SYSTEMATIC ORGANIC CHEMISTRY

MODERN METHODS OF PREPARATION AND ESTIMATION

BY

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PREFACE TO FIRST EDITION (1923)

THE present work is intended as a complete laboratory guide to the preparations and estimations of organic chemistry for undergraduate and post-graduate students. An endeavour has been made to introduce up-to-date methods, some of which are new, having been developed by the authors. In all cases sufficient practical details are given to enable a beginner, with the aid of the sections on apparatus and methods, to carry out the necessary operations for himself. The research student, it is hoped, will often find within the preparations required. To meet the needs of the many students whose ultimate interests are likely to be industrial, several manufacturing methods are described on a laboratory scale. An industrial experience which has been invaluable to the authors in their duties as teachers has led them to include a few notes on costing, since they feel that this subject, of such vital importance in industry, is neglected in our technical institutions.

References to the original literature have been given after almost every preparation, thus affording a means of amplifying, if desired, the practical details. Stress has been laid on the value of consulting original papers through the media of the lexicons of Richter, Beilstein and Stelzner.

Lists of suggested preparations have been included. It is believed that greater interest is developed when the student works through a sequence of preparations which are more or less intimately connected.

The authors have striven to make the book something more than a collection of recipes. Owing to deficiencies in the teaching of the subject, there is to-day a tendency for the student to think that there is a lecture-room and a laboratory variety of organic chemistry. To such an extent does this division exist that a student who in the lecture-room knows the general method for the preparation of, say, anhydrides, in the laboratory is quite at sea when asked to prepare any anhydride other than that of acetic acid. To combat this, the preparations of several compounds of a given type have been included in most sections of the book.

Many reactions of purely theoretical interest have been incorporated, so that the student may gain some real idea of the possibilities of his subject, and that he may feel his practical and theoretical text-books to be very near akin. Indeed, the authors trust that from a theoretical standpoint alone the student may find the book useful in that it will enable him to view his subject from an angle different to the usual, and in this way to gain perspective. The better to accomplish this, they have introduced a new classification of organic reactions in which reaction follows reaction on a definite plan. They hope that the student who carefully reads through this book will not only have acquired much varied theoretical and practical knowledge, but also that his purely theoretical books will take on a new meaning, and that even their current jargon of " reducing A with HI " and " distilling B with lime " will be for him something more than a form of words.

Identifications have not been dealt with beyond including some few tests and tables of reactions. A section has been included dealing with the preparation of such inorganic compounds as are largely used in organic chemistry, and on the correct preparation of which much may depend. The authors would here emphasise the importance of introducing " oleum " of all strengths into the teaching laboratories of this country. It is of great industrial importance, cheap, and not dangerous when properly handled.

The section on estimations is rather more comprehensive than is given in most text-books of this kind, and is composed entirely of examples found to give good results in practice.

The authors beg to acknowledge assistance received directly and indirectly from well-known text-books by the following authors—Adams and others, Barnett, Barrowcliff and Carr, Cain, Cain and Thorpe, Cohen, Elbs, Fiertz-David, Fischer, Gattermann, Henderson, Knecht and Hibbert, Lassar-Cohn, Hans Meyer, Meyer-Jacobson, Meyer-Tingle, Perkin, F. M., Sudborough and James, and Ullmann.

They wish to express their thanks to Professor F. J. Wilson, for his kindly interest and valuable suggestions ; to Professor I. M. Heilbron for useful advice ; to Mr. A. B. Crawford, B.Sc., A.R.T.C., A.I.C., and Mr. E. C. Pickering, B.Sc., A.I.C., for reading the proofs ; and to Messrs. Constable & Co. for the way in which they have carried out their share of the work.

They desire to acknowledge specially the assistance rendered by Mr. James Connell, B.Sc., A.I.C., in drawing the illustrations for the book.

The authors will be grateful for any suggestions or for notification of any errors.

THE ROYAL TECHNICAL COLLEGE, GLASGOW. W. M. C. AND I. V. H.
RESEARCH DEPARTMENT, ROYAL ARSENAL, WOOLWICH. T. S. W.

PREFACE TO SECOND EDITION (1931)

In responding to the call to issue a second edition we have taken the opportunity to bring the book generally up to date in all its sections.

The Apparatus and General Methods section has been increased by the addition of an outline of the mercury vapour lamp and its uses in polarimetry and in catalytic reactions. A laboratory-scale apparatus, devised by us, for the distillation of solids is included. The section on the use of the library has been extended, and attention has been drawn to the changes which have taken place in the German reference literature.

In Part II. several new reactions and preparations—or improved methods of preparation—have been introduced. Several of these are now of industrial importance. References have been brought up to date; and for those preparations described in " Organic Syntheses " references are given to this valuable series of books.

The Analytical section has been subjected to some changes. An electrically heated combustion furnace, some new methods of analysis, and the method of Rast for the determination of molecular weights, are also described. Chapter XLIV on tests for some common organic substances has been completely rewritten.

The nomenclature used throughout the book has been amended. The principal names are those adopted by the Chemical Society. Alternative names—which are in some cases the English equivalent of the usual German names, and in others are based on the Geneva System—are given in most instances to assist the student in making reference to the original literature.

We desire to thank reviewers, teachers and students for suggestions and corrections brought to our notice. We are indebted to Professor F. J. Wilson, D.Sc., F.I.C., for his continued interest and to Mr. H. G. A. Anderson, B.Sc., who made the additional drawings. We have also to thank Professor Thomas Gray, D.Sc., F.I.C., and Mr. Thomas Love, B.Sc., for useful suggestions.

The Royal Technical College, Glasgow. W. M. C. and I. V. H.
June, 1931.

PREFACE TO THIRD EDITION (1937)

The third edition appears during a transition stage in the development of organic analysis. The older macro methods are gradually giving place to micro and hemi-macro modifications. The chapters on combustion have therefore been entirely rewritten, stress being laid on the hemi-macro methods, which are perhaps more accessible to the average student. In this connection the authors have been fortunate in securing the collaboration of Dr. Robert Roger, University College, Dundee, an authority who has published widely on the subject. To him they express their deep indebtedness for his assistance in this and in other directions.

While the main plan of the book has not been altered, sections have been brought up to date by the addition of improved methods and new references, particularly to " Organic Syntheses ".

With the development of large industrial research organisations there is a growing tendency to record new advances through the medium of patent literature. Frequent reference has therefore been made to this source, especially as regards high pressure reactions.

In the miscellaneous analytical section some references are given to additional exercises which the advanced student may undertake after perusal of the original literature.

The authors acknowledge with thanks suggestions made by colleagues and correspondents, and especially the services of Mr. David M. Wilson, B.Sc., who prepared the new diagrams.

The authors also thank Dr. G. D. Muir and Mr. A. C. Syme, B.Sc., A.R.T.C., for reading the proofs, and Messrs. Constable & Co. for their efficient co-operation.

The Royal Technical College, Glasgow. W. M. C.
June, 1937. I. V. H.

PREFACE TO FOURTH EDITION (1950)

In the present edition the authors have endeavoured to modernise and extend all sections of the book so as to include the more important developments which have taken place during the last decade.

The methods and apparatus section has been brought up-to-date, and includes new sections on ozonolysis, hydrogenation, chromatography, azeotropic distillation, etc. Attention has been directed to the increasing use of ground-glass jointed apparatus.

The scope of the reactions has been extended by incorporating many that have become established in modern practice, for example, reactions associated with the names of Ponndorf; Diels-Alder; Hinsberg; Markownikoff; Kharasch; Zerewitinoff; Fischer-Tropsch; and also oxidations by periodic acid (Malaprade) and lead tetra-acetate, formation of amidines, sulphonamides, fluorine compounds. Modern interpretations of reactions by acid or base catalysis have been included where appropriate.

Since the publication of the previous edition, micro analysis has become an essential tool of the organic chemist. Accordingly, macro and hemimacro methods of combustion analysis have been completely replaced by a new section on micro methods. In this, the authors have been fortunate in the collaboration of a colleague, Dr. A. C. Syme, who is in charge of the organic micro analytical laboratory in this College. To him they express their grateful thanks.

Literature references throughout have been revised. Attention has been directed to the more important summaries on reactions and methods included in such standard works as Annual Reports of the Chemical Society, Chemical Reviews, Organic Syntheses, Newer Preparative Methods of Organic Chemistry, Organic Reactions, and text books (Roger Adams, Gilman, Wieland, etc.) to all of which due acknowledgment is made.

The authors tender sincere thanks to their colleagues, Dr. G. Edwards for the new diagrams, to Professor F. S. Spring, Dr. G. T. Newbold and Dr. A. B. Crawford, for their interest and useful suggestions, and to the publishers for their helpful collaboration.

Royal Technical College, Glasgow.
June, 1949.

W. M. CUMMING.
I. V. HOPPER.

ABBREVIATIONS

A. - - - - = Liebig's Annalen der Chemie.
Abs. A. or B. - = British Chemical Abstracts, A or B.
A.C.R. - - = Applied Chemistry Reports (S.C.I.).
A. Ch. - - = Annales de Chimie et de Physique.
A. Spl. - - = Supplement Liebig's Annalen der Chemie.
Am. Chem. - = American Chemical Journal.
Am. Soc. - - = Journal of the American Chemical Society.
An. Chem. - = Analytical Chemistry.
Ann. Chim. app. Annali di Chimica applicata.
Ann. Rep. - = Annual Reports (Chemical Society).
B. - - - - = Berichte der Deutschen Chemischen Gesellschaft.
B.P. - - - = Boiling Point.
Bl. - - - = Bulletin de la Société chimique de France.
C. - - - - = Chemisches Zentralblatt.
C. & I. - - = Chemistry and Industry.
C.I. - - - = Colour Index (F. M. Rowe, 1924).
C. J. R. - - = Canadian Journal of Research.
C. N. - - = Chemical News.
C. r. - - - = Comptes rendus de l'Académie des Sciences.
C. T. - - = Chemical Trade Journal.
C. V. - - = " Organic Syntheses " (Coll. Vol. I—Second Edition, and II—First Edition).
C. Z. - - = Chemiker-Zeitung.
D. - - - = Specific Gravity.
D.R.P. - - = German Patent.
E.P. - - = British Patent.
Far. - - - = Transactions of the Faraday Society.
F.P. - - = French Patent.
G. - - - = Gazzetta chimica italiana.
H. Acta - - = Helvetica Chimica Acta.
In. S. - - = " Inorganic Syntheses ".
J. - - - = Jahresbericht der Chemie.
J. C. Ed. - - = Journal of Chemical Education.
J. C. S. - - = Journal of the Chemical Society.
J. Eng. - - = Journal of Industrial and Engineering Chemistry.
J. pr. - - = Journal fur praktische Chemie.
J. R. C. S. - = Journal of the Physical and Chemical Society of Russia.
J. R. T. C. - = Journal of the Royal Technical College, Glasgow.
J. S. C. I. - = Journal of the Society of Chemical Industry.
J. Soc. Dyers - = Journal of the Society of Dyers and Colourists.
M. - - - = Monatshefte fur Chemie.
M.P. - - = Melting Point.
O. S. - - = " Organic Syntheses " (Roger Adams, and others).
P. A. - - = Poggendorf's Annalen.
P. C. S. - - = Proceedings of the Chemical Society.
P. R. S. - - = Proceedings of the Royal Society.
Phil. Mag. - = Philosophical Magazine.
Phil. Trans. - = Philosophical Transactions of the Royal Society of London.
Rec. - - - = Recueil des travaux chimiques des Pays-Bas.
Rev. - - = Chemical Reviews.
T. R. S. E. - = Transactions of the Royal Society of Edinburgh.
U.S.P. - - = United States Patent.
Z. a.- - - = Zeitschrift fur angewandte Chemie.
Z. Anal. - - = Zeitschrift fur analytische Chemie.
Z. e. - - - = Zeitschrift fur Electrochemie.
Z. ph. - - = Zeitschrift für physikalische Chemie.

Tables showing the dates of issue of most of the above publications is given in the Introduction to Volumes of Beilstein's Handbuch der Organischen Chemie.

