanol or ethanol containing 0.50 to 0.75 equivalent of sodium or potassium hydroxides.[18]

According to Kurz, a fat or oil such as olive oil is converted to methyl esters to the extent of more than 98% by merely allowing a mixture containing 50 parts by volume of a 20% solution of the fat in ethyl ether, 35 parts of neutralized methanol, and 1.0 part of 0.5 *N* solution of potassium hydroxide in methanol, to stand for 24 hours at 20°C.

3. Distillation

Distillation of mixed fatty acids may be carried out to effect one of several different types of separation, namely to separate so-called volatile from nonvolatile acids by means of steam, to separate relatively nonvolatile members of a homologous series by vacuum distillation, and to separate a relatively nonvolatile acid from a nondistillable component such as an oxidized or polymerized component by molecular distillation.

Distillation may also be applied to a mixture of fatty acids containing both saturated and unsaturated fatty acids or it may preferably be applied to the separation of individual components of the saturated and unsaturated acid fractions obtained by prior crystallization from solvents of the original mixed fatty acids, metallic salts, or bromo derivatives at ordinary or low temperatures.

More often than not, distillation of the methyl or ethyl esters of the original mixed acids, or the saturated and sometimes the unsaturated acid fractions, is conducted to obtain a specific acid or to effect separation of the mixture into a series of readily identifiable components. Although one of the most common operations employed in the examination of fatty acid mixtures, it is quite frequently carried out with less attention to pertinent details than almost any other laboratory process.

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[17] H. Kurz, *Fette u. Seifen*, **44**, 144–145 (1937).

[18] Y. Toyama, T. Tsuchiya, and T. Ishikawa, *J. Soc. Chem. Ind. Japan*, Suppl. binding, **36**, 230–231B, 231–232B (1933).

(a) *Steam Distillation*

Most monographs[19,20] and methods of analyses[21] contain directions for conducting the separation of so-called volatile acids from nonvolatile acids by steam distillation. Such methods are necessarily empirical because most of the fatty acids found in common fats are volatile with steam in varying degrees depending on the temperature, pressure, throughput of steam, and other factors obtaining during distillation. The relative degree of volatility of the fatty acids from C_2 to C_{22} is readily apparent from Figure 36 (Chapter VI, page 167).

The method of steam distillation is of some utility in the case of milk fats, nearly all of which contain short chain acids such as butyric, caproic, caprylic, etc. Coconut, palm kernel, and related fats also contain small amounts of acids which are somewhat more volatile than the long chain acids with which they are associated. Isovaleric acid which occurs in the head and jaw oils of the porpoise, is also readily volatile with steam.

Steam distillation may serve to effect a partial separation of the shorter chain from the longer chain acids. The volatilized acids may then be recovered from the condensed distillate by extraction with ethyl ether. After removal of the ether, the acids may be further separated by fractional distillation through an efficient column. If it is desired to recover quantitatively the acids in the steam distillate care must be exercised in the ether extraction because of the tendency of the lower acids to partition themselves between the aqueous and ethereal phases.

(b) *Vacuum Distillation*

Vacuum distillation of fatty acid and ester mixtures constitutes one of the most important methods of separation of these products. The past quarter of a century has seen great activity in the field of petroleum fractionation and during this period many publications have appeared dealing with the theoretical and practical aspects of the process. Similar intense investigations have not been directed to the fractionation of fatty acids and esters with respect to theory, practice, or design of equipment. Only in the past few years have these phases of fatty acid investigation received consideration commensurate with their importance in the laboratory and industry.

Theoretical Considerations.—Under ideal conditions of fractional distillation it should be possible to resolve a mixture of components by completely removing successive molecular species at fixed temperatures and

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[19] G. S. Jamieson, *Vegetable Fats and Oils.* 2nd ed., Reinhold, New York, 1943, pp. 400–403.

[20] T. P. Hilditch, *The Chemical Constitution of Natural Fats.* Wiley, New York, 1941, pp. 369–370.

[21] *Official and Tentative Methods*, V. C. Mehlenbacher, ed. American Oil Chemists' Society, 1946.

pressures. Also ideally, it might be assumed that one component of a given mixture should distill at a fixed temperature and pressure until all of that component has been removed, following which the temperature of the condensate vapor should rise to that of the next higher boiling component and again remain constant until it has been removed. Actually, distillation is dependent on a vapor–liquid equilibrium similar to that represented in Figure 78.

The upper curve in Figure 78 represents the composition of the vapor which will be in equilibrium with the liquid in the lower curve at any given temperature. A liquid corresponding to X_1 mole per cent of component B at a temperature t_1 will give rise to a vapor which, when cooled to temperature t_2, will produce a liquid containing X_2 mole per cent of component B. Re-evaporation of the latter liquid at a temperature t_2 will give rise to a vapor which, on cooling to temperature t_3, will produce a liquid containing X_3 mole per cent of component B. If the process of evaporation and condensation, re-evaporation and condensation were repeated a sufficient number of times, a pure component would theoretically be obtained.

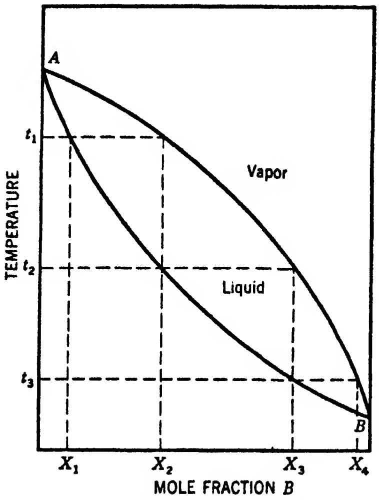

Fig. 78. Hypothetical distillation curve.

In practice, this is accomplished by a process in which distillate vapors leaving the heated liquid are allowed to pass upward through a tube or column at the top of which they are condensed. The condensate, which is designated *reflux*, is returned downward through the tube in which it comes into more or less intimate contact with ascending vapors. Here a heat exchange occurs between the relatively cooler liquid condensate and the warmer vapors so that the more volatile part of the liquid is vaporized while the more readily condensible part of the vapors is converted to liquid. Under ideal conditions the heat lost by the rising vapors is gained by the descending liquid and no gain or loss of heat occurs within the system. This series of interactions results in a concentration of the more volatile component of a mixture in the top of the column and an increasing concentration of less volatile material at the bottom. In an ideally adiabatic distillation complete resolution would result.

Such ideal conditions seldom prevail and, in the case of routine fatty acid or ester fractionation, they are quite frequently not even approximated. Distillation is more often than not carried out over a range of temperatures and pressures without any very exact knowledge of the manner in which these conditions are varying. The resulting fractions cannot, therefore, be expected to be composed of a single component, or if the original mixture is very complex, even of a very small number of components. That this is true in many cases is evident from the examination of the published data on acid and ester fractionation. Many experimenters have assumed, for example, that the distillate fractions are two component systems, or three components if, as in the case of saturated acid fractions, they are found to have an appreciable iodine value. It is generally true that one component predominates in the mixture, but this predominancy depends generally on the relative complexity and percentage composition of the original distilland. Even the assumption that the fraction contains but three components is oftentimes unwarranted, and it is seldom substantiated by rigid physical or chemical criteria of homogeneity. For additional treatment of the theoretical and practical aspects of distillation of fatty acids and esters reference should be made to Chapter VI.

Practical Considerations.—A distillation unit of whatever design must of necessity be a compromise between theory and practice, but it is possible to design and operate such equipment with a relatively high degree of efficiency. Such a unit consists of four essential parts, namely, a boiler and source of heat, a column including the packing and insulation, a still head including a condenser, reflux controller and fraction cutter, and a means of producing and controlling the vacuum.

Column.—In design, the column must have the proper diameter to total height, the packing must have good height efficiency, *i. e.*, low H.E.T.P. (height equivalent to a theoretical plate), good throughput rate, low liquid holdup, and freedom from channeling.

In selecting the proper column diameter for a given distillation it should be remembered that increasing the diameter of the column increases its capacity. The increase in capacity is roughly proportional to the square of the diameter of the column as indicated in the data in Table 151. It is

TABLE 151

EFFECT OF DIAMETER ON CAPACITY AND HOLDUP OF COLUMN PACKED WITH PODBIELNIAK HELI-GRIDS[a]

Packing diameter, mm.	Maximum capacity, ml./hr.	Ratio of capacity to diam.^{2}	Holdup,[b] ml.	Ratio of holdup to diam.^{2}
8.0	240	3.8	4.0	0.063
11.0	360	3.0	7.2	0.059
13.0	560	3.3	11.2	0.066
22.0	1500	3.1	30.0	0.062

[a] F. A. Norris and D. E. Terry, *Oil & Soap*, 22, 41–46 (1945).

[b] Milliliter holdup at 50% maximum capacity for 36-inch column.

also evident from the data of Norris and Terry,[22] which are reproduced in Table 151, that the holdup is likewise proportional to the square of the diameter. In distillations employing large diameter columns it is, therefore, necessary to use relatively large samples to obtain sharp fractionation.

Packing.—A large variety of column packings are now available and have been investigated to determine their relative efficiencies in fractionating fatty acids and esters.[23–33] Norris and Terry have compiled data with respect to the efficiencies of the more common packings which are reproduced in Table 152. Among the more efficient packings for small laboratory stills are single-turn helices[31,32] and conical wire gauze or Stedman packing. According to Bragg,[33] Stedman packing in $^3/_8$-, $^3/_4$-, and 1.0-inch diameter columns having minimum H.E.T.P. values of 0.42, 0.48,

TABLE 152

COMPARATIVE H.E.T.P. FOR VARIOUS TYPES OF COLUMN PACKING ACCORDING TO NORRIS AND TERRY[a]

Type of packing	Ref. No.	H.E.T.P. in cm.
Heli-Grid	23	0.5–1.5
Stedman	24	1.3
Multiple concentric glass tubes	25	1.8
Spinning band	26	2.2
Concentric tubes	27	1.9–5.6
Spiral screen	28	1.7
Glass helices	29	2.9–6.3
Vigreux, indentations only	26	6.0
Widmer, spiraled glass rod	26	8.2
Jackchain, single link, iron, No. 16	30	10.7
Single-turn helices, aluminum, 0.25 in.	30	12.7–27.2
Raschig rings, carbon, 0.25 × 0.25 in.	30	11.9–15.3
Open tower	29	64.7–74.2

[a] F. A. Norris and D. E. Terry, *Oil & Soap*, 22, 41–46 (1945).

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[22] F. A. Norris and D. E. Terry, *Oil & Soap*, 22, 41–46 (1945).

[23] W. J. Podbielniak, *Ind. Eng. Chem., Anal. Ed.*, 13, 639–645 (1941).

[24] A. W. Weitkamp and L. C. Brunstrum, *Oil & Soap*, 18, 47–50 (1941).

[25] M. L. Selker, R. E. Burk, and H. P. Lankelma, *Ind. Eng. Chem., Anal. Ed.*, 12, 352–355 (1940).

[26] R. H. Baker, C. Barkenbus, and C. A. Roswell, *Ind. Eng. Chem., Anal. Ed.*, 12, 468–471 (1940).

[27] S. A. Hall and S. Palkin, *Ind. Eng. Chem., Anal. Ed.*, 14, 807–811 (1942).

[28] H. S. Lecky and R. H. Ewell, *Ind. Eng. Chem., Anal. Ed.*, 12, 544–547 (1940).

[29] A. A. Morton, *Laboratory Technique in Organic Chemistry.* McGraw-Hill, New York, 1938.

[30] C. S. Robinson and E. R. Gilliland, *Elements of Fractional Distillation.* 3rd ed., McGraw-Hill, New York, 1939.

[31] C. O. Tongberg, S. Lawroski, and M. R. Fenske, *Ind. Eng. Chem.*, 29, 957–958 (1937).

[32] M. R. Fenske, S. Lawroski, and C. O. Tongberg, *Ind. Eng. Chem.*, 30, 297–300 (1938).

[33] L. B. Bragg, *Ind. Eng. Chem., Anal. Ed.*, 11, 283–287 (1939).

and 0.50 inch, respectively, throughout the operating range, that is, from incomplete wetting to incipient flooding is equal or superior to the best of the randomly packed columns. This efficiency is about twice that of $^3/_{32}$-inch helices and four times that of small Berl saddles.

In selecting a given packing it must be borne in mind that the lower the efficiency of the packing, the longer must be the column, to obtain a given degree of fractionation. The increased pressure drop through the column as a result of increased height results in increasingly higher temperatures in the still pot and correspondingly greater thermal reaction (polymerization or decomposition) of the distilland.

Pressure Drop.—The pressure at the bottom of a packed column is always greater than that obtaining at the top by an amount which is a function of the packing, vapor velocity, and reflux ratio. In order to maintain the temperature of the distilland at a minimum, the pressure drop should be kept as low as possible. It should also be kept constant in order to maintain constant boiling. With certain types of columns it does not follow that a given reflux setting will insure a constant reflux ratio because the boil-up may vary and produce, for example, increased liquid descending the column. Therefore, the pressure drop should be measured and maintained constant at the best operating level.

Fractionating Efficiency.—With regard to theoretical plate efficiency, Norris and Terry[22] state in substance in their treatment of the fractionation of fatty acid esters that, not infrequently, columns are used without any determination of the number of theoretical plates and thus without any quantitative measurement of their efficiency. Even if the number of plates is determined, investigators may often be misled by assuming that the efficiency determined under conditions of total reflux obtains, for example, at a reflux ratio of 20:1. Experimentally, a column of 25 plates and a reflux ratio of 20:1 may be necessary to provide the same fractionation as a 15-plate column under total reflux.

It is not always recognized that H.E.T.P. varies with the molecular weight of the distillate and tends to increase as the molecular weight increases. This subject has been discussed by Morton[29] who suggests that since the volume of vapor at the boiling point of a unit weight of substance is *indirectly* proportional to molecular weight and *directly* proportional to the absolute temperature, a condition will result, especially in the case of a high molecular weight material, in which an equal volume of vapor will come into contact with a reduced quantity of backflow. It follows, therefore, that H.E.T.P. values as ordinarily determined are minimum in the case of methyl ester distillations, or, stated another way, a column will exhibit less than its rated number of theoretical plates when operating on substances of high molecular weight.

Insulation.—The fractionating column must be operated as nearly adiabatically as possible throughout its length so that the reflux originates at the top of the column and not somewhere along the walls of the column. This condition may be attained by a variety of means, such as silvered vacuum jackets,[23] external ribbon resistors controlled by means of voltage regulators,[34] or combinations of resistors and magnesia insulation, and by external circulating liquid jackets. The last two are perhaps the simplest to construct and control.

Norris and Terry[22] have used a combination of vacuum jacket and metallic reflector for ester fractionation. With this device they found it unnecessary to add heat to the column during distillation of material distilling upwards to 200°C., while the outside of the column was essentially at room temperature. According to these authors, the need for multiple thermocouples and voltage controllers is eliminated and the manipulative procedure during distillation is greatly simplified.

In order to maintain adiabatic conditions and proper control of the distillation by a method other than that of Norris and Terry, it is necessary to provide means of determining the temperature in various parts of the system. Temperatures in the still pot, column, and column packing are best determined by means of an adequate number of thermocouples connected through a selector switch to an accurate potentiometer. A thermometer may be used at the top of the column if preferred.

Reflux Regulation.—It is obvious from the preceding discussion that reflux is essential to good distillation yet it is quite common to find laboratory stills, oftentimes otherwise adequate in design, being operated with no provision for returning condensate. Reflux controllers are an essential part of the still head and much ingenuity has been exercised in the design of these devices. There is often little choice with regard to efficiency of many of these devices, consequently simplicity of design and ease of operation may be the basis of choice. Marshall[35] has described a simple and effective reflux controller and more elaborate designs have been described by Bruun and co-workers,[36–38] Simons,[39] Noonan,[40] Rossini and Glasgow,[41] Richards,[42] and others. Norris and Terry[22] prefer the electrically operated reflux controller of Podbielniak which admittedly is one of the best.

Operating Pressure.—One of the most common faults in the design of the vacuum fractionating equipment, especially where good vacuum is required, is the failure to provide sufficiently large diameter lines between

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[34] C. O. Tongberg, D. Quiggle, and M. R. Fenske, *Ind. Eng. Chem.*, **26**, 1213–1217 (1934).

[35] M. J. Marshall, *Ind. Eng. Chem.*, **20**, 1379 (1928).