CONTENTS

PART I

CHAPTER I

CHAPTER II

APPARATUS AND METHODS

PART II

THE LINKING OF CARBON TO CARBON

CHAPTER III

HYDROGEN COMPOUNDS

CHAPTER IV

HYDROXY COMPOUNDS

CHAPTER V

OXY COMPOUNDS

CHAPTER VI

HYDROXY-OXY COMPOUNDS

CHAPTER VII

OXIDE-OXY COMPOUNDS

CHAPTER VIII

NITROGEN COMPOUNDS

THE LINKING OF HYDROGEN TO CARBON

CHAPTER IX

HYDROGEN COMPOUNDS

CHAPTER X

HYDROXY COMPOUNDS (ALCOHOLS AND PHENOLS)

CHAPTER XI

OXY AND HYDROXY-OXY COMPOUNDS (ALDEHYDES, KETONES AND ACIDS)

CHAPTER XII

HALOGEN COMPOUNDS

THE LINKING OF OXYGEN TO CARBON

CHAPTER XIII

HYDROXY COMPOUNDS (ALCOHOLS AND PHENOLS)

CHAPTER XIV

OXIDE COMPOUNDS (ETHERS)

CHAPTER XV

OXY COMPOUNDS (ALDEHYDES, KETONES AND QUINONES)

CHAPTER XVI

HYDROXY-OXY COMPOUNDS (ACIDS)

CHAPTER XVII

OXIDE-OXY COMPOUNDS (ESTERS AND ACID ANHYDRIDES)

THE LINKING OF NITROGEN TO CARBON

CHAPTER XVIII

NITRO COMPOUNDS

CHAPTER XIX

THE LINKING OF SULPHUR TO CARBON

CHAPTER XX

SULPHONIC ACIDS

CHAPTER XXI

THE LINKING OF HALOGEN TO CARBON

CHAPTER XXII

THE LINKING OF HYDROGEN TO NITROGEN

CHAPTER XXIII

AMINO COMPOUNDS

CHAPTER XXIV

HYDROXYLAMINES AND HYDRAZINES

THE LINKING OF NITROGEN TO NITROGEN

CHAPTER XXV

DIAZONIUM COMPOUNDS, ETC.

CHAPTER XXVI

DYES

CHAPTER XXVII

CHAPTER XXVIII

CHAPTER XXIX

CHAPTER XXX

CHAPTER XXXI

CHAPTER XXXII

PART III

CHAPTER XXXIII

CHAPTER XXXIV

CHAPTER XXXV

CHAPTER XXXVI

CHAPTER XXXVII

GROUP ESTIMATIONS

CHAPTER XXXVIII

CHAPTER XXXIX

CHAPTER XL

PART IV

CHAPTER XLI

CHAPTER XLII

SYSTEMATIC ORGANIC CHEMISTRY

PART I

CHAPTER I

INTRODUCTORY

CAUTIONS

Fire : The locations of the Fire Extinguisher, the Fire Blanket, the Sand Bucket, and the First-Aid box should be known. In the event of fire, turn off any gas burner or heating current and take appropriate measures to extinguish conflagration. Small fires can be put out by excluding air, say by placing a clock glass over the opening of a beaker or flask containing the burning material. Burning oil can be smothered with solid sodium bicarbonate ; sand is useful for fires in general but should be handled so as not to scatter the fire ; patent fire extinguishers employing carbon dioxide under pressure or carbon tetrachloride, if used, should direct the liquid carefully on to the base of the flame—it is often preferable to pour carbon tetrachloride on from a beaker or winchester as this avoids scattering. Since carbon tetrachloride on a fire may generate phosgene the laboratory should be vacated and ventilated until the fume hazard has passed. Avoid carelessness, unsuitable procedures of heating and unsuitable apparatus, and fires will seldom occur.

Volatile, Inflammable Solvents.—Great care is necessary in the use of ether, light petroleum, carbon disulphide, acetone, alcohol, benzene and other easily volatile liquids ; their vapours are highly inflammable. They should always be distilled from a water bath and collected in apparatus of the type shown on p. 21. Extra special care is desirable with carbon disulphide whose vapour inflames in contact with a hot surface even in absence of a flame.

Clothes on Fire.—Rolling on the floor is often the best method for checking a fire on one's own clothing. Running about merely assists the flame. Do not inhale the flame or hot vapours. Coats, towels—but preferably a fire blanket or water spray—should be used at once to extinguish the fire. Do not use carbon tetrachloride. If a carbon dioxide extinguisher is employed get fresh air as quickly as possible afterwards.

Burns (Extensive).—Call medical aid at once. Remove patient from the scene of fire, lay him down comfortably in a quiet room, cover with a blanket or coat and give him a warm drink. If medical aid is not available within 30 minutes, one of the following preparations might be used though there is some objection to applying anything difficult of removal before full treatment is given subsequently by a physician. Suitable preparations include : sulphanilamide cream, crystal violet jelly, gentian violet jelly, butesin picrate, freshly-prepared 5% tannic acid solution in water, acriflavine emulsion; some of these should be available in the laboratory.

Burns (Minor).—(*a*) *By Heat.* If clean, apply one of the above preparations. Alternatively, treat with cold saturated (8%) sodium bicarbonate solution for some time and then with one of the foregoing remedies. Finally cover with pad and gauze bandage.

(*b*) *By Acids.* Wash immediately with much cold water, then with dilute sodium bicarbonate and finally with water. Dry carefully and apply ointment (e.g. butesin picrate).

(*c*) *By Alkalis.* Wash in turn with water, dilute acetic acid and water. Follow with ointment.

(*d*) *By Bromine.* Wash off immediately with light petroleum or benzene (less preferably with alcohol) and apply ointment. Alternatively wash, first, in a stream of water, then with sodium bicarbonate solution, and finally with glycerol before applying ointment.

(*e*) *By Phenol and other substances.* Remove the corrosive substance with a solvent—preferably one not toxic or not readily absorbed by the tissue. Very dilute bromine water, in glycerol, is useful as a final wash for phenol burns.

(*f*) *By Dimethyl Sulphate.* Remove with petroleum or ether, then wash with ammonia solution in plenty.

(*g*) *Phosphorus.* Wash immediately with sodium carbonate solution followed by warm 1% copper sulphate, removing any copper-coated phosphorus by forceps or water. Follow by washing in warm water containing a little boric acid.

Reagents in Eye.—(*a*) *Acids.* Wash with water from wash bottle or eye cup, but get water into eye immediately—face under tap, water from beaker, or somehow. Follow with dilute (1%) sodium bicarbonate solution and finally with a few drops of castor oil or liquid paraffin.

(*b*) *Alkalis.* Wash first with water, then with boric acid solution and finally drop oil into eye.

(*c*) *Glass in eye.* Unless this is easily removed with forceps, do not attempt to dislodge; hold eye open until doctor arrives.

Goggles.—Wear to protect the eyes when there is likelihood of danger, e.g. in handling caustic alkalis where spurting or splashing might occur (during caustic fusions or when dissolving solid or fused alkalis in water); also during vacuum distillations and experiments under pressure in glass vessels.

Triplex Glass Shields (say 2 ft. × 1 ft.), mounted in wooden frames. Set up to protect from accident during dangerous operations.

Vacuum Desiccators.—House in plywood containers or wire cages. The flat-lid type have been known to implode. Those of dome-shaped type are less dangerous.

Asphyxiation : Gas Poisoning.—Remove patient to fresh air, loosen restrictive clothing about neck and chest. If breathing has stopped, apply artificial respiration ; send for doctor.

Ether Extractions.—First test ether (diethyl-, di-isopropyl-, or dioxane) for peroxide and, if present, remove (p. 219).

Sodium Residues.—These should not be dropped into the sink or waste box, but should be added in small portions to alcohol, and, when all action has ceased, the solution poured into the sink.

Gas Masks.—Students should acquaint themselves with gas masks for use in case of fire, explosion, or other emergency.

Attention is directed to "Safety Measures in Chemical Laboratories, 1949," published by the Department of Scientific and Industrial Research.

SCHEME OF ARRANGEMENT OF REACTIONS

The reactions in this book are grouped in sections determined by the linking of elements that occurs in the reaction to form the product. The order of the sections depends on the Richter alphabet—**C, H, O, N, Cl, Br, I, S**, etc. A complete classification by this method would take the form :

$$\text{I. Reactions in which } \left.\begin{array}{r} \mathbf{C}, \\ \mathbf{H}, \\ \mathbf{O}, \\ \mathbf{N}, \\ \mathbf{Cl, Br, I, S}, \text{etc.}, \end{array}\right\} \text{ are linked to } \mathbf{C}.$$

$$\text{II. Reactions in which } \left.\begin{array}{r} \mathbf{H}, \\ \mathbf{O}, \\ \mathbf{N}, \\ \mathbf{Cl, Br, I, S}, \text{etc.}, \end{array}\right\} \text{ are linked to } \mathbf{O}.$$

$$\text{III. Reactions in which } \left.\begin{array}{r} \mathbf{H}, \\ \mathbf{O}, \\ \mathbf{N}, \\ \mathbf{Cl, Br, I, S}, \text{etc.}, \end{array}\right\} \text{ are linked to } \mathbf{N}.$$

Small sections as III are not further subdivided herein. Large sections are subdivided to give a separate subsection for the linking of each separate element to the main one, so to speak, of the section ; and each subsection is further subdivided according to the type of compounds necessarily obtained in the various reactions. An examination of the table of contents and of the **C** to **C** section will make all the details clear. In the various sections the reactions follow one another so that related reactions come together as much as possible.

Of course, in practice, points arise which have to be settled arbitrarily. Some reactions can be placed under two or more headings, e.g. $C_6H_5SH \rightarrow C_6H_5SO_3H$ might be put under **S** to **O** or **O** to **S**. In this case it is more natural to put it in the latter section, but in analogous cases the reaction in question is classified under the section first occurring. No linkings to **H** are considered, **H** is always supposed to be linked to the other element. Some sections do not appear in the book because so few reactions fall within them.

Decomposition reactions in which links are broken rather than made, electrolytic preparations and some others are placed in a separate section.

HINTS TO STUDENTS

1. Before commencing a course on practical organic chemistry, become familiar with the chapter on apparatus and methods. This chapter must be continually referred to as the course proceeds, so that facility in manipulative detail may be gained.

2. Before beginning any individual preparation, read carefully the entire method and also obtain a clear idea of the theory as well as the practice of the operation. Know the reason for every step in the process.

3. Work on a definite plan, never omitting anything essential for the sake of speed.

4. Procure *suitable and sufficient* apparatus. This applies especially to the use of vessels appropriate to the quantities to be used.

5. Clean and, if necessary, dry all apparatus before use. A solution of sodium dichromate in conc. sulphuric acid, contained in a pneumatic trough, is useful for cleaning apparatus.

6. Fit up the apparatus carefully and compactly, paying particular attention to the boring and fitting of corks.

7. Adhere to the instructions given with regard to definite times, temperatures and weights.

8. Cultivate a habit of observation ; observe all changes and record them without delay. This is one of the essentials of successful research.

9. Whenever possible, control the course of the reaction by testing samples. This will in many cases enable the end point to be determined exactly (see Acetanilide, Benzenesulphonic Acid).

10. Remember that the criterion of practical work is the yield of *pure* substance obtained, and if this differs by more than 10% from the yield stated, seek the cause of this difference, and then *repeat* the experiment.

11. After the experiment expand the notes already taken, giving particulars of the yield, physical characteristics (M.P., B.P., D., and microscopic examination for crystalline form) of the product. The ratio of the yield obtained to the theoretical yield also should be recorded as a percentage.

12. Cost the preparation (see p. 7) and compare the price with the catalogue quotation.

13. A sample of each stable product should be kept in a specimen bottle, and details of physical characteristics and yield placed on the label.

14. Above all, keep the bench neat and clean. Use separate dusters for it and for the apparatus.

THE USE OF THE LIBRARY

The references given in this book to the reactions and preparations should be consulted where possible by the student.

A knowledge of the literature is of fundamental importance. Richter's Lexicon can be used where a reference for a preparation is not given. The method of using this lexicon is fully described in the preface to that book. To facilitate the use of this lexicon, molecular formulae have been given in this book.