[36] J. H. Bruun, *Ind. Eng. Chem., Anal. Ed.*, **2**, 187–188 (1930).

[37] J. H. Bruun and S. T. Schicktanz, *Bur. Standards J. Research*, **7**, 851–882 (1931).

[38] J. H. Bruun, *Ind. Eng. Chem., Anal. Ed.*, **7**, 359–360 (1935).

[39] J. H. Simons, *Ind. Eng. Chem., Anal. Ed.*, **10**, 29–31 (1938).

[40] E. Noonan, *Ind. Eng. Chem., Anal. Ed.*, **10**, 34 (1938).

[41] F. D. Rossini and A. R. Glasgow, Jr., *J. Research Natl. Bur. Standards*, **23**, 509–514 (1939).

[42] A. R. Richards, *Ind. Eng. Chem., Anal. Ed.*, **14**, 649–652 (1942).

the pump and still head. It has been found that the introduction of a 3-cm. length of 4-mm. inside diameter tubing in the vacuum line will reduce the pumping speed of a good vacuum pump by a factor of 50% at 0.001 mm. pressure.[43] The lengths of tubing of various diameters which will reduce the pumping speed by a factor of 50% is given in Table 153.

TABLE 153

LENGTH OF TUBING OF DIFFERENT DIAMETERS WHICH WILL REDUCE PUMPING SPEEDS OF VARIOUS CAPACITY VACUUM PUMPS BY A FACTOR OF FIFTY PER CENT AT 1.0 MICRON PRESSURE[a]

Type of pump	Length of tubing (cm.) for diameters of				
	4 mm.	6 mm.	10 mm.	20 mm.	30 mm.
Hyvac	10	33	150	...	...
Megavac (320)	3	13	55	420	...
Megavac (605)	..	3	30	250	...
Hypervac 20	..	..	8	65	250
Hypervac 100	..	..	...	6	25

[a] *Cenco News Chats*, No. 13, 6–7 (1937); No. 45, 12–14 (1944).

The use of three to four or more feet of small diameter tubing between a high vacuum pump and the top of the distillation column is not uncommon. Furthermore, it is not unusual to measure the pressure of the system by inserting a manometer near the pump instead of as near the top of the column as possible. Consequently, the recorded pressures of many acid and ester fractionations bear little relation to that obtaining at the top of the column and, owing to lack of information concerning the pressure drop through the column, almost none at all to that obtaining in the boiler.

Little effort has been expended on the automatic control of the free air pressure within the system, despite the fact that simple, effective, and inexpensive devices are now available which function entirely automatically. An excellent design of an automatic manostat applicable to the operation of fatty acid stills has been described by Oliver and Bickford.[44]

Although the need for producing efficient vacuum and maintaining it relatively constant at a known value have been stressed, it should be pointed out that there is generally no advantage in distilling thermally stable materials at extremely low pressures, especially where an appreciable pressure drop occurs in a packed column. This is made evident from the data and discussion on ester fractionation by Norris and Terry,[22] who have pointed out that methyl palmitate may be distilled at 136°C. at 1 mm. pressure or at 149°C. at 2 mm. pressure, but the pot temperature will vary less than 1°C. if a 26 mm. pressure drop occurs in the column. In such a

[43] Central Scientific Co., *Cenco News Chats*, No. 13, 6–7 (1937); No. 45, 12–14 (1944). See G. S. Muirhead, *Chemistry & Industry*, **1946**, 298.

[44] G. D. Oliver and W. G. Bickford, *Rev. Sci. Instruments*, **16**, 130–131 (1945).

column an increase in pressure from 1.2 to 10.0 mm. at the still head will increase the pot temperature only 7°C. On the other hand, it is unwise to work at very low still-head pressures since small pressure variations will have a large effect on the boiling point of the material being distilled. Thus, in distilling methyl palmitate, a decrease in still-head pressure from 1.0 to 0.5 mm. will lower the boiling point about 12.5°C., while a decrease of 0.5 mm. in pressure at the 10 mm. level will lower the boiling point only about 1°C. Since distillation "cuts" are ordinarily made on the basis of temperature changes, it is obvious that pressure variations must be reduced to the limit and an operating pressure selected so that any unavoidable pressure changes will not seriously affect the boiling point of the distillate.

Construction of Fractionation Stills.—In addition to the requirements previously mentioned, a well-designed laboratory fractionating still should preferably be constructed entirely of glass with a minimum number of joints and stopcocks. Where it is necessary to join different parts of the system, ground-glass joints either of the standard taper or hemispherical ball and socket type should be used. The use of rubber tubing and of cork and rubber stoppers should be avoided and metal to glass joints should be sealed with any one of many available low vapor pressure vacuum sealing compounds. If stopcocks are used in the main vacuum line connecting the pump and the top of the column, they should be of large bore (15–20 mm.). Stopcocks in the fraction cutter and reflux controller may be of smaller bore. Where fatty acids are distilled, highly corrosion-resistant metal such as molybdenum-stabilized stainless steel, Inconel, or pure nickel should be used.

Most of the recently described stills intended for use with fatty acids and esters contain some improvement in design and their use has resulted in increased effectiveness in the separation of the more complex mixtures of these substances. Among the earliest of these improved distillation units may be mentioned that described by Jantzen and Tiedcke.[45] Lepkovsky, Feskov, and Evans,[46] Longenecker[47] and Weitkamp and Brunstrum[48] have also described fatty acid or ester distillation units of undoubted improvement over previously available equipment.

Longenecker[49] has thoroughly reviewed the literature on ester fractionation and pointed out its value and limitations as an analytical tool. Weitkamp and Brunstrum[48] have discussed in detail the criteria requisite to good distillation and have described a distillation unit which incorporates

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[45] E. Jantzen and C. Tiedcke, *J. prakt. Chem.*, **127**, 277–291 (1930).

[46] S. Lepkovsky, G. V. Feskov, and H. M. Evans, *J. Am. Chem. Soc.*, **58**, 978–981 (1936).

[47] H. E. Longenecker, *J. Soc. Chem. Ind.*, **56**, 199–202T (1937).

[48] A. W. Weitkamp and L. C. Brunstrum, *Oil & Soap*, **18**, 47–50 (1941).

[49] H. E. Longenecker, *Oil & Soap*, **17**, 53–57 (1940).

nearly all of the well-established principles of fractionation in the vapor phase. They have also presented experimental data to show the efficiency of the separation which can be obtained with the use of such equipment in the distillation of the methyl esters of hydrogenated sardine oil.

Although extensive literature has been published on the separation of fatty acids and esters by fractional distillation and various types of distillation apparatus have been described, only a small amount of work has appeared on the actual degree of separation which is effected by this process. Wyman and Barkenbus[50] quantitatively determined the fractionation efficiency of one type of column by distilling a known mixture of pure methyl esters. These authors used a Lesesne and Lochte[51] spinning band column 38.5 cm. long with an efficiency of about twenty theoretical plates measured with benzene and carbon tetrachloride at total reflux. The column and head were modified for vacuum operation. Binary, ternary, and one quaternary mixture of pure methyl esters of saturated acids of known composition were submitted to fractionation. The fractionation was followed by changes in the refractive indices of the distillates. The results of these fractionations are shown graphically in Figures 79 to 81. The flat portions of the curves in these figures may be assumed to represent pure esters and the distillate between these portions may be considered as binary or more complex mixtures.

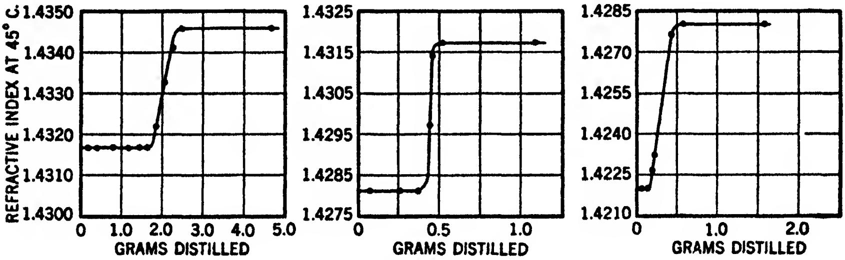

Fig. 79. Fractional distillation of two-component mixtures of saturated fatty acid esters.[50]

The authors found that even with a highly efficient still such as they used, very careful manipulation was required; even the slightest superheating resulted in poor separation. One to two hours and even longer was required to attain equilibrium, and 36 to 48 hours were required to complete a fractionation. These conditions are probably seldom, if ever, observed in ordinary laboratory distillation of methyl esters.

The results obtained by Wyman and Barkenbus[50] in fractionating known

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[50] F. W. Wyman and C. Barkenbus, *Ind. Eng. Chem., Anal. Ed.*, 12, 658–661 (1940). See J. A. Monick, H. D. Allen, and C. J. Marliss, *Oil & Soap*, 23, 177–182 (1946).

[51] S. D. Lesesne and H. L. Lochte, *Ind. Eng. Chem., Anal. Ed.*, 10, 450 (1938).

mixtures of methyl esters under rigidly controlled conditions are reproduced in Table 154. The authors found no very great difficulty in separating binary mixtures, but with a three-component mixture consisting of methyl myristate, methyl palmitate, and methyl stearate, it was difficult to obtain

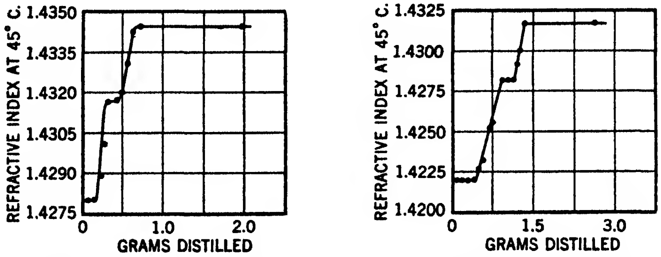

Fig. 80. Fractional distillation of three-component mixtures of fatty acid esters.[50]

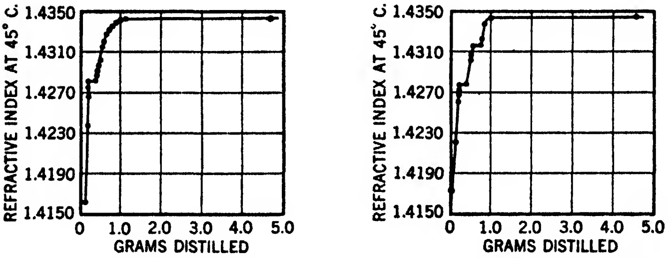

Fig. 81. Fractional distillation of methyl caprate, methyl myristate, methyl palmitate, and methyl stearate mixture.[50]

TABLE 154

RESULTS OF FRACTIONATION OF KNOWN MIXTURES OF METHYL ESTERS[a]

Mixture used, g.	Actual composition, %	Determined experimentally, %
4.983	40.4 palmitate 59.6 stearate	39.6 palmitate 60.4 stearate
2.161	36.4 myristate 63.6 palmitate	35.3 myristate 64.7 palmitate
1.504	21.8 laurate 78.2 myristate	21.5 laurate 78.5 myristate
2.084	11.9 myristate 10.5 palmitate 77.6 stearate	11.3 myristate 10.6 palmitate 78.1 stearate
2.708	26.4 laurate 17.5 myristate 56.1 palmitate	26.4 laurate 17.8 myristate 55.8 palmitate
4.910	3.01 caprate 7.04 myristate 4.97 palmitate 84.97 stearate	1.75 caprate 6.74 myristate 4.79 palmitate 86.72 stearate

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[a] F. W. Wyman and C. Barkenbus, *Ind. Eng. Chem., Anal. Ed.*, **12**, 658–661 (1940).

a distillation plateau corresponding to methyl palmitate. However, reasonably good separation was obtained with a mixture of methyl laurate, methyl myristate, and methyl palmitate. Only one four-component mixture was examined, namely methyl caprate, methyl myristate, methyl palmitate, and methyl stearate. As may be seen in the upper portion of Figure 81, little indication of the presence of methyl palmitate is evident. A second fractionation gave better separation and the calculated composition is not too greatly divergent from the actual composition. It is probable that the fractionation of methyl esters obtained by Wyman and Barkenbus[50] is the most efficient of its kind on record, yet it still leaves much to be desired especially with respect to the number and variation in the proportions of the different components of the mixtures investigated.

Norris and Terry[22] have likewise discussed at length the requisites of good ester fractionation and illustrated it with examples of the degree of separation which is obtainable with binary mixtures of methyl esters of oleic and stearic acids, oleic and linoleic acids, and with U.S.P. stearic acid. When a 50:50 mixture of methyl stearate and methyl oleate was distilled through a Podbielniak column with a reflux ratio of 11:1, the first fractions contained 95% of methyl oleate. When a similar mixture of methyl oleate and methyl linoleate was distilled, no fractionation occurred despite the fact that the difference in boiling points (3.0°C.) of these two esters was the same as between methyl stearate and methyl oleate. The authors concluded that fractionation of the unsaturated acids is probably impossible of attainment owing to their strong association.

Since knowledge of the composition of natural fats is dependent to a large extent on the known efficiency of any given fractionation apparatus and technique employed, there is much need for additional systematic and painstaking investigation in the field. All of the elements, including relatively pure acids and esters, many types of distillation equipment, and a fundamental knowledge of the theory of distillation are at hand for undertaking such investigations.

Analytical Fractionation.—If we assume that adequate distillation equipment is available, the question may arise as to the amount of mixed acids or esters to charge into the still pot. The answer depends on the amount of fat or oil which is available and the purpose for which the fractionation is performed. If the purpose of the fractionation is to determine the percentage composition of the mixed fatty acids and the quantity of original material is limited, *i. e.*, less than 100 g., the largest amount which can be spared for fractionation should be used. Where reasonably large amounts of the original fat are available and the number of component acids is small, the use of 100–150 g. of saturated acids is sufficient when it is merely desired to determine the percentage composition of the original mixture.

If the number of components of the mixed saturated acids is large, then 200–300 g. should be used in order that sufficient product may be available for refractionation. However, it is preferable to carry out the fractionation in batches of 100–150 g. if a still of small capacity (*i. e.*, small vapor velocity of the column) is used, in order to avoid protracted heating of the material in the still. Fractions of corresponding composition can then be combined for further fractionation or analysis. When a highly efficient and automatically controlled distillation unit is employed, the composition of replicated fractions should be quite similar and can be combined without introducing additional components in the corresponding combined fractions. Where it is simply desired to prepare a large quantity of a pure acid or ester for some specific purpose, the amount of mixed acids to be used must necessarily be varied to suit the experimenter's needs.

(*c*) *Molecular Distillation*

Molecular distillation differs from ordinary distillation by virtue of the fact that evaporation and condensation occurs in a highly evacuated atmosphere (0.001 mm. or less), between surfaces separated by a very short distance, usually of the order of 1–2 cm., and by the further fact that evaporation of the distilland occurs from the surface of thin films (0.01 to 0.2 mm.). Under these conditions separation of normally nondistillable, high molecular weight, and thermally unstable substances is possible.

A very extensive literature[52] on molecular distillation has appeared in the past few years during which time the process has passed through all the stages of development from laboratory to large scale commercial operation. From time to time reviews[53–62] covering various phases of these developments have appeared and many types of distillation equipment have been described together with their application to the separation of a variety of substances.

Molecular distillation has been applied to the investigation of fats and oils and particularly to the separation of nonglyceride lipids which are present in these substances. Although some degree of separation of the

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[52] S. B. Detwiler, Jr., and K. S. Markley, *Oil & Soap*, **16**, 2–5 (1939). S. B. Detwiler, Jr., *ibid.*, **17**, 241–243 (1940). S. S. Todd, *ibid.*, **20**, 205–208 (1943).

[53] K. Hickman, *J. Franklin Inst.*, **213**, 119–154 (1932).

[54] K. C. D. Hickman, *Ind. Eng. Chem.*, **29**, 968–975, 1384 (1937).

[55] N. D. Embree, *Ind. Eng. Chem.*, **29**, 975–979 (1937); *Chem. Revs.*, **29**, 317–332 (1941).

[56] K. C. D. Hickman, *Chem. Revs.*, **34**, 51–106 (1944).

[57] C. R. Burch and W. J. D. van Dijck, *J. Soc. Chem. Ind.*, **58**, 39–42 (1939).

[58] E. W. Fawcett, *J. Soc. Chem. Ind.*, **58**, 43–50 (1939); *Kolloid-Z.*, **86**, 34–51 (1939).

[59] G. Burrows, *J. Soc. Chem. Ind.*, **58**, 50–56 (1939).

[60] H. I. Waterman and C. van Vlodrop, *Rev. chim. ind. Paris*, **48**, 314–322 (1939).

[61] E. Blasco, *Ion*, **2**, 753–760 (1942).

[62] H. Dam, *Kem. Maanedsblad*, **20**, 203–207 (1939).

fatty acid glycerides may be effected by molecular distillation, its chief application has been in the separation of sterols, sterol esters, vitamins, hydrocarbons, fatty acids, etc., from natural fats. It has not been extensively applied to the fractionation of fatty acids *per se* primarily because ordinary methods of distillation generally serve to effect the desired separation more efficiently. However, there have been some notable exceptions wherein molecular distillation has made possible separations which could not be accomplished otherwise.

Farmer and van den Heuvel[63] applied molecular distillation ($< 110°$C., 10^{-4} mm. mercury) to the fractionation of the methyl esters of highly unsaturated acids from fish oils. Under these conditions of distillation they were able not only to separate docosahexaenoic acid, $C_{22}H_{32}O_2$, in a relatively high state of purity ($> 99\%$) but to separate the esters of C_{16}, C_{18}, and C_{20} polyunsaturated acids. The C_{22} hexaene acid which was unaltered during the course of the distillation is probably the most highly unsaturated fatty acid ever isolated in pure form.

Schuwirth[64] fractionally distilled the methyl esters of the unsaturated fatty acids of brain phosphatides, employing a vacuum of 10^{-3} to 10^{-4} mm. of mercury and temperatures between 55° and 82°C.

Molecular distillation is particularly useful in separating monomeric and polymeric fatty acids and esters. Lambou and Dollear[65] were unable to prepare linoleic acid or linolenic acids of high purity except by molecular distillation to separate the monomeric acids from the small amount of polymers which invariably accompanied the otherwise pure acid. For this purpose a molecular pot still was employed. The purest fraction of linoleic acid distilled at 113°C. at 1.0×10^{-4} to 4×10^{-5} mm. pressure, whereas the purest linolenic acid was obtained by distillation at 115.5° to 116.0°C. at 10^{-5} mm. pressure.

4. Solubility Methods of Separation

There are available various methods for the separation of fatty acid mixtures which depend on the relative solubilities of individual acids, their salts, or bromo derivatives in different solvents or in the same solvent at different temperatures. These methods make it possible to separate a mixture of fatty acids into saturated and unsaturated fractions, and to separate the unsaturated acids into subfractions of different degrees of unsaturation, or into individual components. None of the methods are strictly quantitative owing to the mutual solubility effects exerted by one component of the mixture on the solubility of the other components or

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[63] E. H. Farmer and F. A. van den Heuvel, *J. Soc. Chem. Ind.*, **57**, 24–31 (1938); *J. Chem. Soc.*, **1938**, 427–430.

[64] K. Schuwirth, *Z. physiol. Chem.*, **277**, 147–158 (1943).

[65] M. G. Lambou and F. G. Dollear, *Oil & Soap*, **22**, 226–232 (1945). See R. T. O'Connor, D. C. Heinzelman, M. Caravella, and S. T. Bauer, *ibid.*, **23**, 5–9 (1946).

vice versa. However, they afford a means of resolving relatively complex mixtures into simpler ones which can in turn be separated further by other means.

The oldest of these methods depends on the relative solubility of the metallic salts of a mixture of fatty acids, while the most recently developed methods depend on the relative solubility of the free fatty acids or esters in a solvent cooled to subzero temperatures.

(*a*) *Separation of Metallic Salts*

Both saturated and unsaturated fatty acids form salts with metallic ions, whose solubility in water and organic solvents varies with the nature of the metallic ion and the chain length, degree of unsaturation, and other characteristics of the acid radical. Many attempts have been made to develop quantitative methods of separating the individual fatty acids on the basis of the solubility of their metallic salts or soaps. The solubility of most of the salts, including those of the alkaline metals (sodium, potassium, and lithium); the alkali earths (calcium, magnesium, barium, and strontium); as well as the heavy metals (lead, zinc, iron, cobalt, nickel, mercury, gold, and silver), have been investigated in a variety of organic solvents, including methanol, ethanol, amyl alcohol, ethyl ether, acetone, benzene, toluene, and in mixtures of these and other solvents. No method has, however, been developed which leads to effective quantitative separation of each component acid of mixtures such as are found in the ordinary fats and oils of commerce, but only to fractions which are relatively homogeneous with respect to certain types of acids.

Lead Salt Methods.—The oldest and most widely used of the metallic salt separation methods depends on the differential solubility of the lead soaps of a mixture of fatty acids in ether or alcohol. It is employed primarily for the separation of saturated from unsaturated acids. The lead salt–ether method is an old one and was first introduced by Gusserow[66] in 1828. Since its introduction, it has been investigated many times and various modifications have been adopted to improve its general applicability. Among the important modifications is one introduced by Twitchell[67] which provides for the use of ethyl alcohol in the place of ether for partitioning the lead salts.

Both the lead salt–ether and the Twitchell lead salt–alcohol methods are in general use. The former method has been adopted by the Association of Official Agricultural Chemists[68] and the latter by the American

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[66] C. A. Gusserow, *Arch. Pharm.*, 27, 153–244 (1828), *cf. Kastners Arch. Chem. Met.*, 1, 69–87 (1830).

[67] E. Twitchell, *J. Ind. Eng. Chem.*, 13, 806–807 (1921).

[68] *Official and Tentative Methods of Analysis.* 5th ed., Association of Official Agricultural Chemists, Washington, D.C., 1940, pp. 434–436.

Oil Chemists' Society.[69] These two so-called official methods are intended for use in quantitative separations employing small amounts (5 to 25 g.) of fats and oils. For larger amounts (200 g. or more) the method of Hilditch, to be described later, is preferable.

Official A.O.C.S. Lead Salt–Alcohol Method.—Details of the official A.O.C.S. lead salt–alcohol method of separating saturated and unsaturated fatty acids are as follows.

Twenty-five grams of the melted fat or oil contained in a 600-ml. beaker are saponified with 15 g. of potassium hydroxide dissolved in a small amount of water and 25 ml. of 95% ethanol. After the saponification is complete, the alcohol is removed by evaporation nearly to dryness and 200 ml. of distilled water is added. The mixture is heated on a steam bath until the soaps are dissolved, after which concentrated hydrochloric acid is added with stirring until the mixture is acid to methyl orange, after which it is heated on a steam bath and transferred to a separatory funnel with the aid of 100–150 ml. of ethyl ether. The ethereal solution is washed with distilled water until it is free of acid after which it is filtered through paper into an Erlenmeyer flask. The ether is then removed by evaporation on a steam bath during which operation the acids are protected from oxidation by a current of inert gas. If it is desired to determine the yield of mixed fatty acids, the flask is weighed before and after the last operation.

A sample of mixed fatty acids containing approximately 1.2 ± 0.3 g. of solid fatty acids, but in no case more than 5 g. of the mixed acids, is weighed into a 250-ml. beaker and 50 ml. of 95% ethanol is added. One and one-half grams of powdered lead acetate is likewise dissolved in 50 ml. of 95% ethanol and both solutions heated to boiling. The lead acetate solution is then slowly added to the solution of fatty acids with continuous stirring. After cooling, first to room temperature and then to 15°C., the mixture is maintained at 15°C. for two hours, following which it is filtered with the aid of suction through a Buchner funnel (3-in. diameter) snugly fitted with a filter paper. The precipitated lead soaps are transferred to the Buchner funnel and washed with the aid of 200 ml. of 95% ethanol cooled to 15°C.

A sample of the filtrate which contains the lead salts of the liquid fatty acids and the excess lead acetate should be tested with concentrated sulfuric acid to determine whether precipitation was complete, *i. e.*, whether the filtrate actually contains an excess of lead acetate.

The collected lead soaps of the solid fatty acids which are slightly colored are transferred from the Buchner funnel to the original beaker with the aid of 100 ml. of warm 95% ethanol. To the alcoholic solution of

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[69] *Official and Tentative Methods.* V. C. Mehlenbacher, ed., American Oil Chemists' Society, 1946.

lead soaps enough glacial acetic acid is added to make a 0.5% solution (0.5 ml. glacial acetic acid per 100 ml. of ethanol). The solution is then heated to boiling and stirred to dissolve the lead soaps after which it is allowed to cool to room temperature, then artificially to a temperature of 15°C., which is maintained for two hours.

The solution is filtered through a Buchner funnel and washed exactly as in the first filtration. After the separated lead soaps of the saturated fatty acids have been freed of ethanol, they are transferred to the original beaker with the aid of 75 ml. of ethyl ether and disintegrated by adding 20–25 ml. of nitric acid (1 to 3). After transferring the solution to a separatory funnel with the aid of ethyl ether, the ethereal solution is washed with distilled water until the wash waters are neutral to methyl orange. The ethereal solution is then transferred to a weighed 150-ml. Soxhlet flask and the ether removed by evaporation under a current of inert gas. The residue is dried for one hour at 101° ± 1°C., cooled, and weighed. The percentage of solid fatty acids is equal to the weight of the solid acids × 100 divided by the weight of the sample of mixed acids used in the determination.

Hilditch Method.—For larger quantities of solid acids, Hilditch[70] dissolves approximately 200 g. of the mixed fatty acids in one liter of boiling 95% ethanol and adds an equal volume of boiling ethanol containing 140 grams of lead acetate and 1.5% of glacial acetic acid. After cooling overnight at 15°C., the lead salts of the saturated acids which are deposited are recrystallized from the same volume of 95% ethanol as was used in the original separation. The saturated acids are then regenerated from the recrystallized lead salts, and the unsaturated acids from the residual lead salts obtained on evaporation of the filtrates from the original precipitation and the recrystallization operations.

Regeneration of Free Acids.—When large quantities of lead salts are prepared and separated, the *saturated acids* are best regenerated by suspending them in a large volume of hot water and adding concentrated hydrochloric acid until the solution is distinctly acid to Congo red. After cooling, the solid acids are separated in a separatory funnel. The aqueous layer and the suspended lead chloride are extracted with ether and the ethereal extract added to the separated acids in the funnel. Sufficient ethyl ether is added to dissolve all of the acids and the ethereal solution is washed until the wash waters are neutral. The ether is then removed by distillation and the solid acids dried *in vacuo*.

The *unsaturated acids* are recovered by distilling the solution of soluble lead salts to remove the ethanol, preferably with the addition of water and under an inert atmosphere of gas. The acetic acid will partially or com-

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[70] T. P. Hilditch, *The Chemical Constitution of Natural Fats*, Wiley, New York, 1941, p. 371.

pletely decompose the lead salts with the formation of soluble lead acetate. After removal of the ethanol, the mixture is transferred to a separatory funnel and extracted with ether. Additional acetic or hydrochloric acid should be added to insure complete decomposition of the lead soaps. The ethereal solution is washed with water until free of acetic and hydrochloric acids, after which the ether is removed by distillation under an atmosphere of inert gas. The unsaturated acid fraction should be maintained under an atmosphere of inert gas at all times to prevent oxidation and polymerization.

Limitations of the Lead Salt Method.—Regardless of the method used, complete and sharp separation of the saturated and unsaturated fatty acids is generally not possible. According to Jamieson[71] the lead salt–ether method, and the same is true of the lead salt–alcohol method, gives unsatisfactory results when applied to butterfat, coconut, palm kernel, and similar oils because they contain saturated acids (myristic and shorter chain length) whose lead salts remain in part or entirely with the unsaturated acid fraction. Also, this method cannot be used in separating the mixed fatty acids of fats and oils which contain erucic (rape and mustard oils), elaeostearic, chaulmoogric, hydnocarpic, or similar acids, because the lead salts of these acids are difficultly soluble in ether.

Sharp separation of the saturated and unsaturated fatty acids derived from hydrogenated fats likewise cannot be accomplished by either the lead salt–alcohol or lead salt–ether methods because of the relative insolubility of the lead salts of the solid iso-oleic acids. The saturated acid fraction will contain most of the solid iso-oleic acid of hydrogenated fats, small quantities (1% to 2%) of *n*-oleic acid, and in some cases, for example, acids from partially hydrogenated fish oils, relatively large quantities of iso acids of a higher degree of unsaturation. The saturated acid fraction may also contain appreciable quantities of long chain (C_{20} and above) monoethenoid fatty acids.

Fortunately not all of these acids are present in any one fat and even when some of them are present minor modifications of the procedure may provide a reasonably good separation. In the case of coconut, palm kernel, and similar oils most of the low molecular weight acids can be removed by steam distillation prior to separation of the saturated and unsaturated fatty acids. For quantitative use with hydrogenated oils (cottonseed, peanut, soybean, etc.) the unsaturation accompanying the saturated acid fraction can be determined by iodine titration and the results corrected on the assumption that the absorption of iodine is due to the presence of iso-oleic acid.

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[71] G. E. Jamieson, *J. Assoc. Official Agr. Chem.*, 11, 303–305 (1928); *Vegetable Fats and Oils*, 2nd ed., Reinhold, New Yokr, 1943, p. 407.

Barium Salt–Benzene Method.—Farnsteiner[72] proposed the use of barium salt–benzene as a means of separating saturated and unsaturated acids. This method, although not widely used, has been employed to effect separations of specific acids not readily amenable to other methods. For example, Bosworth and Helz[73] used the barium salt–benzene method to concentrate and ultimately isolate hydroxypalmitic acid from butterfat.

Lapworth, Pearson, and Mottram[74] and Skellon[75] applied the barium salt crystallization method to the isolation and purification of oleic acid from olive oil and commercial oleic acid. In both cases oleic acid of a high degree of purity was obtained for use in determining certain of its physical properties. Erdmann and Bedford[76] applied the barium salt–alcohol method to the separation of oleic and linoleic acids of linseed oil.

Smith and Chibnall[77] employed benzene containing 5% of 95% ethanol as a solvent for fractionating the barium soaps of the fatty acids of forage grasses. This medium was used to separate the saturated acids and oleic acid (insoluble fraction) from the higher unsaturated acids (soluble fraction). The insoluble fraction was then subjected to the lead salt–alcohol method to separate the saturated acids from the oleic acid.

Lithium Salt–Acetone Method.—Of the many combinations of salts and solvents, the lithium salt–acetone method of Tsujimoto[78,79] has been frequently applied to the separation of individual members in a mixture of acids of various degrees of unsaturation. According to Tsujimoto, the lithium salts of polyethenoid acids containing four or more double bonds are soluble in 95% acetone, whereas less unsaturated acids are relatively insoluble in this medium. In fact, the lithium salt–acetone method can be applied in separating the polyethylenic acids from the monoethylenic and saturated acids, and according to Tsujimoto, it affords the best means of separating the highly unsaturated acids in fish oils.

Lovern[80] has applied the lithium salt–acetone method in the investigation of many oils of aquatic origin. He first separates the saturated and unsaturated acids by means of the lead salt–alcohol method and then submits the unsaturated acid fraction to separation by the lithium salt–acetone method. For the latter separation, the crude liquid acids are dis-

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[72] K. Farnsteiner, *Z. Untersuch. Nahru. Genussm.*, **2**, 1–27 (1899); **4**, 63–65 (1901); **6**, 161–166 (1903).

[73] A. W. Bosworth and G. E. Helz, *J. Biol. Chem.*, **112**, 489–492 (1936).

[74] A. Lapworth, L. K. Pearson, and E. N. Mottram, *Biochem. J.*, **19**, 7–18 (1925).

[75] J. H. Skellon, *J. Soc. Chem. Ind.*, **50**, 131–134T (1931).

[76] E. Erdmann and F. Bedford, *Ber.*, **42**, 1324–1333 (1909).

[77] J. A. B. Smith and A. C. Chibnall, *Biochem. J.*, **26**, 218–234 (1932).

[78] M. Tsujimoto, *J. Chem. Ind. Japan*, **23**, 1007–1010 (1920); *Chem. Umschau Fette Öle Wachse Harze*, **33** 285–291 (1926).

[79] M. Tsujimoto and K. Kimura, *J. Chem. Ind. Japan*, **26**, 891–893 (1923).