Richter also gives references to Beilstein which should afterwards be consulted, and the latter book always gives an indication of the scope of the reference. *A Brief Introduction to the Use of Beilstein's Handbuch der Organischen Chemie* (Huntress) has been published in English (Chapman & Hall, 1930).

The Lexicon of Stelzner should be consulted for references from 1910–1921, while the formula register of Chemisches Zentralblatt, based on the same plan as Richter and Stelzner, continues the index. A general register is also supplied by the Chemisches Zentralblatt from 1925 onwards.

British Chemical Abstracts (Sections A and B) issued by the Bureau of Chemical Abstracts, and *Chemical Abstracts* of the American Chemical Society, should also be consulted for recent references.

Cultivate a habit of reading the current journals, especially J. C. S., J. S. C. I., Berichte and Am. Soc. Do not forget that organic chemistry is only one branch of the subject. Pay particular attention to the Annual Reports issued by the Chemical Society and the Society of Chemical Industry as well as the Quarterly Reviews of the former.

NOMENCLATURE

The nomenclature in this book is that used by the Chemical Society.

Alternative names are given in preparations to assist the student in looking up the literature in Richter and in Beilstein. There are also appended in some cases, in square brackets, the names according to the Geneva Commission of 1892. Although the latter has not been uniformly adopted, it is well that the student should become acquainted with this nomenclature, in which the name is derived, in general, from the parent hydrocarbon, and which is sometimes adopted to designate a compound of complex structure. For a new nomenclature, see *A New Notation and Enumeration System for Organic Compounds*, Dyson (Longmans, 1946).

SUGGESTED LISTS OF PREPARATIONS

Before commencing a course in practical organic chemistry, the student should have a definite list of preparations to follow. These should be arranged in increasing order of difficulty, and in such a way that, as far as possible, each preparation leads naturally to the next. Where several students are working in the laboratory, the best results are obtained when each works through a different list and compares notes with his neighbour.

The following lists are suggested :

I	II	III	IV
199	318	321	200
269	143	257	213
440	281	311	220
482	478	218	187A
75	249	274	268
187A	75	75	75
268	252	464	204

I	II	III	IV
434	379	40	434
209	442	208	225
224	228	224	371
359	361	359	285
278	294	292	141
243	384	278	206
285	56	383	272
141	131	141	274
206	146	242	230
385	274	148	377
28	341	58	385
245	342	25	345
375	34	344	157
426	104	78	43
343	337	176	442
22	494	480	50
82	295	493	314
175	245	52	64A
173	248	117	16
271	52	22	105
265	117	421A	485
169	94	247	169
346	477A	424	154.

More advanced students should work through a synthesis involving several steps, e.g. Collidine, and should also attempt the preparation of homologues of some of the substances given in detail. In the lists given above, several preparations of industrial importance are included.

These preparations should be prefaced by exercises in fractional crystallisation and fractional distillation (pp. 14, 15, 16).

Tests on groups of organic compounds, such as those outlined in Chapter XLII, should be interspersed during the preparation exercises.

NOTE ON COSTING

The student should always acquaint himself with the cost of the materials he uses in a preparation. He should therefore consult the price list of some well-known manufacturer or retailer. Such a list should be available in every laboratory. Having ascertained such prices, he should always, after completing his preparation, calculate the cost of his final product and compare with the price in the catalogue. Many factors control the market prices, such as labour, recovery of by-products, etc. ; it is, nevertheless, a good exercise to make this comparison. In deciding which particular method of preparation should be adopted in a particular case, the student should consider the question of cost, weighing up the cost of starting materials, reagents, solvents, with yield. For example, there is a well-known reaction by which aromatic amines are converted into the corresponding hydrocarbons This reaction is one that can well be studied on the test-tube scale. Only if toluene, for example, were required of a high degree of purity for special purposes, such as determination of physical constants, would it be prepared in quantity from a toluidine.

Such evaluation should be adopted in all the simpler preparations. In this way the student will become acquainted with the elements of costing which play such an important part in his later life in the factory. He should hardly wait until he enters the factory to appreciate the cost of such common substances as sulphuric acid, benzene, aniline, naphthalene ; he should be able to estimate roughly the cost of derivatives such as dinitrobenzene, *p*-nitroaniline, etc. Even should he not take up the industrial side of his profession, he should be acquainted with the relative value of the more common products, and trained to decide for himself whether, for example, it would be more economical to extract with ether or benzene, taking into consideration the relative efficiencies of the two processes.

Moreover, chemically pure products are not essential for preparations, unless for research purposes. The ordinary technical qualities supplied by the well-known manufacturers are quite suitable for most preparations, and are, of course, much cheaper. It should be remembered that the facilities for the purification of many organic products are much greater on the large scale than in the laboratory, and that these technical products are often therefore of remarkable purity. It is a valuable exercise to purify some technical product of poor quality and again to estimate the cost of such purification (see Purification of Crude Anthracene).

The authors would not stress the point further in a book of this kind. Their experience teaches them that too often do students look upon such things as gas and power, bench reagents, and the commoner organic chemicals supplied from the departmental store, as commodities which have no actual value. It is a moot point as to whether educational authorities would not render much greater service to the student by charging say, a nominal fee for instruction followed by a charge for all materials used in the course of his work.

CHAPTER II

APPARATUS AND METHODS

PRACTICAL HINTS

Softening of Corks.—Corks should always be softened before inserting in any flask and the boring performed after softening. Several methods are available. The cork may be softened in the ordinary eccentric iron press between the two rollers. It may also be rolled on the floor underneath the foot. A convenient way is to place the cork in hot or boiling water ; the cork swells somewhat and becomes quite soft so that it can be made to fit various tubes or flasks. An excellent method of reducing the size of a cork is to rotate it in a flame until the outer coating has charred ; it is then rolled and cleaned : a cork thus treated may be used for vacuum distillations as the layer of carbon forms a good seal.

Corks impregnated with sodium silicate solution resist attack by hydrogen chloride and chlorine.

Rubber stoppers should be occasionally rubbed with a little toluene, which prevents hardening and keeps them clean. A trace of vaseline smeared on a rubber stopper affords considerable protection from the actions of halogens. Rubber stoppers should always be removed from vessels while the latter are still warm, to prevent sticking to the glass.

Boring of Corks.—Sharp borers should always be used. The end of the cork is placed against some solid object and bored half-way through from one end. The boring should then be completed from the other end. The boring of rubber stoppers may be greatly facilitated by moistening the borer with caustic soda. Mechanical borers are now available.

Removing Fixed Stoppers.—Hot water should be run on to the neck of the bottle and the stopper gently tapped. The neck of the bottle may be held in a stream of hot water and afterwards gently tapped. If these methods fail, and if the contents of the bottle are not easily inflammable, the neck of the bottle may be rotated in a flame prior to tapping. Similar methods may be applied to fixed stop-cocks which are more easily removed in a special press.

Ground-glass Joints.—Apparatus provided with ground-glass joints for attachment to other pieces are available for most of the common operations and should be employed for the sake of convenience and of avoiding contamination from corks. For examples, see Figs. 12, 13, 17, 33A.

CRYSTALLISATION

The solid product obtained from a chemical reaction is seldom pure, being contaminated with various impurities and by-products. For purification, the process of crystallisation is generally employed. As the process is of such frequent occurrence, the student should early in his course acquire proficiency in it. When dealing with products obtained in plenty, the utmost care should be taken to obtain the maximum yield of pure crystallised compound, as only by doing so can the manipulative skill be acquired which is necessary to obtain a satisfactory yield of pure compound from a product obtained in meagre quantities.

Crystallisation by Cooling.—The ideal solvent is one in which the compound to be obtained in pure crystalline form is insoluble in the cold, but readily soluble in the hot. Further, the impurities should either be insoluble or else very soluble. In practice such a solvent is seldom obtained, but the nearest approach to it should be selected.

The solvents most commonly employed are : water, alcohol (methyl and ethyl), ether, benzene, petroleum ether, acetone, glacial acetic acid ; or mixtures of water and alcohol, water and acetic acid, ether and petroleum ether, benzene and petroleum ether.

The following are frequently used : chloroform, carbon disulphide, carbon tetrachloride, ethyl acetate, pyridine, hydrochloric acid, sulphuric acid, nitrobenzene, aniline, phenol, dioxan.

The following solvents are now manufactured on the large scale for industrial purposes : ethylene dichloride, di-, tri-, and tetra-chloroethylene, tetrachloroethane, dichloroethyl ether, cyclohexane, cyclohexanol, tetra- and deca-hydronaphthalene (tetralin and decalin), triacetin, ethylene glycol and its esters and ethers, butyl alcohol, diacetone alcohol, ethyl lactate, *iso*propyl ether, etc.

Selection of Solvent.—In order to select a suitable solvent small quantities (each about 0·1 gm.) of the finely pulverised product are placed in several test tubes and treated with a *few drops* of single solvents of the above class. Where the substance dissolves easily in the cold on shaking, or does not dissolve appreciably on boiling, the solvents in question may be regarded as unsuitable. Where the substance dissolves on heating or boiling, and separates out again on cooling, the solvents are suitable ; that solvent should be selected which gives good crystals in the greatest abundance. At times crystallisation does not take place owing to supercooling ; in such cases the side of the test tube should be rubbed with a glass rod, or the solution should be " seeded " by the addition of a small portion of the crude product, since such operations frequently induce crystallisation. If necessary, the solution should also be cooled in ice or in a freezing mixture. With substances which are sparingly soluble in the common solvents, solvents of high boiling points such as toluene, nitrobenzene, etc., should be used.

Where no single solvent is found suitable, a mixture of two miscible solvents in one of which the product is soluble and in the other insoluble may be employed with advantage. Substances which are very soluble in cold alcohol or cold acetic acid are frequently but slightly soluble in water, and many substances which are very soluble in benzene are sparingly soluble in petroleum ether. From the preliminary investigation with single solvents it can generally be deduced which are suitable to serve as mixed solvents. The substance is dissolved in a small quantity of one solvent and heated ; the second solvent is then gradually added to the hot solution until a turbidity appears ; heat is again applied until complete solution takes place, and the solution is set aside to cool. Many substances separate in an amorphous or sticky form from an alcohol-water solvent. It is important that the crystals should be sufficiently well defined that their crystalline form as well as the presence of other crystals or impurities can be detected with the aid of a lens. The crystals obtained from these preliminary tests should be preserved, to serve, if needed, to "seed" the solution containing the main bulk of the substance.

Preparation of Solution.—If the substance is readily soluble the heating is generally carried out in a flask (conical or ordinary) on a water bath. If considerable heating is necessary, a reflux condenser should be provided to avoid loss of solvent or danger of fire. A convenient type of reflux condenser when small quantities of liquid are being dealt with is an ordinary glass filter funnel placed stem-wise in the mouth of the flask. Should the vapour catch fire, the flame should be withdrawn and the mouth of the vessel covered with a damp cloth or with a watch-glass. When the solvent is neither very volatile nor easily inflammable (i.e. water or acetic acid), the heating may be performed in a beaker over a flame. Where the resulting solution does not require filtration, a conical flask should always be used (see next section). During the heating, the contents of the vessel should be frequently shaken or stirred, since crystals, especially when they melt to a heavy oil on the bottom of the vessel, render the latter liable to crack.

In preparing the solution an excessive amount of solvent should not be employed at first ; successive small quantities should be added to the boiling or nearly boiling solution until the substance just completely dissolves, or until nothing but impurity remains undissolved. With substances of low melting point care should be taken that concentrated solutions from which the substance commences to separate at temperatures above its melting point are not used. When using mixed solvents, the procedure is similar to that described for the preliminary tests ; if on the addition of the second liquid (e.g. water or petroleum ether) resinous impurities separate, these should be filtered off before proceeding further.

Filtration of Hot Solution (see also **Filtration**).—This operation is usually necessary in order to remove insoluble impurities, filter fibres, etc. When the substance does not separate rapidly from the hot solution, and the liquid filters quickly, the solution may be filtered through an ordinary funnel with a short stem, fitted with a folded filter paper (Fig. 1). Both funnel and paper should previously be warmed in a steam bath. Or, the solution may be filtered with suction, using suitable types of apparatus (Figs. 27, 28). (For use of decolorising carbon, filter aids, etc., see p. 37.) When the filtrate is collected in a thick glass suction flask, the latter should be warmed beforehand by immersion in warm water. The bell-jar form of filtering apparatus (Fig. 29) is recommended, as the hot solution can be collected in a conical flask of suitable size. For "crystallisation by cooling" a rather *wide-mouthed conical flask* should be used to contain the hot filtered solution—a filter flask serves equally well for large volumes ; with *vessels of this conical type* the crystals *do not creep up the sides*, as may occur when beakers or the so-called "crystallisation dishes" are used ; after separation, the crystals can easily be removed with the aid of a glass rod over the end of which a short piece of rubber tube has been drawn.

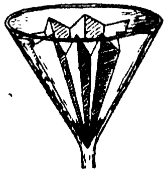


FIG. 1.

If the substance crystallises rapidly from the hot solution, a hot filter should be used. Figs. 2 and 3 show steam-jacketed and hot-water jacketed filters. With a volatile and easily inflammable solvent the flame should be removed from the jacket immediately before filtering, danger of fire being thereby avoided ; in such an instance the steam funnel is preferable when the steam is generated at a safe distance.

After filtration the conical flask is covered with a watch-glass and set aside. If large crystals are required, the rate of cooling should be as slow as possible, and the flask should not be disturbed. The rate of cooling may be lessened by immersing the flask in a bath of warm water and allowing the bath and its contents to cool. If the substance separates in large coarse crystals on slow cooling, or if small pure crystals are required, it is expedient to cool quickly in cold water or in ice water, and to stir or agitate the solution at the same time. Small crystals are generally free from mother liquor, which is liable to be occluded in large crystals. When the substance is very soluble at ordinary temperature, the cooling should be continued in a freezing mixture.

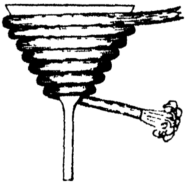


Fig. 2.

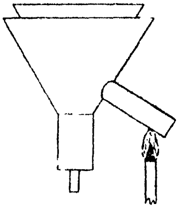


Fig. 3.

The list below gives some useful freezing mixtures, the most convenient for many purposes being a mixture of conc. hydrochloric acid and ice, or sodium chloride and ice.

Separation of Crystals.—This is generally effected by filtration with suction, vessels of size suitable to the quantities dealt with being selected. The crystals left on the funnel should be well pressed down and then washed a few times with small quantities of the pure solvent in order to

Mixture in gms.	Temp. falls from 15° to
250 calcium chloride cryst. + 100 aq.	—8°
8 sod. sulphate + 5 conc. HCl	—12°
25 amm. chloride + 100 ice	—15°
45 amm. nitrate + 100 ice	—17°
50 conc. HCl + 100 ice	—18°
33 sod. chloride + 100 ice	—20°
1 pot. thiocyanate + 1 aq.	—24°
100 dil. H_2SO_4 66% + 100 ice	—31°
3 calcium chloride cryst. + 2 ice	—49°
Solid CO_2 + ether	—100°

remove the last traces of mother liquor. If the substance is easily soluble, too large quantities of solvent must not be employed for washing. When a solvent which is not readily volatile has been used (e.g. nitrobenzene, acetic acid, etc.), it must be removed from the crystals by washing with an easily volatile solvent with which it is miscible. After being thoroughly drained on the funnel, the crystals are dried (see also p. 40). They may be placed on filter paper or porous plate, covered to protect from dust, and allowed to dry in the air, or left in a desiccator over a suitable substance to absorb the solvent; the operation may be hastened by evacuating the desiccator. If the crystals have a high melting point, the drying may be effected in a bath at temperatures below the fusion point. In this connection it should be noted that the presence of small quantities of solvent may produce a considerable lowering of the melting point. A test portion should therefore first be dried.

Often further crops of crystals can be obtained by concentrating the mother liquor; generally these are less pure and require to be recrystallised. In some cases the first crop has to be recrystallised before the crystals are pure (determined by M.P.). It is often convenient, in order to separate a second crop, to dilute the mother liquor with a liquid in which the dissolved substance is sparingly soluble. Crops separated in this way generally require recrystallisation.

Crystals which are very soluble in the solvent at laboratory temperature, and which have been obtained by cooling the solution in a freezing mixture, should be filtered through an ice-jacketed funnel (Fig. 4).

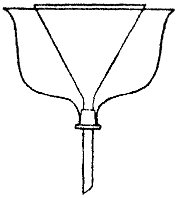


FIG. 4.

In all cases the process of crystallisation must be continued until no change in melting point occurs on further crystallisation, or until the product obtained by evaporating a sample of the mother liquor has the same melting point as the crystals separated from it.

On the larger laboratory scale centrifuges may be used for separating and draining crystals.

Crystallisation by Evaporation.—This method is employed when the substance is so easily soluble in all solvents (hot and cold) that it will only separate after partial evaporation. The solvent is allowed to evaporate spontaneously in the air or in a desiccator; if in the latter the evaporation is greatly hastened by using a suitable absorbent as well as evacuating the desiccator. The type of vessel employed depends on the volatility of the solvent; obviously the conical flask already recommended for " crystallisation by cooling " is not suitable for spontaneous evaporation, while a beaker or shallow " crystallising dish " is. When the latter type of vessel is used, " crusts " often form on the sides above the surface of the liquid. Such crusts seldom consist of pure substance, and they should be carefully removed with a spatula before attempting to filter off the crystals.

Since the purifying effect of crystallisation depends on the fact that the impurities remain dissolved in the mother liquor—except in cases where the impurities being insoluble are first filtered off—the solvent should never be completely evaporated, but the crystals should be filtered off while still covered with mother liquor.

Special Methods.—With some substances it is difficult to obtain good crystals by the methods already described. A method which frequently gives excellent results consists in dissolving the substance in some solvent, then adding a second solvent miscible with the first, but in which the substance is sparingly soluble. The first solvent is then gradually removed and the substance separates out—usually in the crystalline form. If the first solvent is the more volatile in air, spontaneous evaporation in air may diminish its concentration in the solution. The solution may be placed in a desiccator over some substance which absorbs the first solvent but not the second; in this way water may be removed from a water-alcohol solution by solid caustic potash or quicklime.

Another method—applicable when the substance is soluble in alcohol and in ether, but insoluble in water—consists in making a saturated solution in cold alcohol, adding water until considerable precipitation has taken place, then adding ether until the precipitate has redissolved, and finally allowing the ether to evaporate spontaneously.

When a substance is soluble without change in concentrated sulphuric acid, but insoluble in water, a saturated solution in the former medium when left exposed to water-vapour—say, side by side with a vessel of water under a bell-jar—gradually absorbs water, and the substance frequently separates out in crystalline form.

The purification of many products can be facilitated by distillation, prior to crystallisation, provided they distil without decomposition. Generally it is preferable to conduct the distillation under reduced pressure (p. 30).

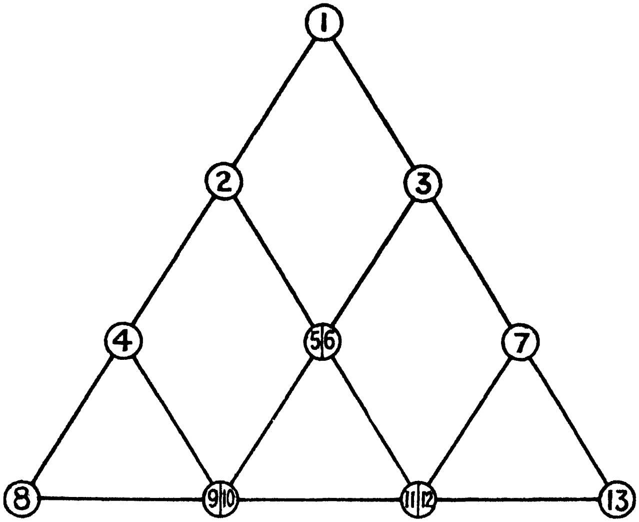
FRACTIONAL CRYSTALLISATION

The process of fractional crystallisation is employed to separate two or more substances, all of which are soluble in the solvent used. When only two substances are present, it is often possible to find, by preliminary tests, a solvent which, when used in suitable quantity, will dissolve the whole of the more soluble compound, but only a small quantity of the less soluble. In such a case, a preliminary separation may be effected by shaking the mixture with a quantity of solvent (hot or cold—as found suitable by trial), and filtering the solution from the residue remaining undissolved. For extracting a mixture of this nature with a hot solvent the Soxhlet apparatus (Fig. 30) is specially useful; in fact this apparatus should be employed for all extractions where a residue remains undissolved, since filtration as well as extraction is accomplished; also, only a relatively small quantity of solvent is required (see p. 38).

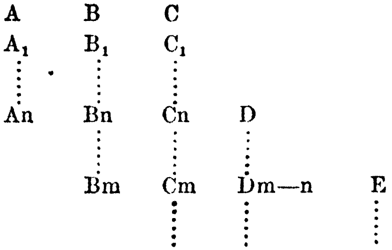
When commencing a fractional crystallisation, preliminary tests similar to those described under "Crystallisation" are first carried out, and the crystals which separate during such tests examined with a lens. The crystals which form first are either the least soluble or most abundant constituent of the mixture. If a second or further type of crystal appears, its shape and time of formation relative to cooling should be noted; it is often necessary to filter off the first crop while the mixture is still warm.

When dealing with a finely-powdered or amorphous mixture, it is often useful to examine a small portion placed on a watch-glass under the microscope. The action of a few drops of various solvents (hot or cold) can be examined in this position, and valuable information—which might not be obvious to the naked eye—perhaps gained concerning the solubility or insolubility of some constituent in a particular solvent.

No definite plan can be given which will suit all examples of fractional crystallisation. The scheme outlined in *Text-book of Inorganic Chemistry*, Vol. IV, p. 324 (J. Newton Friend), when applicable, affords a convenient method of marking and recording the various fractions involved in a fractional crystallisation ; it also avoids the accumulation of a vast number of small crops and mother liquors :



The mixture is dissolved with the aid of heat in a solvent to give solution (1). From this solution on cooling, crystals separate which are filtered off, and solution (1) is thereby divided into crop (2) and mother liquor (3). Crop (2) is dissolved in the minimum quantity of hot solvent, and from the resulting solution after cooling, crop (4) and mother liquor (5) are obtained. Mother liquor (3) is concentrated, and from the concentrated solution after cooling, crop (6) and mother liquor (7) are obtained. Crop (6) and mother liquor (5) are united to form a single fraction, and after being heated to dissolve and subsequently cooled give rise to crop (10) and mother liquor (11). Crop (4) is dissolved in a small portion of pure solvent by heating and after cooling is divided into crop (8) and mother liquor (9). Mother liquor (7) after concentration and cooling yields crop (12) and mother liquor (13). (9) and (10), likewise (11) and (12), are united to give single fractions. Proceeding in this way, the least soluble compound goes to the left in the diagram, while the most soluble goes to the right, and compounds of intermediate solubility lie between these extremes. Each crop should be tested for purity. If, when examined with the aid of a lens, two or more types of crystals are present, the crop must be recrystallised. When a crop appears uniform, a small portion should be withdrawn, dried by exposure on porous porcelain or on filter paper, and its melting point taken. In the above scheme if crop (2), say, is pure it takes no further part in the recrystallisation ; mother liquor (3) is then worked up. When the principal product is moderately soluble in the hot solvent, but not very soluble in the cold solvent, the following method might be serviceable. The product is divided into three (say) equal portions, A, B and C. A is recrystallised from the minimum quantity of pure solvent, yielding crop A_1. The mother liquor from A_1 and small quantity of washings are used to recrystallise B, yielding crop B_1. The mother liquor from B_1 is similarly used to recrystallise C. In this way the mother liquor from C_1 should be more or less saturated with the impurities present, while it contains but little more of the principal product than was contained in the mother liquor from A_1. If crop A_1 is impure, it is recrystallised from fresh solvent yielding crop A_2. Crops B_1 and C_1 are recrystallised from mother liquors A_2 and B_2, and mother liquors C_1 and C_2 are united. The process is continued after this fashion until the crop under A is pure. The crop under B then becomes the first fraction, and the mother liquors from the C's are combined and evaporated, so as to give a crop D, which becomes the new end-fraction and enters into the recrystallisations.