[80] J. A. Lovern, *The Composition of the Depot Fats of Aquatic Animals*, Dept. Sci. and Ind. Res., Food Investigation Special Report No. 51, H. M. Stationery Office, London, 1942. See T. P. Hilditch and L. Maddison, *J. Soc. Chem. Ind.*, **51**, 169–173 (1942); O. B. Bjarnason and M. L. Meara, *ibid.*, **53**, 61–63 (1944).

solved in anhydrous acetone (960 ml. per 100 g.) neutralized with ammonia, and an equivalent amount of lithium chloride or acetate in aqueous solution (50 ml. per 100 g. of original acids) is added. After shaking the mixture for at least thirty minutes, it is cooled to 0°C. for an hour and the precipitated salts filtered off. The monoethylenic acids are contained in the precipitate and the polyethylenic members are in the filtrate. Since the process is not strictly quantitative each fraction must again be submitted to the lithium salt–acetone procedure.

Brown and Stoner[81] prepared a concentrate containing 82% of linoleic acid by crystallizing the lithium soaps of the mixed fatty acids of cottonseed oil from butanol at 30°, 0°, and −20°C. The precipitate at −20°C. contained 60% of linoleic acid and the filtrate 82%. Ault and Brown[82] applied the lithium soap–acetone method to the separation of the arachidonic acid of suprarenal phosphatides. A single crystallization gave a product containing 30% of arachidonic acid. The mixed fatty acids from suprarenal phosphatides were found to contain 19.8% of arachidonic acid by the lithium salt–acetone method compared to 22.2% on the basis of the polybromide number. When the results were corrected for the arachidonic acid which remained with the saturated fatty acids (4.4%), the agreement between the two methods was almost exact.

The lithium soap–alcohol method was used by Tsujimoto and coworkers[83,84] and by Toyama and Tsuchiya[85] in isolating and purifying clupanodonic acid from various marine animal oils.

Dorée and Pepper[86] found that the lithium salt–alcohol method was ineffective in separating erucic acid from the unsaturated acids of rapeseed oil. Only about 20% of acid was recovered and it had a low iodine value indicative of the presence of other acids.

Magnesium Salt–Alcohol Method.—Efforts have been made to separate specific acids from various fatty acid mixtures on the basis of the relative solubility of the magnesium salts in alcohol. Kerr[87] and later Thomas and Yu[88] attempted to develop methods for separating arachidic acid from the saturated acid fraction obtained from peanut oil. The method, while possessing some merit as a qualitative means of separation, was shown by Voorhies and Bauer[89] to be far from quantitative.

Chibnall, Piper, and Williams[90] applied the magnesium salt–alcohol

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[81] J. B. Brown and G. G. Stoner, *J. Am. Chem. Soc.*, **59**, 3–6 (1937).

[82] W. C. Ault and J. B. Brown, *J. Biol. Chem.*, **107**, 615–622 (1934).

[83] M. Tsujimoto, *Bull. Chem. Soc. Japan*, **3**, 299–307 (1928).

[84] M. Tsujimoto and H. Koyanagi, *J. Soc. Chem. Ind. Japan*, Suppl. binding, **38**, 271–272B (1935).

[85] Y. Toyama and T. Tsuchiya, *Bull. Chem. Soc. Japan*, **10**, 192–199, 232–241 (1935).

[86] C. Dorée and A. C. Pepper, *J. Chem. Soc.*, **1942**, 477–483.

[87] R. H. Kerr, *Ind. Eng. Chem.*, **8**, 904 (1916).

[88] A. W. Thomas and C.-L. Yu, *J. Am. Chem. Soc.*, **45**, 113–128 (1923).

[89] S. T. Voorhies and S. T. Bauer, *Oil & Soap*, **20**, 175–178 (1943).

[90] A. C. Chibnall, S. H. Piper, and E. F. Williams, *Biochem. J.*, **30**, 100–114 (1936).

method to the purification of the hydroxy acids separated from the cerebrosides, phrenosin and kerasin.

Combination and Comparison of Methods.—Toyama and co-workers[91,92] employed the sodium soap–acetone, lithium soap–alcohol methods individually or in sequence for the separation of gadoleic, eicosenoic, and other acids in Japanese fish and whale oils. The lithium soap–alcohol and magnesium soap–alcohol methods were employed by Toyama and Tsuchiya[93] in isolating selacholeic acid from cod liver and whale liver oils. These authors[94] also used a combination of the barium soap–acetone and lead salt–alcohol methods for separating tetradecenoic and dodecenoic acids from sperm blubber oil.

Bertram[95] prepared highly pure oleic acid by crystallizing the silver and mercury salts of the unsaturated fatty acids obtained by the lead salt–alcohol separation of crude or commercial oleic acid.

In the course of the preparation of oleic acid from teaseed oil, Hartsuch[96] compared the lead soap–alcohol, barium soap–benzene, and low temperature crystallization methods for the separation of oleic acid from the saturated acids and from linolenic acid. He found that the low temperature crystallization method was the most efficient of the three for the separation of saturated from unsaturated acids and also that crystallization from acetone at −60°C. was the most efficient method for the separation of oleic and linoleic acids.

Keffler and McLean[97] investigated the efficiency of the lead salt–alcohol method for the separation of the solid and liquid fatty acids, and of the lithium salt–alcohol method for the purification of oleic acid using a large quantity (750 g.) of the mixed acids. In neither case was the separation complete or efficient regardless of variations in the experimental conditions. After twelve recrystallizations of the lithium salt, the composition of the separated fraction and that of the mother liquor became constant with a maximum iodine value of 86.7. This value could be raised only by fractional distillation.

The foregoing references are but a few of the many similar ones which are to be found in the literature on the subject. They are sufficient, however, to indicate the general applicability and limitations of these methods.

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[91] Y. Toyama and T. Tsuchiya, *J. Soc. Chem. Ind. Japan*, Suppl. binding, **37**, 14–17B, 17–20B, 530–534B (1934).

[92] Y. Toyama and T. Ishikawa, *J. Soc. Chem. Ind. Japan*, Suppl. binding, **37**, 534–536B, 536–537B (1934).

[93] Y. Toyama and T. Tsuchiya, *J. Soc. Chem. Ind. Japan*, Suppl. binding, **38**, 684–687B (1935).

[94] Y. Toyama and T. Tsuchiya, *Bull. Chemical Soc. Japan*, **10**, 563–569, 570–573 (1935).

[95] S. H. Bertram, *Rev. trav. chim.*, **46**, 397–401 (1927).

[96] P. J. Hartsuch, *J. Am. Chem. Soc.*, **61**, 1142–1144 (1939).

[97] L. Keffler and J. H. McLean, *J. Soc. Chem. Ind.*, **54**, 362–367T (1935).

(*b*) *Separation of Bromo Derivatives*

Most of the unsaturated fatty acids when treated with bromine in cold organic solvents, *e. g.*, chloroform or ethyl ether, add bromine at the double bonds to form bromo derivatives. Advantage has been taken of the fact that these bromo derivatives differ sufficiently in their solubility characteristics to permit resolution of mixtures of these acids into their individual components. For example, unsaturated fatty acids containing four or more double bonds form polybromides which are practically insoluble in almost all of the common organic solvents. Clupanodonic acid containing five or six double bonds forms a polybromide insoluble in nearly all organic solvents, arachidonic acid containing four double bonds forms an octabromide insoluble in cold ethyl ether and benzene. Linolenic acid forms a hexabromide which is insoluble in ethyl ether and many other solvents. Linoleic acid forms a tetrabromide which is soluble in ethyl ether but nearly insoluble in cold petroleum naphtha. Oleic, ricinoleic, erucic, and other monoethenoid acids for dibromides which are soluble in most of the common organic solvents. The properties of the bromo derivatives of a number of unsaturated fatty acids are given in Tables 155 and 156.

TABLE 155

BROMO DERIVATIVES OF MONOETHENOID ACIDS

Acid	Dibromo derivative	Formula	Molecular weight	Bromine content, %
Obtusilic	4,5-Dibromocapric	$C_{10}H_{18}O_2Br_2$	330.08	48.42
Caproleic	9,10-Dibromocapric	$C_{10}H_{18}O_2Br_2$	330.08	48.42
Lauroleic	9,10-Dibromolauric	$C_{12}H_{22}O_2Br_2$	358.13	44.63
$\Delta^{5,6}$-Tetradecenoic	5,6-Dibromomyristic	$C_{14}H_{26}O_2Br_2$	386.18	41.39
Myristoleic	9,10-Dibromomyristic	$C_{14}H_{26}O_2Br_2$	386.18	41.39
Palmitoleic	9,10-Dibromopalmitic	$C_{16}H_{30}O_2Br_2$	414.23	38.58
Petroselinic	6,7-Dibromostearic	$C_{18}H_{34}O_2Br_2$	442.28	36.14
Oleic[a]	9,10-Dibromostearic	$C_{18}H_{34}O_2Br_2$	442.28	36.14
Vaccenic	11,12-Dibromostearic	$C_{18}H_{34}O_2Br_2$	442.28	36.14
Gadoleic	9,10-Dibromoeicosanoic	$C_{20}H_{38}O_2Br_2$	470.34	33.98
$\Delta^{11,12}$-Eicosenoic	11,12-Dibromoeicosanoic	$C_{20}H_{38}O_2Br_2$	470.34	33.98
Cetoleic	11,12-Dibromobehenic	$C_{22}H_{42}O_2Br_2$	498.39	32.07
Erucic[b]	13,14-Dibromobehenic	$C_{22}H_{42}O_2Br_2$	498.39	32.07
Selacholeic	15,16-Dibromotetracosanoic	$C_{24}H_{46}O_2Br_2$	526.44	30.36

[a] Also elaidic acid.
[b] Also brassidic acid.

Bromination and separation of the bromides on the basis of solubility have been applied for many years for the qualitative and quantitative examination of the unsaturated fatty acids present in fats and oils. The method has been the subject of numerous investigations[98] and many modi-

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[98] J. Lewkowitsch, *Chemical Technology and Analysis of Oils, Fat and Waxes.* 6th ed., Vol. I, Macmillan, London, 1938 (reprint; original ed. 1921), pp. 585 *et seq.*

TABLE 156

BROMO DERIVATIVES OF THE POLYETHENOID ACIDS

Acid	Bromo derivative	Formula	Mol. wt.	Polybromide number		Bromine content, %	M. p., °C.
				Theoretical[a]	Observed[b]		
Heragonic	Hexabromopalmitic[c]	$C_{16}H_{26}O_2Br_6$	729.86	291.52	...	65.70	40
Linoleic	Tetrabromostearic[d]	$C_{18}H_{32}O_2Br_4$	600.10	213.99	102.9	53.27	115.5–116.0
Linolenic	Hexabromostearic[e]	$C_{18}H_{30}O_2Br_6$	757.92	272.22	96.0	63.26	185.5–186.0
Elaeostearic	Hexabromostearic	$C_{18}H_{30}O_2Br_6$	757.92	272.22	...	63.26	141
Parinaric	Octabromostearic	$C_{18}H_{28}O_2Br_8$	915.73	331.30	...	69.82	...
Arachidonic	Octabromoeicosanoic[f]	$C_{20}H_{32}O_2Br_8$	943.79	309.99	84.2	67.74	227–228
Clupanodonic[g]	Decabromodocosanoic[h]	$C_{22}H_{34}O_2Br_{10}$	1129.65	341.81	...	70.74	Melts above 200° with decomp.
Nisinic	Dodecabromotetracosanoic	$C_{24}H_{36}O_2Br_{12}$	1315.52	368.98	...	72.90	...

[a] The theoretical polybromide number is the percentage of bromo derivative which would be obtained if the acid yielded 100% of insoluble bromides on the addition of bromine.

[b] Observed polybromide number is the percentage of bromo derivative actually obtained and varies with the method of bromination. The values reported are for the purest acids prepared to date.

[c] Soluble in benzene.

[d] Two tetrabromides, one soluble and one insoluble in petroleum ether.

[e] Two hexabromides, one soluble and one insoluble in ethyl ether.

[f] Insoluble in cold ether and benzene.

[g] Exact number and position of double bonds not entirely settled.

[h] Insoluble in most organic solvents.

fications have been introduced to improve its utility. No more conclusive evidence can be had for the presence of linolenic or linoleic acids in a mixture of unsaturated acids than a positive hexabromide or tetrabromide test. Unfortunately, the work of the past few years has shown that the method is far from quantitative even after various correction factors have been applied to improve its accuracy. Its failure as a reliable quantitative method is due to the fact that bromination of polyethenoid acids results in the formation of two or more isomeric bromo derivatives of different solubilities. Only the insoluble isomerides are ordinarily isolated from the reaction mixture and the ratios of the insoluble isomerides to the soluble isomerides are not always constant.

Within the limits of the method, the composition of a mixture of linolenic, linoleic, and oleic acids can be determined by determining the hexabromide and tetrabromide numbers. When the yields of hexa- and tetrabromostearic acids are corrected by the factors to be discussed later it is possible, at least in the case of some fats and oils, to obtain a fairly quantitative idea of the composition of the unsaturated fatty acid fractions but in other instances the results are merely approximations.

Bromination Procedure.—Where it is desired to separate the unsaturated acids in a fairly large sample of mixed acids either for purposes of identification or for use in other investigations the following procedure is satisfactory.

Bromination is best carried out by dissolving the mixture of unsaturated fatty acids in sufficient dry ethyl ether to form a 10% solution. The mixture is cooled to $-10°C.$ or below and bromine is added very slowly from a finely drawn pipette or burette. The mixture should be constantly shaken during the addition of bromine and the temperature should not be permitted to rise even perceptibly. Any noticeable rise in temperature of the whole solution indicates a very high local temperature at the point of bromine addition. Addition of bromine is continued until a persistent reddish yellow color is obtained indicating an excess of bromine.

If sufficient amounts of tetra- and/or triethenoid acids are present, octa- and/or hexabromides will begin to separate immediately. After standing ten to fifteen minutes in the brominating bath the excess bromine is destroyed by adding β-amylene drop by drop until the color disappears. The reaction mixture is then maintained at the temperature of ice for several hours to permit as complete separation as possible of the ether-insoluble bromides which are then removed by filtration, washed with ether, and recrystallized from benzene. The octabromo derivative of arachidonic acid is insoluble in benzene. Octa- and hexabromides are distinguishable by their solubilities in benzene, melting points, and content of bromine.

After separation of the ether-insoluble bromides, the ethereal solution is evaporated and the residue is extracted repeatedly with successive portions of boiling petroleum naphtha or, if preferred, in a Soxhlet apparatus. The petroleum naphtha extract is allowed to stand to permit separation of the crystalline tetrabromides. After removal of the separated tetrabromides the filtrate is concentrated and allowed to stand to permit the separation of any further quantities of tetrabromides. It is oftentimes possible to recover additional quantities of tetrabromides by a repetition of the process of concentrating the solution and permitting it to stand at a low temperature for long periods either with or without the addition of a few seed crystals.

The recovered tetrabromostearic acid is readily purified by recrystallization from petroleum naphtha. The addition of a small amount of ethyl ether to the petroleum naphtha solution is helpful in purifying tetrabromides. Tetrabromostearic acid can be identified by its characteristic solubility, melting point, and bromine content.

The filtrate, after extraction of the tetrabromides, contains the dibromides of any monoethenoid acid which was originally present in the mixed unsaturated fatty acids but it also contains, in addition, varying quantities of higher bromides isomeric with the insoluble polybromides previously separated. It has become an established practice to refer to the insoluble polybromides as α-bromides and to the isomeric soluble polybromides as β-bromides (see Chapters III and XIII).

Differences in the composition of the original fatty acid mixture and in the ratio in which insoluble and isomeric soluble bromides are formed during bromination affect the solubility of the individual bromo derivatives. The recovery of the individual insoluble bromides may, therefore, not be quantitative. If the mother liquors obtained on recrystallization of the insoluble fractions are added to the filtrate fractions, the final filtrate will contain, in addition to the liquid dibromides, the liquid polybromides and any normally insoluble polybromides rendered soluble by the mutual solubility effect of the mixed bromides. Some information concerning the composition of this final filtrate fraction may be obtained by debrominating it, esterifying the recovered unsaturated acids, fractionally distilling them, and determining the iodine and thiocyanogen values of the distilled fractions.