This method was found very useful for the purification of *d*-α-phenyl ethylamine *l*-malate (p. 375).

When the product separates from the solvent in compact crystalline masses, the mother liquor may be decanted on to the next fraction, and thus filtration, which is always attended with some slight loss of material, is avoided.

It sometimes happens that after a fractional crystallisation has been continued for some time, a solution is obtained from which two products crystallise side by side, the solution being apparently saturated with regard to each product. In such a case a separation might be effected by evaporating off the solvent and proceeding with a different solvent in which the ratio of the solubilities of the two compounds differs from the corresponding ratio in the first solvent. In some such cases mechanical means of separation might be effective ; if one set of crystals is heavier than the other, the lighter set may be separated by stirring the supernatant liquor (or by rotating the vessel) and rapidly decanting. The mother liquor after filtration from the lighter crystals may be agitated a second time over the heavier crystals in order to remove any of the lighter which still remain. If one or both sets of crystals separate in fairly large form, a separation may be effected by hand picking.

DETERMINATION OF MELTING POINT

In order to identify a substance, or to test its purity, the melting point of the substance is determined, a process which can be rapidly carried out. If a substance does melt, it should, if pure, melt sharply at a definite temperature. This figure should agree with the figure given in the literature, and is valuable in the identification of a compound. If the figure is considerably lower than the one given, one must suspect impurity or else a different compound from that stated. In every case, however, the melting point should be verified by reference to Beilstein or Richeter's Lexicon or Stelzner. If the melting point is higher than the figure given, the compound may be a different one, or the melting point may have been carelessly taken, for example, by heating too quickly. In general, a pure substance melts within 1° of the figure given. If the melting point is not sharp, the substance should be recrystallised from a suitable solvent before a further determination is made. From this it is obvious that great care should be observed in making this simple determination, and the following points should be carefully observed.

The choice of a thermometer is an important one. In the first place it should have a small bulb, and the range should be suitably chosen. For example, if it is known that a substance has a low melting point, a thermometer of range 0°–100° should be used. If the substance has a high melting point, a range of say 200°–300° should be chosen, and so on. All thermometers used for the determination of melting points should be standardised against a standard thermometer.

The preparation of the capillary tube requires a little practice. A piece of thin-walled glass tubing or a test tube is heated in an ordinary Bunsen flame or blowpipe until it softens, when it is withdrawn from the flame and carefully drawn out for 2 or 3 feet. Draw slowly at first, then quickly as the glass cools and hardens. The central part, consisting of the capillary tube, is then cut into sections of about 8–10 cms. in length, and one end of each section fused in the flame. A supply of melting-point tubes should always be in readiness.

The substance of which the melting point has to be taken should be perfectly dry. A sample is ground to a fine powder on a watch-glass with a clean glass rod, introduced into the capillary tube and shaken to the bottom ; light scratching of the tube with a file often brings this about. The tube is then ready for fixing to the thermometer. The liquid used in the melting-point apparatus is usually liquid paraffin. Conc. sulphuric acid, dibutylphthalate, or silicon esters may also be used. Above 200° sulphuric acid should not be employed alone, but should be mixed with 30% or more of potassium sulphate. As this mixture is solid at ordinary temperature it should be poured out while hot. An electrically-heated apparatus (Fig. 6A) may be used.

The melting-point apparatus consists of a small beaker or a large-sized test tube containing liquid up to a convenient level. The thermometer can be held in position with its bulb well immersed in the bath by means of a clamp in the former case, or by means of a cork in the latter. It is advisable to have some kind of mechanical agitation in the liquid (Figs. 5, 6) although if the heating is carefully done this may be dispensed with,

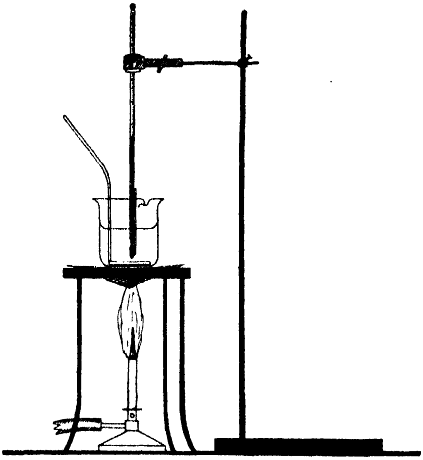


Fig. 5.

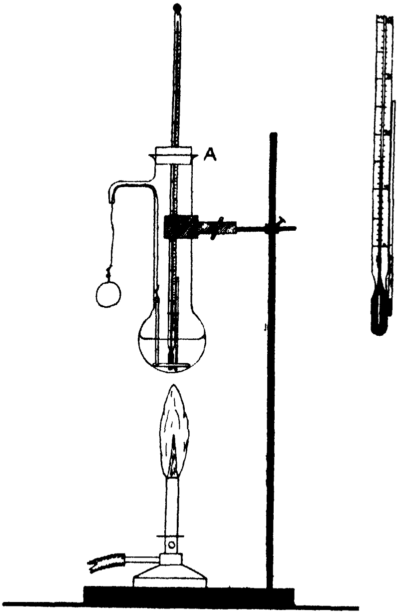


Fig. 6.

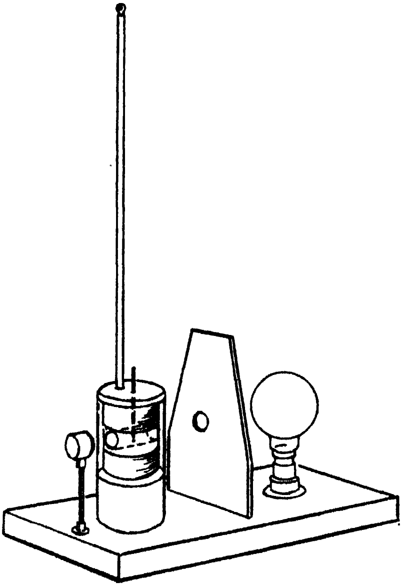


Fig. 6a.

especially when a long (22 cms.) pyrex tube of 2 cms. diam. with a bulb of 4 cms. diam. is used in place of the vessel shown in Fig. 6.

Figs. 5 and 6 show the arrangement in the two cases where a glass rod is used as a stirrer, the stirring being maintained while the bath is slowly heated. The cork at A in Fig. 6 should be as thin as possible so as to obscure the minimum amount of the scale, and if no agitator is used passing through the cork, then a slit should be made in the cork to allow exit to the vapours on heating.

The thermometer is first dipped in sulphuric acid, if this is used, and then the drop which clings to the bulb is smeared on the side of the capillary tube. The capillary tube is then made to adhere to the thermometer (Fig. 6) by capillary attraction, so that the substance in the tube is just opposite the bulb of the thermometer. This method is much better than using a rubber band, which is apt to perish in the sulphuric acid fumes, and gives rise generally to a speedy discoloration of the acid. A rubber band or fine copper wire is desirable with paraffin.

A cloth should be placed on the bench below the apparatus when heating is commenced, to protect the observer should an accident occur. The Bunsen burner should be held in the left hand and the stirrer worked with the right. The heating should be moderated on approaching the melting point, and the Bunsen lowered to give a flame about 2 cms. in length. The range of temperature over which the substance melts is recorded.

Correction.—Melting points are usually given as "uncorrected"; for correction the following formula is employed :

$$T_c = T_o + 0{\cdot}000156l(T_o - T_m).$$

T_c = corrected temperature.
T_o = observed temperature.
0·000156 = apparent coefficient of expansion of mercury in glass.
l = length of mercury column in degrees above surface of liquid.
T_m = mean temperature of mercury column, i.e. the temperature of the middle point of the mercury column, taken by another thermometer.

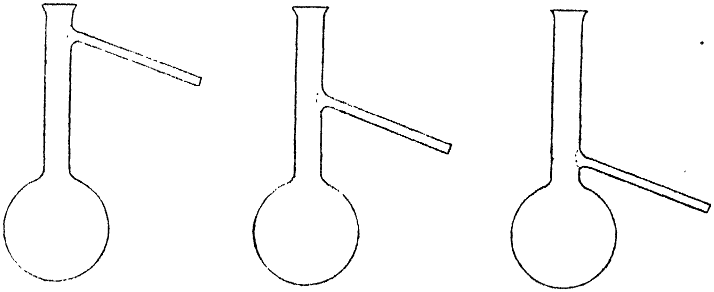
Some Corrected Melting Points for Standardising Thermometers.—

p-Toluidine	45°	Salicylic acid	159·8°
α-Naphthylamine	50°	Anthracene	216°
Naphthalene	80·8°	Carbazole	246°
Benzoic acid	122·5°	Anthraquinone	285°

"Mixed" Melting Points.—Impurities generally lower the melting point of a substance. To determine whether two substances of the same melting point are one and the same, a convenient method is to mix equal quantities of the two and take melting points of the mixture and the two substances—all three tubes being attached to the thermometer simultaneously. If the melting point of the mixture is lowered the two substances are not identical.

Setting Point.—When a large quantity of the substance is available a very speedy determination of its setting point (freezing point) may be made as follows. The method is used largely on the technical scale, and is specially suitable for controlling chemical operations.

The substance is placed in a large test tube and melted. This is placed in a boiling tube which serves as air jacket. A thermometer reading in tenths or hundredths of a degree is placed in the melted substance which is stirred by means of the thermometer. The mercury in the thermometer gradually falls as the liquid cools, until it reaches a point when it rises suddenly (due to the heat liberated on the appearance of the solid phase). The stirring is continued, and the highest temperature reached after this upthrust is taken as the setting point. The determination can usually be carried out with rapidity where super-cooling of a few degrees only takes place.



(*a*) For low B.P. liquids. (*b*) For medium B.P. liquids (*c*) For high B.P. liquids.

FIG. 7.

DISTILLATION AND DETERMINATION OF BOILING POINT

The same apparatus (Fig. 8) is used for the distillation of a liquid and for determining its boiling point. A pure liquid should boil at a constant temperature, and the whole should pass over within a very small range.

The liquid to be distilled, or of which the boiling point is required, is placed in a suitable round-bottomed flask, fitted with a side tube. The flask chosen should be of suitable capacity, e.g. one should not use a 500-c.c. distilling flask to distil 10 c.cs. of a liquid. The liquid should half-fill the bulb of the distilling flask. Fig. 7 above shows the position of the side tube for particular boiling ranges. This is important, and a proper choice will well repay the trouble taken.

Determination of Boiling Point.—After the liquid has been placed in the distilling flask, the thermometer which is chosen to suit the substance, as in the determination of melting points, is fixed in the neck of the flask by means of a thin cork, so that the bulb of the thermometer is opposite the exit tube.

The flask is then fixed to a Liebig or air condenser by means of a cork placed near to the neck of the flask. The condenser is attached to an adapter at its lower end to deliver the condensed liquid into a receiver. The cork should be placed reasonably far from the end of the condenser tube. The sketch (Fig. 8) shows how the complete apparatus should appear. The ordinary Liebig condenser should be replaced by an air condenser for liquids boiling over 160° (see Fig. 9).

When inflammable liquids are distilled, the receiver, as shown, should take the form of a Buchner flask, with a rubber tube connected to the side tube, and dipping over the side of the bench. In this way inflammable vapours are removed from the region of the Bunsen burner.

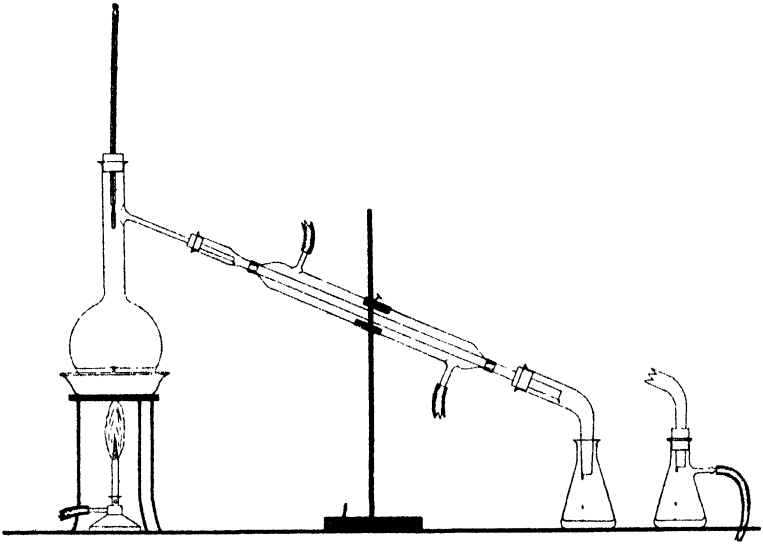


Fig. 8.

Before heating is commenced, a small piece of unglazed porcelain or magnesite is introduced into the flask in order to prevent " bumping " or too vigorous boiling. Heat is applied very gradually, and the temperature raised very slowly at first, until it reaches a point at which the liquid distils regularly. This temperature, which is the boiling point of the liquid, remains constant.

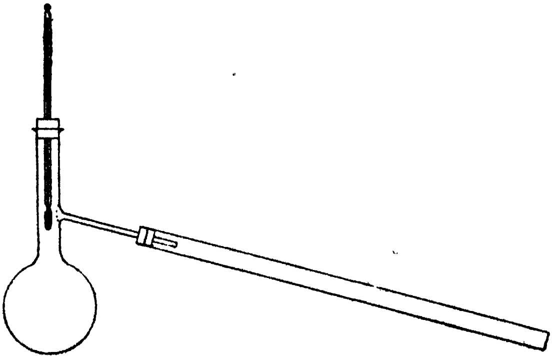


Fig. 9.

When there is only a very small quantity of liquid available, two methods may be applied :—

1. A very small distilling flask, preferably pear-shaped, may be used. The sketch (Fig. 10) shows a very useful type of flask for this purpose. These flasks can be obtained of capacity down to 1 c.c. The hood prevents condensed liquid returning to the bulb.

2. This method may be employed for even one drop of liquid. The latter is placed in a narrow tube which has been sealed at one end, and this tube is attached to a thermometer by means of a rubber band in such a position that the liquid is opposite the bulb of the thermometer. Into the liquid is now placed the open end of a sealed melting-point tube (Fig. 11). If the inverted tube is bent near its closed end and hung from the narrow tube so as to be clear of the bottom of the latter, better results are obtained.

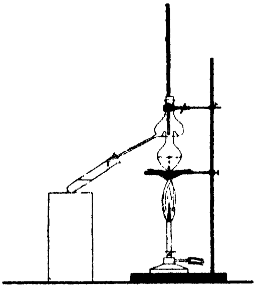


FIG. 10.

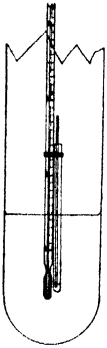


FIG. 11.

At first bubbles of air are expelled from the end of the capillary tube due to expansion as soon as heat is applied to the bath; the heating should be very carefully carried out. Ultimately a point will be reached at which there is a regular stream of bubbles emitted from the tube. This temperature is the boiling point. At least two observations should be made by this method, a new capillary tube being used each time. The mean is taken as the true boiling point. These boiling points are " uncorrected " —the " corrected " figure is obtained as with melting points.

Corrections.—(*a*) *Thermometer Reading.*

$$T_c = T_o + 0{\cdot}000156l(T_o - T_m)$$

T_o = observed boiling point.

T_c = corrected boiling point.

l = length of mercury column not heated by the vapours.

T_m = mean temperature of mercury column (see Melting Point).

(*b*) *Barometric Pressure.*

$$T_c = T_o + 0{\cdot}043(760 - P)$$

P = atmospheric pressure in millimetres.

Some Corrected Boiling Points for Standardising Thermometers.—

Chloroform	61·3°	Nitrobenzene	210·9°
Benzene	80·2°	Quinoline	237·5°
Chlorobenzene	131·2°	Benzophenone	305·9°
Aniline	184·4°	Mercury	356·8°

FRACTIONAL DISTILLATION

Fractional distillation, using the ordinary distillation apparatus, is employed for separating substances whose boiling points differ by at least 40°. The mixture is distilled slowly and the distillates are collected in separate receivers. For example, a mixture of benzene (B.P. 80·2°) and nitrobenzene (B.P. 210·9°) can be separated by collecting the distillate which comes over at about 80° in one receiver and at about 210° in another receiver. By careful redistillation of these two fractions the two receivers will ultimately contain pure benzene and pure nitrobenzene respectively. It is always necessary to repeat the process when the boiling points of the liquids are fairly close.

When the boiling points lie near one another the same method can be used, but before a separation can be obtained the process may have to be repeated ten or twenty times, and even then the separation will probably not be complete. By using still-heads or fractionating columns this difficulty can be obviated. Fig. 12 indicates the types of still-heads most commonly used in the laboratory for this purpose. The principle of all is similar ; they offer a large cooling surface to the rising vapours which are always in contact with the falling condensed liquid. In this way only the more volatile portion passes over to the condenser. Fig. 12A shows a column attached to a flask. Such an apparatus could be used for separating, say, a mixture of benzene (B.P. 80·2°) and toluene (B.P. 110°). It is always necessary to repeat the process at least once until the constituents of the mixture give definite boiling points.

Efficient fractionation depends on the column operating under approximately adiabatic conditions. Consequently insulation in the form of a paper or asbestos jacket is advantageous in ensuring better separation. For temperatures above 100° lagging can take the form of a commercial asbestos-magnesia mixture fixed to the column, or as an air, vacuum, hot water, or liquid jacket surrounding the column. See Fig. 12. (J. Eng., 1932, 408 ; Am. Soc., 1935, 878).

For efficient fractionation a large proportion of the vapours in the column must be condensed and returned to the still. The ratio of the quantity returned to that collected in the receiver is the *reflux ratio*. Where the boiling points of the components of a mixture are close to one another, this ratio should be high.

Fig. 13 shows a convenient apparatus for effecting fractionation. The column is heated by vertically-suspended nicrome wire (28 s.w.g.) with a current about 2 amp. The packing can be of glass helices or other suitable material (see Fenski, J. Eng., 26, 1169). The still-head (Corad) consists of a condenser with an inner " cold finger ", the latter being interchangeable with others of different surface area. These control the reflux ratio which is measured by the ratio of the area of the inner condensing surface to that of the " cold finger ". With this apparatus, in which all joints are of ground glass, the reflux ratio is independent of the rate of distillation. Tap A is fully open throughout distillation ; tap B is for admission of air when dismantling the apparatus ; tap C is for connecting to vacuum pump (An. Chem., 1947, 120).

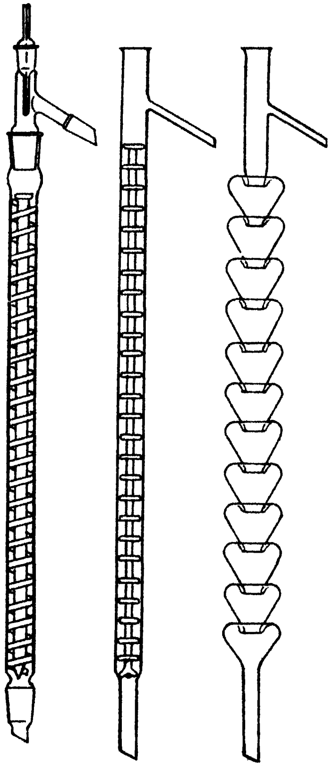


Fig. 12.

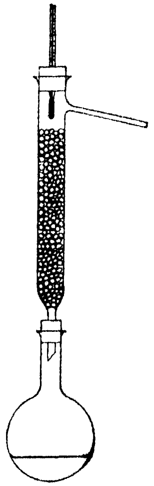


Fig. 12a.

AZEOTROPES

In some cases, liquids with different boiling points cannot be separated in this way, owing to the formation of constant boiling mixtures (azeotropes). The excess of each constituent beyond that required to form the constant boiling mixture would, of course, pass over either before or after the constant boiling mixture which has either a maximum or minimum boiling point compared with any other mixture of the substances (see table below).

Azeotropic Distillation.—Azeotropic mixtures of two compounds may be separated by distillations under varying pressures, by chemical or physical methods, or by adding a third component. When a mixture of ethyl alcohol, benzene and water is distilled at atmospheric pressure, a ternary mixture of minimum B.P. (64·85°) and containing by volume

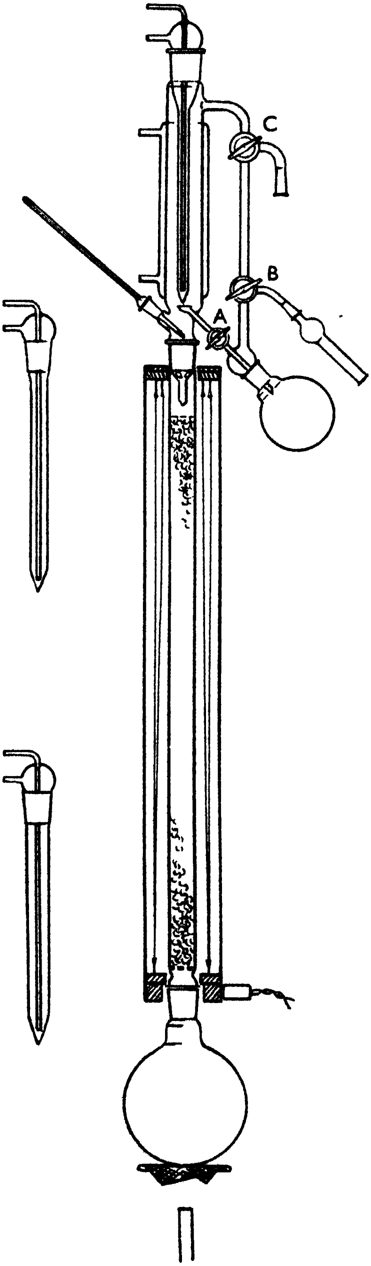


FIG. 13.

18·5% alcohol, 7·4% water, and 74·1% benzene forms the first fraction, the second being a binary azeotrope (B.P. 68·24°) consisting of 32·41% alcohol, and 67·59% benzene. The final fraction is pure alcohol (B.P. 78·3°). Benzene is recovered by dilution with water. Similarly, water may be separated from ethyl alcohol by using small quantities of trichloroethylene (C. r., 1923, 1623), and paraffins removed from commercial toluene with acetone or methyl ethyl ketone (J. S. C. I., 1944, 329). All these processes are used on the industrial scale.

CONSTANT BOILING MIXTURES

Minimum B.P. Type I.

A	B.P.	B	B.P.	B.P, of constant mixture	% of A in constant mixture.
Iethyl alcohol	65·5°	Acetone	56·6°	55·95°	13·5
Vater	100°	Ethyl alcohol	78·3°	78·15°	4·43
Vater	100°	Isopropyl alcohol	82·45°	80·35°	12·10
Vater	100°	*n*-Propyl alcohol	97·2°	87·7°	28·31
Vater	100°	Butyric acid	159·5°	99·2°	80
enzene	80·2°	Ethyl alcohol	78·3°	68·25°	67·64
enzene	80·2°	Methyl alcohol	65·5°	58·35°	60·45
yridine	115°	Water	100°	92·5°	59

Maximum B.P. Type II.

A	B.P.	B	B.P.	B.P, of constant mixture	% of A in constant mixture.
Water	100°	Formic acid	99·9°	107·1°	23
Water	100°	HCl	about —80°	110°	79·76
Water	100°	HBr	,, —73°	126°	52·5
Water	100°	HI	,, —35°	127°	43
Water	100°	HNO_3	86°	120·5°	32
Chloroform	61·2°	Acetone	56·6°	64·7°	80

B.Ps. at 760 mm.

References. Reilly, *Distillation.* Robinson and Gilliland, *Fractional Distillation.* Young, *Stoichiometry.* Morton, *Laboratory Technique in Organic Chemistry.* Swietoslawski, *Ebulliometric Measurements.*

For review of fractional, azeotropic, and molecular distillation, see Ann. Rep., 1943, 216.