Polybromide Numbers.—It has long been recognized that the yield of bromo derivative from any given polyethenoid acid is not quantitative. Arachidonic acid gives only about one-fourth, linolenic approximately one-third, and linoleic approximately one-half of the theoretical yield of bromides. However, by carrying out the bromination and separation of the bromides in a rigidly prescribed manner certain empirical values have been obtained which have been designated octabromide, hexabromide, and tetrabromide numbers or collectively as polybromide numbers. By means of suitable equations these polybromide numbers can be related to the percentage of the individual components of a given mixture of unsaturated acids.

From time to time various empirical constants have been proposed for calculating the composition of mixtures of unsaturated fatty acids on the basis of their observed polybromide numbers. The constants proposed by Brown and co-workers which are discussed below are perhaps the most reliable proposed to date. These constants were obtained by determining under certain rigidly prescribed conditions the actual yield of insoluble polybromides which were obtained by bromination of highly purified unsaturated acids.

For arachidonic acid, Ault and Brown[99] found that the percentage of unsaturated acid equaled *the polybromide number of the mixed acids* × 100/80.4, *or* 100/91.8 for the methyl esters. A similar factor was proposed by Shinowara and Brown[100] for calculating the percentage of linolenic acid which is equal to *the hexabromide number* × 100/92. For determining the percentage of linoleic acid, Brown and Frankel[101] proposed the use of the equation: percentage of linoleic acid equals *the tetrabromide number* × 100/90.6. These equations are summarized as follows:

$$\text{Per cent arachidonic acid} = \frac{(\text{Octabromide No. of mixed acids}) \times 100}{80.4}$$

$$\text{Per cent methyl arachidonate} = \frac{(\text{Octabromide No. of mixed methyl esters}) \times 100}{91.8}$$

$$\text{Per cent linolenic acid} = \frac{(\text{Hexabromide No. of mixed acids}) \times 100}{92}$$

$$\text{Per cent linoleic acid} = \frac{(\text{Tetrabromide No. of mixed acids}) \times 100}{90.6}$$

The various polybromide numbers in the above equations were obtained by dividing 100 × *the weight of the corresponding bromides* recovered by *the weight of mixed fatty acids* used in their determination.

When these empirical values are used in calculating the composition of an unknown mixture of unsaturated fatty acids, reasonable quantitative results may be obtained in the case of some fats but with many others the calculated composition may be considerably in error. One reason for the failure of the method from the quantitative point of view results from the mutual solubility effect which the various bromo derivatives exert on each other. For example, if the amount of linolenic acid is small and the amounts of linoleic and oleic acids are large, as for example in the case of soybean oil, the ether-insoluble hexabromostearic acid may not separate from the reaction mixture. Similarly, if the fatty acid mixture contains

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[99] W. C. Ault and J. B. Brown, *J. Biol. Chem.*, 107, 615–622 (1934).

[100] G. Y. Shinowara and J. B. Brown, *J. Am. Chem. Soc.*, 60, 2734–2738 (1938). D. T. Mowry, W. R. Brode, and J. B. Brown, *J. Biol. Chem.*, 142, 671–678 (1942); J. P. Kass, W. R. Roy, and G. O. Burr, *Anal. Chem.*, 19, 21–24 (1947).

[101] J. B. Brown and J. Frankel, *J. Am. Chem. Soc.*, 60, 54–56 (1938).

an unduly large proportion of oleic acid, the dibromostearic acid may dissolve and retain in solution an appreciable amount of petroleum naphtha-insoluble tetrabromide. For this reason it is often possible to obtain several crops of tetrabromide crystals from the dibromide fraction by maintaining the solution of dibromides, or the oily dibromide fraction itself, for long periods at a low temperature.

Effect of Isomers on the Polybromide Number Determination.—The validity of the polybromide number determination as a quantitative method of estimating the composition of a mixture of unsaturated acids is based on the assumptions that the unsaturated acids in a natural mixture of fatty acids are either identical with or react on bromination exactly as the fatty acids used in establishing the values of the constants of the polybromide equations.

Actually there are many cases where these assumptions do not hold, probably because both positional and stereoisomers of linolenic and linoleic acids do not form soluble and insoluble bromides in the invariant ratios assumed for the standard acids. Elaeostearic acid, for example, does not add bromine in the same manner as linolenic with which it is isomeric.

Evidence is available which indicates that naturally occurring fats and oils may contain stereoisomeric linoleic acids. For example, Frankel, Stoneburner, and Brown[102] found that linoleic acid obtained by low temperature crystallization of the fatty acids from olive oil is not identical with the linoleic acid prepared by the same method from sesame, cottonseed, corn, grapeseed, and poppyseed oils, since it does not form soluble and insoluble bromides in the same manner as do the acids from the latter oils. These authors concluded that linoleic acid from olive oil contains in addition to *cis-cis*-$\Delta^{9,10,12,13}$-octadecadienoic acid, one or more stereoisomers which possesses either a *trans-cis*- or a *cis-trans*-, but not a *trans-trans*-configuration. The *cis-trans*- and *trans-cis*-isomers add iodine monochloride normally but produce petroleum naphtha- and ether-soluble tetrabromides instead of the insoluble α-tetrabromide melting at 115.5–116.0°C.

It has been established by spectrophotometric methods that many natural fats contain small amounts of conjugated isomers of the principal unconjugated acids previously known to be present in these fats. Also by spectrophotometric examination before and after alkali isomerization, it has been found that these fats often contain small amounts of acids of a higher degree of unsaturation than has heretofore been supposed. The failure to detect these small quantities of higher polyunsaturated acids previously has been due to the fact that the corresponding polybromides generally do not separate from the bromination mixture where, on the basis

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[102] J. S. Frankel, W. Stoneburner, and J. B. Brown, *J. Am. Chem. Soc.*, **65**, 259–262 (1943).

of solubility of the pure compound, they should have. However, they frequently separate with the next lower polybromide with a consequent lowering of the melting point of that product. This effect is most frequently observed in the case of hexabromostearic acid which is often reported to melt between 180° and 184°C. instead of 185.5° to 186.0°, and of tetrabromostearic acid which is reported to melt at 113.0° to 114.0°C. instead of 115.5° to 116.0°.

The polybromide number method is especially unsuited for investigating hydrogenated fats because of the presence in these products of both positional and stereoisomers which behave quite differently on bromination with respect to the relative yield of soluble and insoluble polybromides or in some cases even of dibromides.

It has not generally been appreciated that debromination of polybromides, unless carefully conducted, may yield mixtures of isomeric acids instead of the so-called α-form of the acid. The unsaturated acid is usually regenerated by refluxing its bromo derivative with zinc in alcohol solution or in alcohol containing a small amount of mineral acid, usually hydrochloric acid. Other solvents have been used including pyridine, ethyl ether, isopropyl ether, dioxane, and glacial acetic acid. Petroleum naphtha is ineffective as a solvent for this reaction and the use of glacial acetic acid produces acids with anomalously low iodine values indicative of hydrogenation reactions.

According to Frankel and Brown,[103] the best solvent for debrominating tetrabromostearic acid is ethyl ether although methanol, isopropyl ether, and dioxane are satisfactory. The use of ethyl ether obviates the necessity of saponifying the debrominated acids in order to remove any esters formed during the debromination when alcohol is used as a solvent. When ethyl ether, isopropyl ether, or dioxane is used it is only necessary to filter the reaction mixture, wash out the last traces of zinc bromide with water, and remove the solvent in order to recover the unsaturated acid.

Applications of the Bromination Method.—Even though the bromination method may be limited in its quantitative applications, it still has merit from the preparative points of view. Crystalline polybromo acids can be prepared in pure form from many types of fats and oils and from these bromo derivatives the corresponding unsaturated acids may be regenerated by debromination. Many valuable applications of the bromination method for the detection and separation of unsaturated acids from fats can be cited, for example: Eckstein[104] identified traces of arachidonic acid in human fat; Ellis and Isbell[105] and Brown and Deck[106] identified

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[103] J. S. Frankel and J. B. Brown, *J. Am. Chem. Soc.*, **65**, 415–418 (1943).

[104] H. C. Eckstein, *J. Biol. Chem.*, **64**, 797–806 (1925).

[105] N. R. Ellis and H. S. Isbell, *J. Biol. Chem.*, **69**, 219–238, 239–248 (1926).

[106] J. B. Brown and E. M. Deck, *J. Am. Chem. Soc.*, **52**, 1135–1138 (1930).

this acid in lard; and Brown and co-workers[107-110] found it in the glandular organs of animals, in avian oils, and elsewhere. Brown and Hansen[111] determined the content of arachidonic and linoleic acid in human blood serum of normal and eczematous subjects by means of bromination.

An interesting application of the bromination method was the separation of traces of decenoic acid from butterfat by Bosworth and Brown.[112] A fraction consisting of the methyl esters of capric and decenoic acids was treated with bromine and distilled. The methyl dibromocaprate distilled *in vacuo* 60°C. above the associated methyl caprate and was therefore readily separated from the saturated acid.

On the basis of the data obtained by fractionating the polybromides of the insoluble fatty acids of menhaden oil, McGregor and Beal[113] concluded that the maximum unsaturation of the C_{14} acids of this oil was two double bonds, of the C_{16} acids, three double bonds, of the C_{18} acids, four double bonds, of the C_{20} acids, five double bonds, and of the C_{22} acids, six double bonds.

(c) *Low Temperature Crystallization*

A marked advance in the technique of separating fatty acid mixtures followed the application of fractionation from solvents at low temperatures by Brown and co-workers.[114-120] This solubility method (*cf.* Chapter VII) is not universal in its applications but with the mixed acids of many fats and oils rather good separation of the saturated and unsaturated acids can be obtained, and individual fatty acids, especially of the unsaturated series, can be separated with little difficulty by a combination of low temperature crystallization and distillation. The method, in general, involves solution of the mixed fatty acids in a suitable solvent or mixture of solvents and cooling to various prescribed temperatures followed by separation of the crystalline acids from the mother liquor. The procedure must necessarily be varied depending on the source of the fatty acid mixture and the type of separation which it is desired to effect.

Separation of Saturated and Unsaturated Acids.—The separation of a

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[107] W. C. Ault and J. B. Brown, *J. Biol. Chem.*, **107**, 607–614 (1934).
[108] J. B. Brown, *J. Biol. Chem.*, **83**, 783–791 (1929).
[109] J. B. Brown, *J. Biol. Chem.*, **80**, 455–460 (1928).
[110] J. B. Brown and C. C. Sheldon, *J. Am. Chem. Soc.*, **56**, 2149–2151 (1934).
[111] W. R. Brown and A. E. Hansen, *Proc. Soc. Exptl. Biol. Med.*, **36**, 113–117 (1937).
[112] A. W. Bosworth and J. B. Brown, *J. Biol. Chem.*, **103**, 115–134 (1933).
[113] R. R. McGregor and G. D. Beal, *J. Am. Chem. Soc.*, **48**, 3150–3161 (1926).
[114] J. B. Brown and G. C. Stoner, *J. Am. Chem. Soc.*, **59**, 3–6 (1937).
[115] J. B. Brown and G. Y. Shinowara, *J. Am. Chem. Soc.*, **59**, 6–8 (1937).
[116] J. B. Brown and J. Frankel, *J. Am. Chem. Soc.*, **60**, 54–56 (1938).
[117] G. Y. Shinowara and J. B. Brown, *J. Am. Chem. Soc.*, **60**, 2734–2738 (1938).
[118] J. Frankel and J. B. Brown, *J. Am. Chem. Soc.*, **63**, 1483–1484 (1941).
[119] J. B. Brown, *Chem. Revs.*, **29**, 333–354 (1941).
[120] J. S. Frankel, W. Stoneburner, and J. B. Brown, *J. Am. Chem. Soc.*, **65**, 259–262 (1943).

mixture of fatty acids or monoesters into saturated and unsaturated acid fractions is generally carried out in acetone solution. However, the same type of separations can be effected from methanol, methyl acetate, ethyl acetate, methyl ethyl ketone, and petroleum naphtha solutions. Fatty acid mixtures of different compositions require modification of the method but in general separation is more or less readily accomplished by dissolving the mixed fatty acids in acetone or methanol sufficient to make a 10% solution, cooling to −20° to −25°C., and filtering off the precipitate, either in a room maintained at −20°C. or by filtration at room temperature on a precooled Buchner funnel. Filtration is usually sufficiently rapid to permit separation and washing of the crystalline precipitate with precooled solvent at room temperature.

Brown and Stoner[114] found that a saturated fatty acid fraction having an iodine value of 7.2 or lower could be obtained by cooling a 10% solution of the mixed acids of cottonseed oil in acetone or methanol to −20°C. Frankel, Stoneburner, and Brown[120] separated the solid and liquid fatty acids of corn, sesame, cottonseed, grapeseed, and poppyseed oils by crystallizing at −20° to −25°C. the mixed fatty acids from an acetone solution containing 75 g. of acids per liter of solvent.

Brown,[119] Hartsuch,[96] Hilditch and Riley,[121] and others have compared the low temperature crystallization and the lead salt–alcohol methods for the separation of the saturated and unsaturated acids obtained from a variety of fats and oils, and concluded that, in general, the former is superior to the latter. Singleton, Lambou, and Bailey[122] investigated the effect of solvent, temperature, and other factors on the degree of separation of solid and liquid fatty acids obtained from hydrogenated and unhydrogenated cottonseed oils. They found that at any fixed temperature the most efficient separations were obtained in the highly polar solvents, acetone and methyl acetate. However, it was found possible in any case to make equally efficient separations with a nonpolar solvent such as petroleum naphtha by conducting the crystallization approximately 10°F. below that employed with the polar solvent.

When large amounts of mixed fatty acids are submitted to low temperature fractionation from solvents, a somewhat sharper separation of saturated and unsaturated acids can be obtained by redissolving the saturated fatty acid fraction and repeating the operation. The combined filtrates and washings which contain the unsaturated fatty acids can be reduced in volume and the crystallization repeated to recover any additional saturated acids which may separate. The mixed unsaturated acids may then be recovered by evaporating the solvent under reduced pressure or they may be

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[121] T. P. Hilditch and J. P. Riley, *J. Soc. Chem. Ind.*, **64**, 204–207 (1945).

[122] W. S. Singleton, M. Lambou, and A. E. Bailey, *Oil & Soap*, **22**, 168–174 (1945).

fractionated by cooling to still lower temperatures as will be described later.

Earle and Milner[123] found that the method could be used for the quantitative determination of the saturated fatty acids in soybean oil. The procedure described by these authors is as follows:

> "A sample of about 5 g. of mixed acids is placed in a test tube, and 50 ml. of acetone is added. The tube and its content are suspended in a cold bath consisting of acetone and dry ice at about −41°C., and the sample is stirred occasionally with a thermometer until the temperature reaches −40°C. The soluble acids are then removed by filtering through a glass filter stick which has been previously cooled to the temperature of the bath. The solid materials clinging to the thermometer and filter stick are washed back into the test tube with 50 ml. of acetone and permitted to dissolve. After two more crystallizations the solid acids are dissolved in acetone and transferred to a small tared flask. The solvent is removed on a steam bath, and the residue is dried in an oven at 105°C. for one-half hour. The flask and contents are cooled and weighed, and the amount of 'solid' acids is calculated. The iodine number of the 'solid' acids is determined and used to calculate the amount of unsaturated acid in the 'solid' acid fraction, assuming that the only unsaturated acid present is oleic. Subtraction of the 'oleic' acid from the 'solid' acids gives the amount of saturated acids present in the original sample of mixed fatty acids."

As a quantitative method, low temperature crystallization is no doubt of limited application but in most cases it is probably as accurate as the lead salt–alcohol method, and for the preparation of large quantities of saturated and unsaturated acid fractions it is simpler, more rapid, and more economical than any other method.

Separation of Specific Unsaturated Acids.—The method of fractional crystallization from solvents at low temperature as a means of separating specific unsaturated acids from a mixture of such acids has been especially fruitful in the hands of Brown and co-workers. They have applied the method to the preparation of oleic, linoleic, linolenic, and arachidonic acids from the mixed unsaturated fatty acids of a variety of fats and oils. For example, Brown and Shinowara[115] isolated oleic acid from olive oil by crystallization of the mixed fatty acids from acetone at −60°C. The properties of the oleic acid prepared by this method were: m.p. 13°C., molecular weight 282.4, iodine number 89.90, n^{20} 1.4585.

Smith[124] prepared oleic acid of extreme purity by a combination of distillation and low temperature cyrstallization. Methyl oleate was first distilled through an efficient column which removed most of the solid acids and the regenerated acid was then fractionally crystallized at low temper-

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[123] F. R. Earle and R. T. Milner, *Oil & Soap*, **17**, 106–108 (1940). See W. C. Bull and D. H. Wheeler, *ibid.*, **20**, 137–141 (1943).

[124] J. C. Smith, *J. Chem. Soc.*, **1939**, 974–980.

ature to separate the higher unsaturated acids. The purified oleic acid had the following characteristics: α-form, f.p. 13.34°C., m.p. 13.36° ± 0.04°C.; β-form, m.p. 16.25°C. Smith demonstrated that the presence of 1% of stearic acid lowers the melting point of oleic acid by only 0.13°C., therefore, freezing and melting points to be of value as criteria of purity of this acid must be taken with the thermometer in the liquid and must be accurate to ±0.05°C.

Brown and co-workers[114,116,118,120] prepared linoleic acid from corn, sesame, cottonseed, grapeseed, and poppyseed oils by crystallization of the mixed fatty acids from acetone at $-20°$, $-50°$ and $-70°$C., followed by recrystallization from petroleum naphtha at $-60°$. The linoleic acid thus obtained had the following properties: iodine number 180.8, n^{20} 1.4699, m.p. $-5.4°$C, tetrabromide number 100.6.

The procedure of low temperature crystallization followed by Brown and co-workers for preparing pure linoleic acid is as follows: The mixed fatty acids of an oil are dissolved in acetone (75 g. per liter of solvent), cooled to $-20°$ to $-25°$C., and the crystalline fraction removed by filtration. The filtrate is cooled to $-50°$ with slow stirring and the crystalline material separated as before. The filtrate from this operation is cooled to $-70°$ and the solidified portion again removed. The crystalline product from the last operation, which contains approximately 90% linoleic acid, is dissolved in petroleum naphtha (65 g. per liter of solvent, b.p. 30–60°C.) and cooled to $-48°$. The solid which separates under these conditions contains approximately 95% linoleic acid. This product is dissolved in petroleum naphtha (6.25 g. per liter of solvent) and cooled to $-60°$ to $-62°$. The product separating under these conditions is practically pure linoleic acid. The success of the over-all operation is dependent on maintaining the linoleic to oleic acid in a ratio that will minimize mixed crystal or compound formation.

Shinowara and Brown[117] prepared linolenic acid from linseed and perilla oils by fractionation of the mixed fatty acids from acetone at $-23°$, $-45°$, $-60°$ and $-75°$C. and from petroleum naphtha at $-50°$. However, crystallization alone, as well as crystallization followed by distillation of the most concentrated fraction, failed to yield pure linolenic acid. The best product obtained contained only 88% of linolenic acid. Methyl arachidonate was prepared by Shinowara and Brown[125] and by Mowry, Brode, and Brown[126] from adrenal and suprarenal phosphatides by crystallization of the mixed esters from acetone at $-20°$, $-65°$ and $-75°$. The final crystallized product was 70% pure but on distillation it gave a product containing 97.7% of methyl arachidonate.

A unique application of the low temperature crystallization method was

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[125] G. Y. Shinowara and J. B. Brown, *J. Biol. Chem.*, **134**, 331–340 (1940).

[126] D. T. Mowry, W. R. Brode, and J. B. Brown, *J. Biol. Chem.*, **142**, 671–678 (1942).

made by Brown and Green[127] in the preparation of methyl ricinoleate and ricinoleic acid from castor oil. Because of the tendency of ricinoleic acid to undergo various changes in structure when it is subjected to heat and chemical agents, its isolation in pure form is extremely difficult. However, by low temperature crystallization of the methyl esters prepared by direct alcoholysis of castor oil, products were obtained which contained 97% to 99.5% of methyl ricinoleate. The ester melted at −4.0° to −4.5°C., and had the following properties: n^{20} 1.4628, acetyl number 137.0, molecular weight 311.6, iodine number 80.7, optical rotation in acetone $[\alpha]_D^{27}$ 5.19. It was not possible to prepare pure ricinoleic acid from the methyl esters since saponification, even in the cold, and distillation result in dehydration. Cold saponification of the crude esters and fractional crystallization gave an acid which was only 95% pure.

Cramer and Brown[128] applied the method of low temperature crystallization from methanol, acetone, or petroleum naphtha to the separation of the methyl esters of C_{14}, C_{16}, and C_{18} acids obtained from human body fat. De la Mare and Shorland[129] submitted the methyl esters derived from pork fat to low temperature (−35°C.) crystallization from acetone (15 ml. per g. of esters) prior to ester fractionation of the insoluble and combined soluble esters.

Emersol Process for the Separation of Fatty Acids.—According to recent trade literature,[130] Emery Industries, Inc., began investigations on the solvent fractionation of fatty acids in 1934 which culminated in the development of a pilot plant and subsequently a semicommerical unit for effecting this operation. In 1942 the first of two commercial units for the production of a variety of fatty acid fractions by low temperature fractionation was placed in operation. The process, which is a continuous one, employs methanol as solvent and as the heat interchange medium in the multitubular crystallizer. A crystal promoter is added to the methanol solution of mixed fatty acids to assist the formation of readily filterable crystals of the solid acids.

The process has been applied to the production of stearic and oleic acids from Twitchellized and distilled tallows at a rate of approximately two million pounds per month. It is claimed that the process has been applied to the separation of solid and liquid acids of linseed, soybean, sardine, palm, and cottonseed oils and ucuhuba fat.

It is evident from the foregoing discussion that the low temperature fractionation of fatty acids and esters from solvents has, within a very few

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[127] J. B. Brown and N. D. Green, *J. Am. Chem. Soc.*, **62**, 738–740 (1940).

[128] D. L. Cramer and J. B. Brown, *J. Biol. Chem.*, **151**, 427–438 (1943).

[129] P. B. D. De la Mare and F. B. Shorland, *Analyst*, **69**, 337–339 (1944).

[130] R. E. Kistler, V. J. Muckerheide, and L. D. Meyers, *Oil & Soap*, **23**, 146–150 (1946). See also *Emersol Process for the Separation of Fatty Acids*, Bull. No. 2051, Blaw-Knox Division of Blaw-Knox Co., Pittsburgh, Pa., 1945.

years, passed through various stages of development from laboratory to commercial practice. To some extent it has been developed as a quantitative method but its greatest utility lies in the ease and effectiveness with which separations can be made into saturated and unsaturated fatty acids on one hand, and preparation of relatively pure unsaturated acids on the other.

The process is comparatively simple and rapid, and except for the process of saponification, without the introduction of any steps which might result in isomerization or other changes in chemical structure of the final product. It obviates the use of the operations involved in the lead salt separation, esterification, distillation, and subsequent saponification of the distilled esters. The operation requires a minimum of equipment and the solvent can be recovered and reused.

5. Chromatographic Separation

Chromatographic analysis, so-called because it was first applied by Tswett to the separation of plant pigments, has been successfully applied to the separation and purification of various components and derivatives of fats and oils, including fatty acids, esters, glycerides, phosphatides, hydrocarbons, sterols, ketones, and fat-soluble vitamins. Although it has not been equally effective in separating all types of lipids, chromatography has made possible the isolation of certain substances which could not otherwise have been obtained in equal degree of purity by any other method.

The method, in general, comprises solution of the products to be separated in a suitable solvent and passing the solution through a column of adsorbent. As a result of the difference in the degree to which each molecular species is adsorbed, the various components of the solution will be separated into a series of bands. Separation into bands results from the fact that the weakly adsorbed substances will move through the column more rapidly than those components which are more strongly adsorbed. Subsequent washing of the column results in more complete separation and ultimately in the development of distinct bands or adsorption zones. When the adsorption bands have been developed, the column can be separated into series of zones each one of which contains either a simple mixture or, in an ideal separation, a specific component which can then be recovered by elution with a suitable solvent.

Various adsorbents have been used in separating fatty components, the most effective of which is activated alumina. Various fat solvents, including petroleum naphtha, benzene, and chlorinated solvents, have been used and, of these, petroleum naphtha and benzene are generally the most effective. Detailed directions for the preparation of adsorption columns and the technique of carrying out various types of separations are given in standard works on the subject of chromatographic analysis.[131,132]

(a) Separation of Saturated and Unsaturated Acids

Kondo[133] obtained a partial separation of a mixture of oleic and stearic acids, and of oleic and palmitic acids, on passing a solution of the mixed acids through a column of alumina. The acids were dissolved in petroleum naphtha containing a little benzene and the chromatogram developed by washing the column with benzene. The oleic acid was adsorbed in the upper portion of the column and the saturated acid in the lower portion, while the unresolved mixture was contained in the central portion.

Manunta[134] prepared a mixture of palmitic, stearic, and oleic acids in petroleum naphtha and subjected it to chromatographic analysis using hydrated magnesium sulfate, $MgSO_4 \cdot \frac{1}{2}H_2O$, as adsorbent. When the solution was passed through the column, several zones or bands were developed. The uppermost band contained oleic acid; the lower portion of the column contained a mixture of palmitic and stearic acids. By reuniting the products of similar melting point and refractionating on a column of the same material, relatively pure palmitic and stearic acids were obtained.

As part of a comprehensive investigation of the applicability of adsorption technique to the separation of a variety of fatty products, Kaufmann[135] prepared mixtures of saturated with unsaturated acids, as well as mixtures of various unsaturated acids, including oleic–linoleic, oleic–erucic, palmitic–oleic, erucic–stearic, stearic–oleic–linoleic, etc., and submitted them to chromatographic analysis using various solvents, fatty acid concentrations, and adsorbents. Many other mixtures of acids, as well as the mixed fatty acids from coconut and palm oils and butter, were submitted to chromatographic adsorption with varying degrees of success. He concluded that the method was especially valuable for producing concentrates of fatty acids, and for the isolation of specific acids, as for example unaltered linolenic acid, and further, that it was a practical process for refining fats and separating fatty acids on an industrial scale.

Swift, Rose, and Jamieson[136] applied chromatography to the preparation of pure methyl linoleate from cottonseed oil. The mixed methyl esters of

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[131] L. Zechmeister and L. Cholnoky, *Principles and Practice of Chromatography.* Chapman & Hall, London, 1941.

[132] H. H. Strain, *Chromatographic Adsorption Analysis*, Interscience, New York, 1942. See also N. R. Fisk, *Paint Tech.*, 10, 85–89, 107–112 (1945); T. I. Williams, *An Introduction to Chromatography*, Blackie, London, 1946.

[133] H. Kondo, *J. Pharm. Soc. Japan*, 57, 832–839, in German 218–229 (1937).

[134] C. Manunta, *Helv. Chim. Acta*, 22, 1156–1160 (1939).

[135] H. P. Kaufmann, *Fette u. Seifen*, 46, 268–273 (1939); *Angew. Chem.*, 53, 98–99 (1940); French Patents 853,065 and 853,066 (March 9, 1940); British Patents 541,002 541,003 (Nov. 10, 1941).

[136] C. E. Swift, W. G. Rose, and G. S. Jamieson, *Oil & Soap*, 20, 249–255 (1943).

cottonseed oil were prepared by ester interchange using methanol and metallic sodium as catalyst. The esters were distilled and a single fraction representing 95% of the total acids was collected and submitted to chromatographic separation. Aluminum oxide was used as the adsorbent and hexane as the solvent. The recovered methyl linoleate had the following properties: Wijs iodine value 170.4, thiocyanogen value 87.3, n_D^{25} 1.4594. Distillation of the ester effected no change in these constants. It was computed that the product consisted of 97.7% methyl linoleate and 2.3% methyl oleate.

Dutton[137] described a method of adsorption analysis of colorless compounds which employs a highly sensitive differential refractometer for measurement of changes in the refractive index of percolates from adsorption columns during continuous flow. The method was applied to the separation of artificial mixtures of oleic and stearic acids of known composition.

Claesson[137a] has recently developed a method whereby long chain saturated, branched chain, and unsaturated fatty acids may be separated by a flowing chromatographic method which employs a nonpolar solvent (heptane) and activated silica as adsorbent. Each homologous series can in turn be separated into individual components by a similar technique which employs activated carbon as adsorbent.

(b) *Separation of Saturated Fatty Acids*

In connection with the investigation of the applicability of chromatography to the separation of fatty acids, which has already been referred to, Kaufmann[135] determined the degree of separation which could be effected with mixtures of long chain saturated acids. With a 1:1 mixture of stearic and myristic acids, pure stearic and myristic acids were obtained in the top and bottom zones, respectively, of the chromatographic column employing Brockmann aluminum oxide as adsorbent and benzene as solvent. A similar mixture of palmitic and myristic acids yielded a fraction containing 96% myristic and 4% palmitic acids.

Graff and Skau[138] separated mixtures of stearic and myristic acids, and of stearic and oleic acids, by adsorption on magnesium oxide columns impregnated with phenol red. Development of zones containing the separated acids was followed by changes in color of the dye-impregnated adsorbent.

Cassidy[139] investigated the adsorption isotherms of petroleum naphtha solutions of lauric, myristic, palmitic, and stearic acids using various acti-

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[137] H. J. Dutton, *J. Phys. Chem.*, **48**, 179–186 (1944).

[137a] S. Claesson, *Arkiv. Kemi Mineral. Geol.*, **23A**, No. 1, (1946); *Rec. trav. chim.*, **65**, 571–575 (1946).

[138] M. M. Graff and E. L. Skau, *Ind. Eng. Chem., Anal. Ed.*, **15**, 340–341 (1943).

[139] H. G. Cassidy, *J. Am. Chem. Soc.*, **62**, 3073–3076, 3076–3079 (1940).

vated carbons, aluminas, magnesium oxide, clay, and silica gel. Of the various combinations of acids and adsorbents used only one mixture namely, lauric and stearic acids, was readily separated on activated charcoal from a petroleum naphtha solution. About 93% of the acids were recovered in pure form; lauric acid was less strongly adsorbed than stearic and, therefore, was found in the earliest percolates.

(c) *Separation of Other Lipids*

Walker and Mills[140] subjected linseed oils of various origins to chromatographic analysis in which aluminum oxide was employed as the adsorbent and commercial hexane as solvent. After two fractionations only four adsorption zones were obtained. The recovered fractions possessed iodine numbers of 202.8, 174.8, 146.3, and 116.2, respectively. The authors concluded, therefore, that linseed oil contains relatively few types of triglycerides of which oleodilinolenin and dilinoleolinolenin predominate. In a subsequent publication, Walker and Mills[141] reported the separation from linseed oil, by means of chromatography, of a fraction having an iodine number of 246.5 and consisting therefore primarily of trilinolenin.

Winterstein and Stein[142] found that dipalmityl ketone and hentriacontane which occur in the unsaponifiable fraction of ethereal extracts of plant materials can be successfully separated by chromatography. Wagner-Jauregg[143] applied chromatography to the purification of the tribromanilide of tuberculic acid, $C_{35}H_{60}NOBr_3$. The melting point of the crude product was raised from 60° to 68°C. by adsorption on a column of aluminum oxide from benzene solution.

Ralston, Harwood, and Pool[144] found that the reaction products produced by catalytic cracking of long chain nitriles consisted exclusively of hydrocarbons and unreacted nitrile which could be quantitatively separated by chromatographic adsorption on a column of silica gel. The cracked fraction was allowed to flow down a column of silica gel which retained all the components of the fraction. The hydrocarbons were then removed by washing the column with petroleum naphtha. The silica gel column was then treated with ammonia gas and the nitriles removed by heating the adsorbent to 400°C.

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[140] F. T. Walker and M. R. Mills, *J. Soc. Chem. Ind.*, **61**, 125–128 (1942).

[141] F. T. Walker and M. R. Mills, *J. Soc. Chem. Ind.*, **62**, 106–109 (1943).

[142] A. Winterstein and G. Stein, *Z. physiol. Chem.*, **220**, 247–277 (1933). See also K. A. Williams, *Analyst*, **71**, 259–263 (1946).

[143] T. Wagner-Jauregg, *Z. physiol. Chem.*, **247**, 135–140 (1937).

[144] A. W. Ralston, H. J. Harwood, and W. O. Pool, *J. Am. Chem. Soc.*, **59**, 986–993 (1937).