Purification and Fractionation of 90s Benzol.—Commercial benzene is far from pure and contains homologues (chiefly toluene) and thiophene as well as basic substances. On removal of the bases with dilute acid and the thiophen with conc. sulphuric acid, fairly pure benzene may be obtained by fractional distillation of the residue. " 90s benzol " contains about 80–82% benzene, 14–15% toluene, and about 3% xylenes. The term means that 90% by volume of the benzol can be distilled off up to 100°.

Shake up 200 c.cs. of 90s benzol in a large separating funnel with 10 c.cs. of conc. sulphuric acid, allow to settle, and run off the acid layer. Repeat with 10 c.cs. of fresh acid. Wash the residue first with water, then with dilute caustic soda, and finally with water. Dry by standing for

12 hours over granular calcium chloride. Decant into a round-bottom flask and add a small piece of unglazed porcelain (to prevent bumping). Attach a fractionating column (Fig. 12) with thermometer and condenser. Place the apparatus in a fume cupboard or other place free from draughts. Clean, dry, and label a number of small flasks to serve as receivers.

Heat the liquid to boiling, using a very small flame and adjusting it so that a drop of distillate is obtained per second. Collect the fraction boiling up to 80° in the first receiving flask, from 80°–85° in the second, 85°–90° in the third, and so on up to 100°, then finally a fraction from 110°–115°. Remove the flame when the temperature exceeds 115° and discard the residue in flask. To the empty distilling flask add the first fraction and redistil, rejecting distillate below 79°, but collecting what distils at 79°–82°. Similarly add fractions 3 and 4 in turn, collecting the distillate at 79°–82° in the same receiver. Redistil the fraction 79°–82°, collecting the distillate between 80°–81°, which consists almost entirely of benzene. Place this fraction in a flask surrounded by ice. When it has almost completely solidified pour off the still liquid portion, the remaining crystals being practically pure benzene.

The residue in the distilling flask after removing the fraction 79°–82° may be distilled up to 100° and the earlier fraction boiling at 100°–115° then added. Fractions may be collected as before and the final fraction redistilled, the portion distilling at 109·5°–110·5° being collected. This consists of toluene.

For use of Raney Nickel (see p. 521) in removing thiophen, thiotolen, etc., see Ann. Rep., 1945, 100.

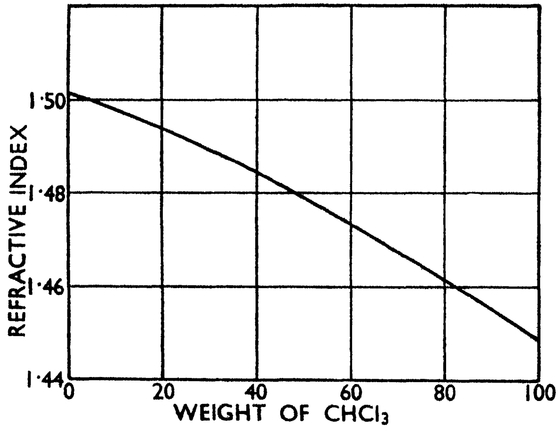
Control by Refractive Index.—A simple and rapid method for following the course of fractional distillation is by the determination of refractive index of the fractions (see J. S. C. I., 1947, 451).

The following illustrates the method :

Mix 100 c.cs. of chloroform (B.P. 61°) with 100 c.cs. of benzene (B.P. 80°), and place in a distilling apparatus (Fig. 8) fitted with one or other of the columns illustrated in Fig. 12. Collect the distillate over 5° intervals in separate receivers, determine the refractive index (*n*) of each fraction and from the table or curve given below estimate the composition of the mixture. Repeat this experiment using a distillation apparatus fitted with an efficient reflux, preferably with reflux control (see Fig. 13) and again determine the refractive index of the various fractions. It will be found that the more efficient distillation effected in the second series results in a more complete separation of the components. The experiment illustrates the application of a well-known physical method of determining the purity of the fractions.

Chloroform Weight %	*n* at 20°
0	1·5012
13·54	1·4960
33·67	1·4876
43·88	1·4828
50·64	1·4790
56·93	1·4760
57·55	1·4759
62·72	1·4729

Chloroform Weight %	*n* at 20°
68·86	1·4692
75·86	1·4650
83·26	1·4595
96·49	1·4579
100	1·4485



Refractive Index-Composition Diagram. Benzene-Chloroform Mixtures (20°).

STEAM DISTILLATION

Steam distillation is sometimes employed for separating substances of high boiling point which have an appreciable vapour pressure at 100°. It consists in passing a current of steam through the mixture. The sketch (Fig. 14) shows the apparatus usually employed. The steam is generated in a tin canister or a glass flask which is provided with a long glass safety

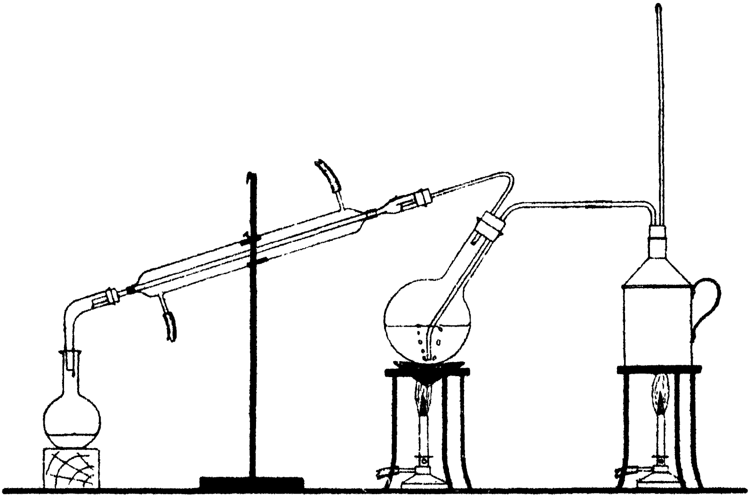


Fig. 14.

tube dipping below the surface of the water. The distilling flask should be large, and should be sloped to prevent the liquid splashing up into the condenser. The steam delivery tube should be slightly bent, as shown. Rubber stoppers should not be used. In order to prevent excessive condensation of steam the distilling flask should be directly heated, and a soluble salt may be added to raise the temperature. The distillate may consist of a solution in water (acetic acid—see p. 251), or of two layers (aniline—see p. 365), or a solid may separate (*o*-nitrophenol—see p. 281). If the last tends to choke the condenser the cooling water should be turned off occasionally. Steam may be substituted by alcohol or ether vapour in particular cases. Control tests should be made occasionally to determine the completion of the distillation; these tests may be physical or chemical, depending on the nature of the substance. For theoretical discussion, see text-books on Physical Chemistry.

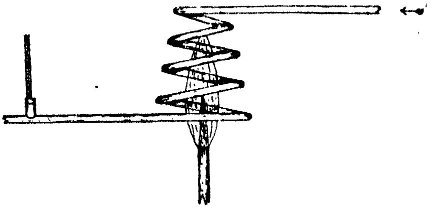


FIG. 15.

Superheated Steam.—This is used for distilling substances which are difficultly volatile. Steam is passed through a lead coil heated in an oil bath or a copper spiral (Fig. 15) heated by a Bunsen flame, and having a side tube for a thermometer. This tube is placed on the exit tube, and as far away as possible from the flame.

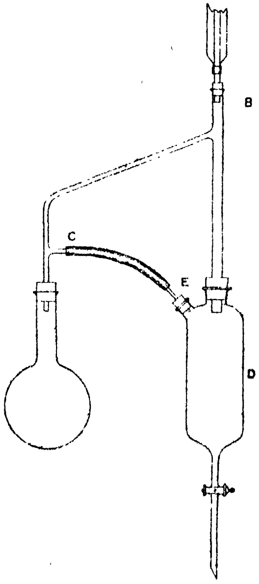


FIG. 16.

Continuous Steam Distillation.—The apparatus (Fig. 16) is very convenient when this process has to be carried on for some time. The substance to be steam distilled is placed in the round-bottomed flask A along with water if none is present. To the flask is attached through a cork a tube delivering to a vertical tube B, and with a small side tube C. A condenser is fitted to the top of the vertical tube and a receiver D of the type shown or a flask with a two-holed stopper. The small side tube C is attached to a delivery tube E fixed to the receiver by means of a rubber tube. The capacity of D must, of course, be less than the volume of liquid in A. When the flask is boiled the vapour is condensed in the condenser and the liquid falls into the receiver. When this process has been continued for some time, the top layer of water in the receiver gradually rises, and when it reaches the level of the small side tube C passes back automatically into A. The process is now continuous. The liquid in the receiver can be separated when desired by opening the tap on the bottom of the receiver.

When the liquid to be distilled is lighter than water, the small glass tube E is extended to the bottom of the receiver.

DRY DISTILLATION

This is a process which is occasionally used in the laboratory ; it is usual to perform the distillation in an iron or copper vessel as glass will not stand the heat. In order to prevent a cake forming, and thus secure uniform heating, it is advisable to mix the substance to be distilled with iron turnings which conduct the heat into the interior of the mass, provided, of course, that the iron turnings have no chemical action on the substance.

VACUUM DISTILLATION

Some liquids decompose when distilled in the ordinary way ; these can generally be distilled under reduced pressure. The apparatus is shown in the sketch (Fig. 17) and may be of glass, provided large vessels are not used. It is usual to heat the distilling flask in a bath and not by direct heat. The distilling flask, which may be of the ordinary type or, better, having two necks (Figs. 18, 18A), should be wrapped in asbestos cloth, which acts as a protection as well as a preventative of loss of heat by radiation. To the flask is attached a glass tube drawn out to a fine capillary which in turn is drawn out in a small luminous flame to a still finer and more flexible capillary and which dips below the surface of the liquid. By the passage of small quantities of air, or some other gas if air is unsuitable, regular boiling is maintained, and this is of extreme importance. Provided the liquid has no action on rubber, rubber stoppers should be used ; they should be smeared with vaseline before inserting. Good corks, however, are quite satisfactory if covered with collodion or cellulose acetate solution

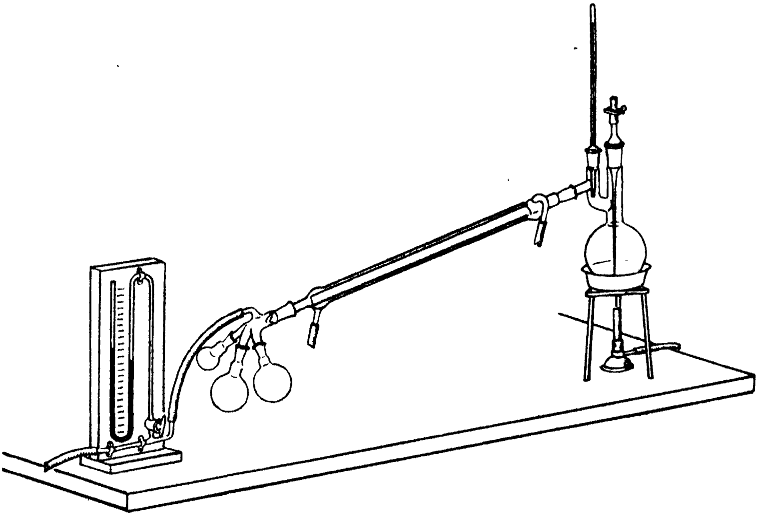


FIG. 17.

after insertion, or charred as described on p. 9. Between the receiving flask and the pump is placed a manometer for reading the pressure. If a water pump is used a water trap (Fig. 19) must be inserted between the pump and the manometer to catch water sucking back. When the distillation is to be discontinued the flame should be extinguished and air allowed to enter by carefully opening the tap attached to the water trap.

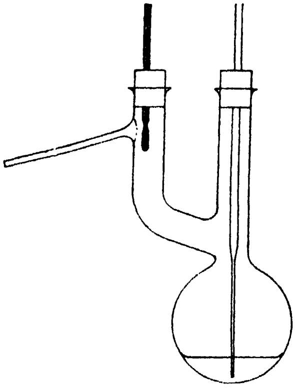


FIG. 18. (Claisen.)