CHAPTER XXIII

IDENTIFICATION OF INDIVIDUAL FATTY ACIDS

1. Introduction

In any investigation involving the isolation of a fatty acid it is generally desirable not only to establish its identity but also its degree of purity. If resolution of a complex mixture does not result in the isolation of a pure acid but yields instead a simpler and still incompletely resolved mixture, it may be highly desirable to determine the composition of the product. These ends may generally be accomplished by determining certain characteristic properties of the isolated product and comparing them with those established for the pure components.

The physical properties most commonly relied upon for purposes of identifying fatty acids and esters are melting, freezing, and transition points, refractive index, density, x-ray diffraction spacing, and absorption spectra, each of which has been dealt with at length elsewhere in this volume. Chemical properties applied for the same purpose are neutralization equivalent, iodine, thiocyanogen, and hydrogen absorption, oxidation, and preparation of various derivatives having additional characteristic properties. No one of these methods should be relied upon solely for either identification of an acid or determination of its relative purity. Owing to the increasingly smaller difference in the numerical values of the physical properties of adjacent members as the series is ascended, and the additive nature of certain of these properties, it becomes more and more difficult to identify unequivocably a given higher fatty acid or mixture of acids by any one or any combination of molar properties.

2. Identification of Saturated Acids

Saturated acids and their methyl or ethyl esters, if extremely pure, can readily be identified by comparison of their neutralization or saponification equivalents, melting, freezing, and transition points, refractive indices, and crystal spacings which have been recorded and discussed in previous chapters. If the acid is isolated from a complex mixture by means of fractional distillation or a combination of solvent fractionation and distillation, it may still comprise a binary, ternary, or even more complex mixture of components of the same or a different homologous series.

Many workers are not cognizant of the fact that the preparation of a highly pure acid or ester is extremely difficult, and that numerical equivalence of a given physical property of a known and unknown acid or ester does not necessarily establish its identity. For example, Phillips and Mumford[1] demonstrated that fractionation alone, even through an efficient column, does not necessarily lead to the separation of a pure acid or ester, and that the melting points of the α-form of esters, which in the case of esters such as ethyl margarate is the melting point of the compound itself, afford no information as to their purity. Furthermore, so far as the presence of homologs is concerned, recrystallization of the α-form may serve to make an ester *less*, instead of *more* pure. For purposes of identification, therefore, all saturated acid esters should be recrystallized to a constant β-melting point.

It is now generally agreed that no single quantitative method or combination of methods of fractionation of a complex mixture of fatty acids or esters derived from a natural fat will result in a series of fractions each composed of a single component. Therefore, when these fractions are composed predominantly of saturated acids or esters recourse is made to calculation of their compositions on the basis of neutralization or saponification equivalents. In order to do so, a number of assumptions have to be made or the necessity for making them must be eliminated.

It is generally assumed that the saturated acid or ester fraction contains no more than three components, *two saturated* and *one unsaturated.* The two saturated components are assumed to be the two homologs between which the observed neutralization equivalent or molecular weight is found to lie. The unsaturated component is generally assumed to be oleic acid. The amount of unsaturated component in the saturated acid fraction is determined by means of iodine and thiocyanogen absorption, or in the case of esters, the unsaturated component may be destroyed by permanganate oxidation prior to determining the saponification value of the mixture.

Mattil and Longenecker[2] and Baldwin and Longenecker[3] have discussed the inherent difficulties of determining the composition of mixed fatty acids by virtue of the limitations of available analytical methods. These authors point out the fact that in a mixture of methyl palmitate and methyl stearate the saponification equivalent must be determined accurately to ±0.28 units in order to calculate the composition to ±1.0% of the true value. This represents a maximum analytical error of ±0.1% in the determination of the saponification equivalent of an ester which corresponds to ±0.02 ml. of 0.5 *N* acid used in the titration.

Mattil and Longenecker proposed a method of determining the composi-

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[1] J. W. C. Phillips and S. A. Mumford, *Rec. trav. chim.*, **52**, 175–180 (1933).

[2] K. F. Mattil and H. E. Longenecker, *Oil & Soap*, **21**, 16–19 (1944).

[3] A. R. Baldwin and H. E. Longenecker, *Oil & Soap*, **22**, 151–153 (1945).

tion of methyl ester fractions based on their refractive indices which they claim can be accomplished with a high degree of accuracy, provided there is available a refractometer of the requisite precision. In order to determine the validity of the refractive index method it was necessary to establish the variation of this property as a function of temperature. A series of highly purified methyl esters was therefore prepared and the refractive index–temperature relationships established. They also determined the refractive indices of known binary mixtures of saturated and unsaturated methyl esters as reference standards. On the basis of this work (see Chapter VIII, sections *5b* and *5c*) it was found that the composition of a binary mixture could be determined to an accuracy of ±0.5% with an Abbe refractometer and even more accurately with an instrument of greater precision.

If the assumption that the unsaturated component of the saturated acid fraction is oleic acid is invalid, *e. g.*, where this component is of different chain length, either longer or shorter than oleic acid, or if it is of a higher degree of unsaturation, then the calculation of the composition of the fraction becomes more involved. Hilditch[4] and also Charnley[5] have indicated various mathematical treatments for calculating the composition of these more complex fractions.

However, the application of spectrophotometric methods has greatly simplified the problem of determining the composition of such mixtures. Baldwin and Longenecker[3] subjected artificial mixtures of methyl esters of lauric, myristic, palmitic, stearic, oleic, linoleic, and linolenic acids to fractional distillation and then determined the iodine value, saponification value, refractive index, and absorption spectra after alkali isomerization of each fraction, and on the basis of these data calculated the compositions of the individual fractions and the original mixture. The agreement between the known composition of the original mixtures and that calculated from the distilled fractions was found to be exceedingly good. The method proposed by these authors is undoubtedly the most reliable and accurate suggested up to the present for the analysis of the ordinary fats and oils of commerce.

3. Identification of Unsaturated Acids

Many unsaturated fatty acids can be identified by conversion into their corresponding bromo derivatives as indicated in Chapter XIII and earlier in the present section. However, this conversion to crystalline derivatives is not always quantitative, hence this method provides only qualitative in-

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[4] T. P. Hilditch, *The Chemical Constitution of Natural Fats.* Wiley, New York, 1941, pp. 400 *et seq.*

[5] F. Charnley, *Can. Biol. Fisheries*, 8, No. 35 (Ser. C. Ind., No. 23), 509–529 (1934); *J. Biol. Board Can.*, 2, 285–297 (1936).

formation concerning the identity of a given acid. Furthermore, many unsaturated acids yield liquid rather than solid derivatives or do not react to yield a completely halogenated derivative. This latter is especially true of conjugated unsaturated fatty acids.

More often than not, mixtures of unsaturated fatty acids or esters cannot be separated into pure components and recourse must, therefore, be had to indirect methods of determining the composition of the mixture. Under certain conditions this may be accomplished with reasonably good accuracy, whereas under others the available methods lead only to approximations. In any case, it is necessary to know that the mixture contains only nonconjugated unsaturated acids and that it is free of saturated, polymerized, and oxidized components. The presence or absence of saturated acids can be determined by means of the Bertram oxidation method (see Chapter XV). The presence or absence of polymerized and oxidized acids is less readily determined.

In this connection it might be mentioned that Farmer and van den Heuvel[6] have pointed out the fact that highly unsaturated fatty acids, such as occur in cod liver and other fish liver oils, are very sensitive to heat and that even at temperatures below 200°C. they undergo polymerization and isomerization reactions. Norris and co-workers[7] investigated by spectrophotometric methods the changes occurring during the vacuum distillation of the methyl esters of the highly unsaturated acids of cod liver and linseed oils. They found that the fatty acids containing up to three double bonds were fairly stable under ordinary conditions of vacuum distillation. The more highly unsaturated acids were, however, found to be less resistant to heat and a certain amount of conjugation and polymerization was observed to occur under various conditions of temperature and length of heating. Conjugation was first observed to increase and then decrease owing to subsequent polymerization. However, they concluded in their first publication that various fractions obtained by vacuum distillation of methyl esters of highly unsaturated acids from cod liver oil are sufficiently representative of the original material to permit their use for purposes of isolation and structural characterization, but they did not state in either communication whether they are sufficiently representative to be used in the quantitative determination of the composition of the original mixture of acids.

If it has been established that the unsaturated acid fraction consists only of a single acid or no more than two unsaturated acids having no conjugated double bonds, identity may be established by determining the neutralization equivalent and iodine value of the fraction. The two acids

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[6] E. H. Farmer and F. A. van den Heuvel, *J. Chem. Soc.*, **1938**, 427–430.

[7] F. A. Norris, I. I. Rusoff, E. S. Miller, and G. O. Burr, *J. Biol. Chem.*, **139**, 199–206 (1941); **147**, 273–280 (1943).

may be of the same chain length and different degrees of unsaturation or of different chain lengths if they are adjacent members of the same homologous series, *e. g.*, C_{18} and C_{20} or C_{20} and C_{22}. If the mixture contains unsaturated acids of different chain lengths and different degrees of unsaturation, the calculations are somewhat more involved as has been shown by Hilditch[4] and Charnley.[5]

Iodine–Thiocyanogen Method

If the unsaturated acid fraction contains three components of the same chain length and different degrees of unsaturation, *e. g.*, oleic, linoleic, and linolenic acids, the composition of the mixture can be determined with reasonably good accuracy in many cases by the iodine–thiocyanogen method. The development by Kaufmann,[8,9] in 1925, of the thiocyanogen addition method for the determination of unsaturated acids led to a marked increase in our knowledge of the composition of fats and oils.

The iodine–thiocyanogen method is based on the assumption that one mole of iodine adds quantitatively to each double bond of unsaturated fatty acids, whereas the thiocyanogen radical, SCN, adds quantitatively to the single bond of a monoethenoid acid, to one of the two double bonds of a diethenoid acid, and to two of the three double bonds of a triethenoid acid. On the basis of these assumptions it is possible, therefore, to determine by calculation from the iodine value the composition of a mixture of fatty acids containing only saturated, oleic, and linoleic acids, provided that the saturated acids are determined by some method such as the lead salt–alcohol or low temperature crystallization method. If the saturated acids are not separately determined, the percentage of total saturated acids and of oleic acid and linoleic acid can be determined from the iodine and the thiocyanogen values. If, on the other hand, the mixture is known to contain only saturated acids and oleic, linoleic, and linolenic acids, its composition can be determined by calculation from the iodine and thiocyanogen values and the percentage of saturated acids determined by an independent method such as the lead salt–alcohol or low temperature crystallization method.

The same methods can be applied with other mixtures, as for example, one containing erucic, but no oleic acid, together with linoleic and/or linolenic acid. It cannot be applied to glycerides or mixtures of fatty acids or esters containing conjugated double bonds since addition of iodine and thiocyanogen is not quantitative in these cases. Elaidic acid adds iodine and thiocyanogen in the same manner as oleic acid so that the method can be used in the presence of either or both acids, but it cannot distinguish

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[8] H. P. Kaufmann, *Arch. Pharm.*, **263**, 675–721 (1925); *Z. Untersuch. Lebensm.*, **51**, 15–27 (1926).

[9] H. P. Kaufmann, *Studien auf dem Fettgebiet.* Verlag Chemie, Berlin, 1935.

between them. Whether it can be applied to glycerides and mixtures of fatty acids containing more than three double bonds has not been established with certainty.

The iodine and thiocyanogen value determinations can be made directly on a fat or oil, or on the mixed fatty acids derived therefrom, or on the mixed unsaturated fatty acids and their methyl or ethyl esters. It is possible to calculate the composition of a fat or oil on the basis of determinations made on any of these related products but generally the mixed fatty acids or the mixed unsaturated fatty acids are used for this purpose. It would be preferable to make the determination directly on the fat or oil since even under the best manipulative conditions alterations occur in the unsaturated fatty acids during saponification and subsequent separation.

It was stated that the validity of the iodine–thiocyanogen method rested on the assumption of the quantitative addition of iodine and thiocyanogen in the manner indicated. Although the assumption is valid for iodine addition, it is not valid for the thiocyanogen addition. It has been shown by numerous investigators[10–18] that with relatively pure acids the addition of thiocyanogen is quantitative in the case of oleic, elaidic, and other monoethenoid acids, whereas addition to linoleic acid is somewhat greater than that required by theory, and in the case of linolenic acid it is considerably less than theory; also that in both latter cases the addition is dependent on the normality of the thiocyanogen reagent used in the determination. This discovery has not invalidated the method but has made it necessary to replace the theoretical constants in the original Kaufmann equations by empirical constants[19] obtained by determining the thiocyanogen value on very pure unsaturated acids under rigidly standardized conditions.

Experience of many investigators has revealed a number of anomalous behaviors in the application of the thiocyanogen method to the analysis of the ordinary fats and oils of commerce. These observations led Lambou and Dollear[20] to undertake a comprehensive investigation of the factors

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[10] W. Kimura, *J. Soc. Chem. Ind. Japan,* **32,** 451–461 (1929); Suppl. Binding, **32,** 138–141B (1929).

[11] R. W. Riemenschneider, C. E. Swift, and C. E. Sando, *Oil & Soap,* **18,** 203–206 (1941).

[12] R. W. Riemenschneider and D. H. Wheeler, *Oil & Soap,* **16,** 219–221 (1939).

[13] J. P. Kass, W. O. Lundberg, and G. O. Burr, *Oil & Soap,* **17,** 50–53 (1940).

[14] J. P. Kass, H. G. Loeb, F. A. Norris, and G. O. Burr, *Oil & Soap,* **17,** 118–119 (1940).

[15] T. P. Hilditch and K. S. Murti, *Analyst,* **65,** 437–446 (1940).

[16] H. I. Waterman, S. H. Bertram, and H. A. van Westen, *J. Soc. Chem. Ind.,* **48,** 50–51T (1929).

[17] G. Y. Shinowara and J. B. Brown, *J. Am. Chem. Soc.,* **60,** 2734–2738 (1938).

[18] N. L. Matthews, W. R. Brode, and J. B. Brown, *Oil & Soap,* **18,** 182–187 (1941).

[19] V. C. Mehlenbacher, *Chem. Eng. News,* **22,** 606–608 (1944). See also M. G. Lambou and F. G. Dollear, *Oil & Soap,* **22,** 226–232 (1945).

[20] M. G. Lambou and F. G. Dollear, *Oil & Soap,* **22,** 226–232 (1945); **23,** 97–101 (1946).

which influenced the course of thiocyanogen addition to unsaturated acids. As a result of this investigation various modifications have been introduced in the preparation of the thiocyanogen reagent which, together with refinements in the technique, have extended its application and increased its accuracy. For details of the method which are too extensive to be reproduced here the reader should consult the publications of Lambou and Dollear.[20]

4. Characteristic Derivatives of Saturated and Unsaturated Acids

Much effort has been expended in the preparation of a variety of derivatives of both saturated and unsaturated fatty acids with the object of finding a reagent which would yield with each acid a derivative whose properties would not only serve to distinguish it from all other acids, but which would also provide a means of quantitatively resolving a mixture of acids into its individual components.

Since the carboxyl is the most reactive group common to all fatty acids most investigators have sought to introduce, in place of its hydrogen or hydroxyl, an organic radical of relatively large molecular weight. By such a procedure it was hoped that the low molecular weight acids and the liquid unsaturated acids would yield well-formed, characteristic crystalline compounds. In some cases, derivatives of this type have been obtained but many of the reagents investigated produced only liquid or oily products of little or no value for identification purposes.

(*a*) *Phenacyl Derivatives*

One of the earliest attempts to systematically characterize the fatty acids was made by means of the phenacyl esters, including the *p*-bromo-, *p*-iodo-, and *p*-phenylphenacyl derivatives. To this end, Judefind and Reid[21] prepared the *p*-bromo- and *p*-iodophenacyl esters of eleven saturated fatty acids including both even- and odd-numbered members of the series. All of the acids from acetic to stearic gave crystalline derivatives as indicated by the melting points shown in Table 157. The melting points of the saturated acid derivatives were found to increase with increase in the atomic weight of the halogen but the melting points of individual members of the homologous series of acids were not sufficiently distinctive to permit their use as identifying criteria.

Kass, Nichols, and Burr[22] prepared the *p*-phenylphenacyl esters of a series of octadecenoic acids in the hope of obtaining derivatives which would be suitable for purposes of isolating and characterizing individual members of this series of acids. All of the derivatives possessed satisfac-

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[21] W. L. Judefind and E. E. Reid, *J. Am. Chem. Soc.*, **42**, 1043–1055 (1920).

[22] J. P. Kass, J. Nichols, and G. O. Burr, *J. Am. Chem. Soc.*, **64**, 1061–1062 (1942).

TABLE 157

MELTING POINTS (IN DEGREES CENTIGRADE) OF *p*-HALOGENOPHENACYL ESTERS OF FATTY ACIDS[a]

Acid	*p*-Bromophenacyl ester	*p*-Iodophenacyl ester	Acid	*p*-Bromophenacyl ester	*p*-Iodophenacyl ester
Acetic	85	114	Caprylic	65.5	77.0
Propionic	59	94.9	Capric	66	80.0
Butyric	63.2	81.4	Palmitic	81.5	90.0
Valeric	63.6	78.6	Margaric	78.2	88.8
Isovaleric	68.0	78.8	Stearic	78.5	90.5
Caproic	71.6	81.5	Erucic	61	73.8

[a] W. L. Judefind and E. E. Reid, *J. Am. Chem. Soc.*, **42**, 1043–1055 (1920).

tory melting points as indicated by the data in Table 158, but only the *p*-phenylphenacyl oleate and elaidate gave theoretical iodine numbers.

TABLE 158

MELTING POINTS (IN DEGREES CENTIGRADE) OF *p*-PHENYLPHENACYL ESTERS OF SOME UNSATURATED FATTY ACIDS[a]

Acid	*p*-Phenylphenacyl ester	Acid	*p*-Phenylphenacyl ester
Oleic	61–62	Linolelaidic	73–75
Elaidic	72–73	Linolenic	37.5–38 38.0–39
Linoleic	37–37.5 46.5–47	β-Elaeostearic	89–90

[a] J. P. Kass, J. Nichols, and G. O. Burr, *J. Am. Chem. Soc.*, **64**, 1061–1062 (1942).

(*b*) *Amino Derivatives*

Dermer and King[23] investigated the possibility of characterizing fatty acids by means of *N*-benzylamide derivatives prepared by reaction of benzylamine and carboxylic acids or esters according to the following equation:

$$RCOOR' + C_6H_5CH_2NH_2 \longrightarrow RCONHCH_2C_6H_5 + R'OH$$

They found that although the fatty acids readily formed *N*-benzylamides, the melting points of the derivatives were relatively low and differed from member to member by too small increments to be satisfactory for purposes of identification.

In contrast to the amides of benzylamine, the diamides of 4,4′-diaminodiphenylmethane were found by Ralston and McCorkle[24] to possess relatively high melting points and a sufficient temperature increment be-

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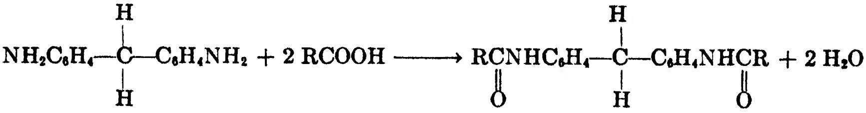
[23] O. C. Dermer and J. King, *J. Org. Chem.*, **8**, 168–173 (1943).

[24] A. W. Ralston and M. R. McCorkle, *J. Am. Chem. Soc.*, **61**, 1604–1605 (1939).

tween adjacent members to render them valuable for purposes of characterizing fatty acids. When the fatty acids were heated with theoretical proportions of 4,4′-diaminodiphenylmethane, diamides were formed according to the following equation:



$$NH_2C_6H_4\text{—}\overset{H}{\underset{H}{C}}\text{—}C_6H_4NH_2 + 2\,RCOOH \longrightarrow R\underset{O}{\underset{\|}{C}}NHC_6H_4\text{—}\overset{H}{\underset{H}{C}}\text{—}C_6H_4NH\underset{O}{\underset{\|}{C}}R + 2\,H_2O$$

All of the saturated acids from acetic to stearic yielded well-crystallized, relatively high melting derivatives with this reagent. The difference in melting points of the diamides of adjacent acids is relatively large for the lower members but becomes increasingly less as the series is ascended. As indicated in Table 159, appreciable depression of the melting point occurs on addition of the diamide of the next higher homologous acid. The extent of the depression of the melting point also decreases as the series is ascended. Despite these limitations the derivatives are especially useful for characterizing specific saturated acids.

TABLE 159

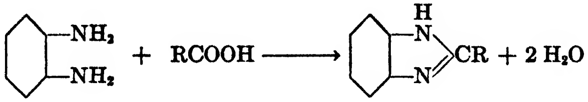
MELTING POINTS (IN DEGREES CENTIGRADE) OF FATTY ACID DIAMIDES OF 4,4′-DIAMINODIPHENYLMETHANE[a]

Acid	Diamide	Mixture with next higher homolog	Acid	Diamide	Mixture with next higher homolog
Acetic	227–228	205–210	Undecanoic	175–176	172–174
Propionic	212–213	188–193	Lauric	174–175	171–173
Butyric	197–198	185–188	Tridecanoic	172–173	170–172
Valeric	188–189	179–181	Myristic	170–171	167–169
Caproic	185–186	179–181	Pentadecanoic	167–168	166–168
Heptanoic	183–184	176–178	Palmitic	167–168	164–166
Caprylic	182–183	176–179	Margaric	164–165	163–165
Nonanoic	176–177	175–177	Stearic	164–165	.....
Capric	178–179	173–175			

[a] A. W. Ralston and M. R. McCorkle, *J. Am. Chem. Soc.*, **61**, 1604–1605 (1939).

The preparation of the derivative is accomplished by heating in a Pyrex tube a mixture of 1 g. (0.005 mole) of 4,4′-diaminodiphenylmethane and slightly more than 0.01 mole of a fatty acid. The reaction mixture is maintained at the boiling temperature until water ceases to be evolved, after which the product is crystallized from a mixture of benzene and methanol until a constant melting point is obtained. With the lower molecular weight acids, a reflux condenser and a reaction period of about one hour are required. The time required to complete the reaction decreases as the series is ascended and in the case of stearic acid five minutes is sufficient.

Pool, Harwood, and Ralston[25] prepared the 2-alkylbenzimidazoles of all the aliphatic acids from formic to heptadecanoic acid. The acids were found to react with *o*-phenylenediamine according to the following equation:



The 2-alkylbenzimidazoles are readily prepared with small amounts of fatty acids. They have comparatively high melting points and, in the case of the lower members of the series, the melting point interval between adjacent members is large and the depression in melting point resulting from the addition of the next higher homolog is considerable, as may be observed in Table 160. These derivatives of the fatty acids are perhaps the most useful ones thus far described for characterizing fatty acids and especially for the lower members of the series.

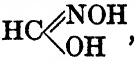
TABLE 160

MELTING AND MIXED MELTING POINTS OF 2-*n*-ALKYLBENZIMIDAZOLES[a]

n-Alkyl	Melting point, °C.	M. p. of mixture with next higher homolog, °C.	*n*-Alkyl	Melting point, °C.	M. p. of mixture with next higher homolog, °C.
Hydrogen-	172.0–173.0	130–132	Nonyl-	127.0–127.5	117–120
Methyl-	177.0–177.5	157–158	Decyl-	114.0–114.5	106–107
Ethyl-	174.5	155–156	Undecyl-	107.5	107–108
Propyl	157.0–157.5	141–143	Dodecyl-	109.0–109.5	105–106
Butyl-	155.0–155.5	152–153	Tridecyl-	105.0–105.5	100–102
Pentyl-	163.0–163.5	138–143	Tetradecyl-	98.5–99.5	97–98
Hexyl-	137.5–138.0	132–135	Pentadecyl-	96.5–97.0	94–96
Heptyl-	144.5–145.0	136–137	Hexadecyl-	93.5–94.5	93–94
Octyl-	139.5–140.5	128–131	Heptadecyl-	93.5–94.5	.....

[a] W. O. Pool, H. J. Harwood, and A. W. Ralston, *J. Am. Chem. Soc.*, **59**, 178–179 (1937).

(*c*) *Hydroxamic Acids*

Hydroxamic acids may be prepared by the reaction of hydroxylamine, NH_2OH, on the esters, anhydrides, chlorides, and amides of fatty acids. For example, formhydroxamic acid,  $HC\begin{smallmatrix}\nearrow NOH \\ \searrow OH\end{smallmatrix}$, is produced when equimolecular quantities of formic ester and hydroxylamine are allowed to stand in a solution of absolute ethanol. The resulting hydroxamic acid is a crystalline product melting at 81–82°C.

The more general method of preparation of hydroxamic acids comprises

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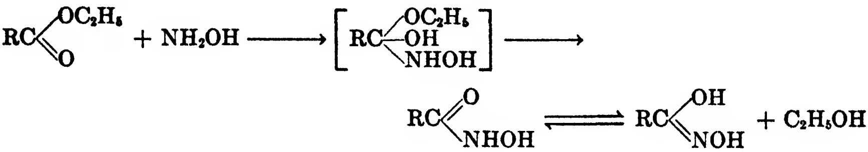
[25] W. O. Pool, H. J. Harwood, and A. W. Ralston, *J. Am. Chem. Soc.*, **59**, 178–179 (1937).

treatment at room temperature of the ethyl esters of aliphatic acids with hydroxylamine hydrochloride and sodium ethoxide. The resulting hydroxamic acids are white crystalline compounds which give an intense reddish-violet color with ferric chloride, $FeCl_3$, in alcoholic solution. With an excess of cupric acetate, $Cu(OAc)_2$, solution they produce green-colored, voluminous amorphous precipitates of the corresponding copper salts. The parent fatty acids may be regenerated from the hydroxamic acids by hydrolysis in dilute alcoholic sulfuric acid solution. Hydroxamic acids are presumed to be formed from fatty acids as shown in the following equation:



The only systematic investigation of the hydroxamic acids as characterizing derivatives of the normal aliphatic acids has been reported by Inoue and co-workers[26] who prepared the hydroxylamine derivatives of all the even-numbered fatty acids from acetic to behenic. They also prepared the corresponding derivatives of oleic, elaidic, linoleic, and linolenic acids. All of the products, with the exception of that derived from butyric acid, were crystalline compounds melting above room temperature (Table 161).

TABLE 161

MELTING POINTS OF ALKYLHYDROXAMIC ACIDS DERIVED FROM NORMAL AND UNSATURATED FATTY ACIDS

Original acid	Hydroxamic acid, m.p., °C.	Original acid	Hydroxamic acid, m.p., °C.
Formic	81–82	Myristic	98–98.5
Acetic	88	Palmitic	102.5
Propionic	92.5–93	Stearic	106.5–107.0
Butyric	[a]	Arachidic	109
Valeric	73.5–76	Behenic	112.5
Caproic	63.5–64	Oleic	61
Caprylic	78.5–79	Elaidic	91
Capric	88–88.5	Linoleic	41–42
Lauric	94	Linolenic	37–38

[a] Reported as a viscous liquid and as a solid melting at 127°C.

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[26] Y. Inoue and H. Yukawa, *J. Agr. Chem. Soc. Japan*, **16**, 504–509, 510–512 (1940), **17**, 411–413 (1941); *Bull. Agr. Chem. Soc. Japan*, **16**, 100–101 (1940), **17**, 44 (1941). Y. Inoue, H. Yukawa, and H. Katumata, *J. Agr. Chem. Soc. Japan*, **17**, 491–493, 493–494 (1941); *Bull. Agr. Chem. Soc. Japan*, **17**, 59–60 (1941); *cf.* H. L. Yale, *Chem. Revs.*, **33**, 209–256 (1943).

Inoue, Yukawa, and Katumata[26] investigated the possibility of separating the saturated and unsaturated acids of soybean oil by way of the corresponding hydroxamic acids. Soybean oil was converted directly to a mixture of hydroxamic acids and the latter separated by crystallization at 0°C. from ethanol, ethyl ether, petroleum naphtha, and carbon tetrachloride. The corresponding saturated acids were found to represent 12.3% to 13.6% of the total acids and little difference was found in the yield regardless of the solvent used. The authors also applied the method to the determination of the volatile and nonvolatile acids of coconut oil. Hydroxamic acids were prepared from the ethyl esters of coconut oil fatty acids and the alcoholic solution of reaction products was diluted with water to form a 15% alcoholic solution. The insoluble product which separated was removed by filtration and the filtrate was evaporated *in vacuo* to recover the soluble acids, after which both fractions were decomposed with sulfuric acid. The mean molecular weight of the two fractions indicated that the separation of volatile and nonvolatile acids was equally as effective as steam distillation.

(*d*) *Thiuronium Derivatives*

Kass, Nichols, and Burr[22] prepared the *S*-benzylthiuronium salts of a series of octadecenoic acids with a view of obtaining specific derivatives which could be used in characterizing these acids. High melting derivatives (Table 162) were obtained, but only that from elaidic acid was definitely crystalline and none of the derivatives gave theoretical iodine values.

TABLE 162

MELTING POINTS OF THIURONIUM DERIVATIVES OF FATTY ACIDS

Fatty acid	*S*-Benzylthiuronium salt, m.p.,°C.	Fatty acid	*p*-Chlorobenzylpseudothiuronium derivative, m.p., °C.
Oleic	134–134.5	Formic	148
Elaidic	125–125.5	Acetic	140
Linoleic	123.5–125	Propionic	143
Linolelaidic	122–123	Butyric	139
Linolenic	122–124	Valeric	142
		Caproic	143
		Palmitic	146
		Oleic	131

Dewey and Sperry[27] prepared a number of *p*-chlorobenzylpseudothiuronium chloride salts of aliphatic acids. Derivatives were readily obtained by adding an equivalent quantity of a cold 10% alcoholic solution of *p*-

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[27] B. T. Dewey and R. B. Sperry, *J. Am. Chem. Soc.*, **61**, 3251–3252 (1939).

chlorobenzylpseudothiuronium chloride to an aqueous solution of the salt of the fatty acid. The derivative usually precipitated immediately on addition of the reagent but if it did not, the solution was concentrated under reduced pressure until precipitation occurred. The melting points of the derivatives are given in Table 162.

(e) *Other Derivatives*

Ford[28] and Gilman and Ford[29] prepared a diversified series of derivatives of lauric, myristic, palmitic, stearic, and oleic acids. As indicated by the data in Table 163, all of the saturated acids gave solid derivatives, but differences in melting points between the various members in the homologous series were usually no greater than those between the individual acids. Except for the *p*-phenylphenacyl ester, the ureide, and thioureide, all of the derivatives of oleic acid were oily products.

TABLE 163

MELTING POINTS (IN DEGREES CENTIGRADE) OF VARIOUS DERIVATIVES OF LAURIC, MYRISTIC, PALMITIC, STEARIC AND OLEIC ACIDS[a]

Derivatives	Lauric	Myristic	Palmitic	Stearic	Oleic
N-Acylcarbazole	78–79	81–82	85–86	91–92	oil
N-Acylphenothiazine	70	75	80	86	oil
N-Acyl-*p*-toluenesulfonamide	83–84	89–90	93–94	98–99	oil
p-Phenylphenacyl ester	86	90	94	97	60
p-Nitroanilide	78	84	93	96	. . .
N-Acylsaccharin	88–89	90–91	90	95	oil
2,4-Dinitrophenylhydrazide	110–111	118	120–121	123	oil
N-Acyl-2-nitro-*p*-toluidine	62–63	73–74	78–79	85	. . .
p-Tolylmercuric salt	93–94	95–96	99	102–103	oil
Phenylmercuric salt	82	86	93	95	oil
Triphenyllead salt	91	102–103	110	112	. . .
Monoureide	182	178	175	174	160
Monothioureide	138	135	135–136	133	113
p-Xenylamide	146	143	142	143	. . .
p-Diphenyl ketone	101–102	102–103	103–104	106–107	. . .
2,8-Diacylcarbazole	176	169	162	163	. . .
p-Acylaminobenzoic acid	227–228	224–225	226–227	221	. . .
Diacylbenzidine	248	241–242	233	232	. . .

[a] G. M. Ford, *Iowa State Coll. J. Sci.*, **12**, 121–122 (1937). H. Gilman and G. M. Ford, *ibid.*, **13**, 135–147 (1939).

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[28] G. M. Ford, *Iowa State Coll. J. Sci.*, 12, 121–122 (1937).
[29] H. Gilman and G. M. Ford, *Iowa State Coll. J. Sci.*, **13**, 135–147 (1939).

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