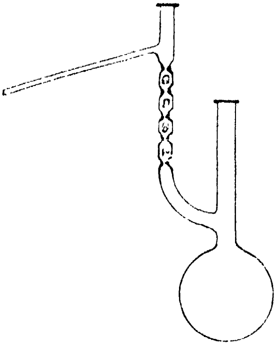


FIG. 18A.

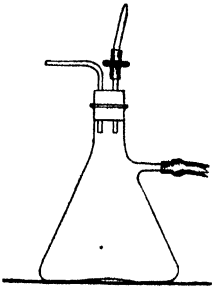


FIG. 19.

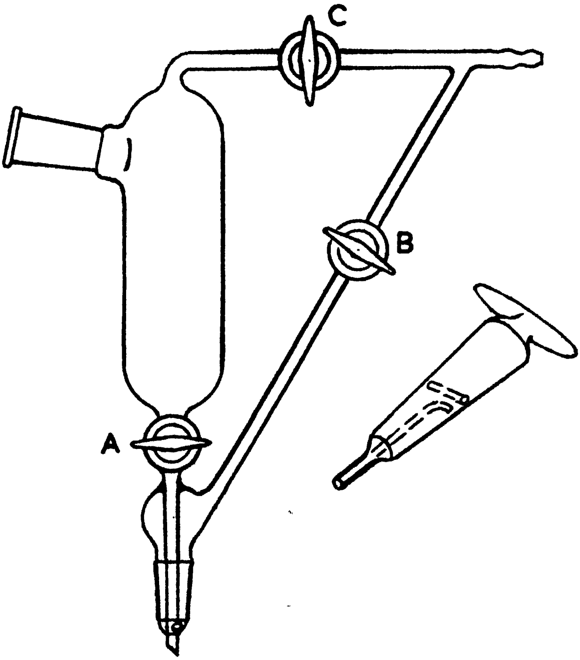


FIG. 20.

Vacuum distillation may be used in fractionating liquids. The apparatus is similar except that facilities are provided for collecting different fractions. Two sketches (Figs. 17, 20) show suitable types of receivers for use in fractionating under reduced pressure. Fig. 20 shows a single receiver which can be emptied without breaking the vacuum. While a fraction is being collected, A and B are closed while C is open. The receiver is emptied by closing C and opening A and B. While the next fraction is being collected the receiving flask may be removed.

It sometimes happens that a liquid "bumps" violently even with the addition of a few porcelain chips and the passage of a fine gas current through the flask. The best plan in such cases is to add glass wool so that it is immersed in the liquid and occupies space above the liquid. In this way—or by heating the flask deeply immersed in an oil bath—the vapour is superheated, and bumping is minimised.

A convenient apparatus for distilling liquids of high boiling point under reduced pressure is shown in Fig. 21, in which the receiver is an ordinary distilling flask, and is kept cool by a current of cold water (see also Fig. 23).

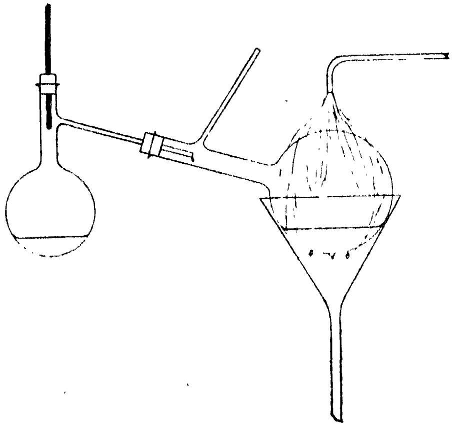


FIG. 21.

A cylinder, fitted at one end with a good cork and drawn out to a tube at the other, may be packed with test tubes and used in such a manner as to function as a fractional receiver by rotation of the cylinder as required. An adapter passing through the cork delivers the distillate into the test tubes. The pump is attached to the drawn-out end of the cylinder.

As with glass flasks there is a risk that they may collapse under a vacuum, especially when heated to high temperatures, the eyes should be protected by goggles and "safety glass" screens employed.

PRESSURE JACKETED CONDENSER

The apparatus (Fig. 22) is convenient to use when it is desired to distil at ordinary pressure or *in vacuo* a solid of high boiling point which would solidify in an ordinary condenser, e.g. α- or β-naphthol, or benzidine.

The condenser, made of steel tubing, consists of a 4-inch diameter outer jacket A, surrounding 4 or 6 tubes of ½-inch diameter expanded into the plates B. Plate C is in the form of a flat ring, while to plate D is attached the delivery tube from the cast-iron still H. The chamber E then serves as a receiving chamber for the vapours. Similarly, chamber F acts as a delivery chamber for the condensed liquid, which then flows out to a receiving flask in the form of an ordinary distilling flask at the exit tube I. The condenser is filled with water at the removable safety valve J, which has previously been set to "blow off" at any desired pressure, say, 80 lbs. per square inch. The safety valve is replaced on the reservoir K and the still firmly screwed to the condenser by the movable nut L.

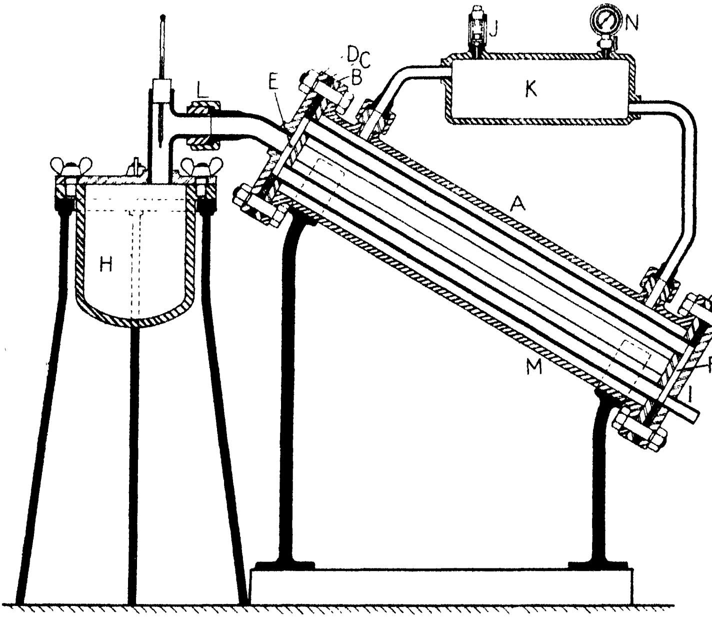


Fig. 22.

The substance to be distilled is placed in the still, and the lid screwed tight by means of the thumb screws, a suitable jointing material being used between lid and pot. The condenser is then heated by a Bunsen at M and when boiling point has been reached, pressure begins to be recorded on the pressure gauge N. The table below gives the temperatures corresponding to various pressures. When the required pressure has been registered on the pressure gauge, the still H is heated.

An electric vacuum pump is attached, through traps (see below), to the glass receiving flask. The substance distils when the boiling point is reached, as shown on the thermometer, and may solidify on entering the flask, but by the application of heat it can be delivered to the bulb of the flask before it solidifies.

Pressure lbs. sq. in.	Temperature °C.	Pressure lbs. sq. in.	Temperature °C.
0	100·0	30	134·4
5	108·4	40	141·1
10	115·0	50	147·7
15	121·1	60	152·7
20	126·1	70	157·7
25	130·5	80	162·2

Pumps.—The pressure obtainable by a good water pump is approximately the vapour pressure of water at the temperature (10–15 mms.). For pressures below this a mechanical pump must be employed, which in some cases reduces the pressure to less than 1 mm. Traps should be inserted between the mechanical pump and the apparatus so as to avoid contamination of the oil in the pump. A very efficient trap consists of a large test tube immersed in solid carbon dioxide in a vacuum flask (Fig. 22A). Mercury or oil diffusion pumps can be used to reinforce the effect of mechanical pump giving pressures down to 10^{-5} or 10^{-6} mm. of mercury.

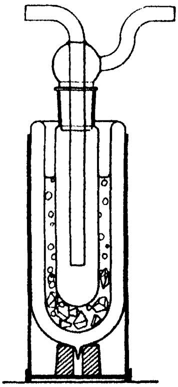


FIG. 22A.

Note.—The boiling points at atmospheric pressure of high boiling liquids are reducedby about 100° at 10–15 mms.

A Receiver for Distillation in a Current of Gas or under Reduced Pressure.—The receiver shown in Fig. 23 can be used to fractionate liquids in a current of gas or under reduced pressure.

The condensing liquid is first collected in A, the tap B being turned so as to connect tubes *b* and *c*. The gas current meanwhile passes from A into C, where it displaces air and prepares C for the reception of the fraction. The tubes *d* and *e* are shown as for a heavy gas, e.g. CO_2; for a light gas the relative depths to which they enter the flask must be reversed.

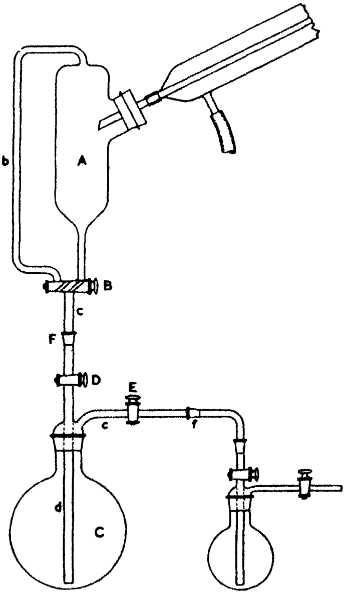


FIG. 23.

To isolate the fraction, B is turned to put *c* in communication with A. The liquid, helped by the gas current, passes into C, B is turned through

180°, and the tube *c* swept out by gas passing from *b*. Taps D and E are closed, and the ground-glass joint F opened. A new flask is put on at the joint, and when the air in it has been swept out, the next fraction can be collected. If it is necessary to collect the fractions at very short intervals, several flasks can be swept out simultaneously by connecting them in series to *f*. If glass joints are unnecessary throughout, pieces of rubber tubing can be used for connecting the flasks together.

As shown, the apparatus is adapted for the collection of very readily oxidisable liquids. In many cases it will not be necessary to have taps D and E ; and F can be replaced by a rubber connection. The apparatus can also be used for fractionation *in vacuo*. The vacuum pump is connected at *f*, and while a fraction is collecting, exhaustion takes place from *b* to *c*. The fraction, after being sucked into C by turning B through 180°, is isolated by closing B by a right-angle turn, closing E and disconnecting at *f*. Air or other gas can then be admitted through E, and F disconnected. If preferred, E can conveniently be a three-way tap. Another flask is then fitted on, and when exhausted, *b* and *c* are put in communication. To save time, several flasks can be kept exhausted by attaching them in series to *f* and to the pump (J. S. C. I., 41, 59 (T)).

SUBLIMATION

Sublimation is a process used for the purification of some compounds, especially when the quantity of substance is small. The first point to determine is that the substance does actually sublime. This is done by heating a little of the substance in a dry test tube held in an almost horizontal position. The sublimate, if any, will collect on the colder parts of the tube.

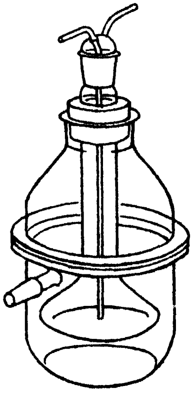


FIG. 24.

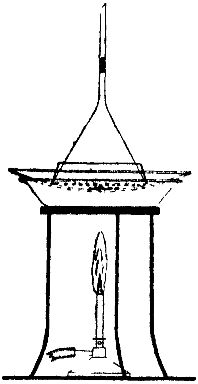


FIG 25.

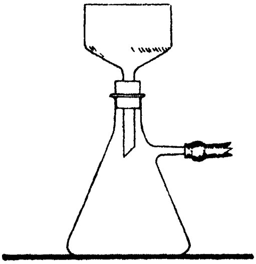


FIG. 26.

Several types of apparatus are available for sublimation. If the substance sublimes readily, the following apparatus is convenient. Fig. 24 shows a convenient form of apparatus. The crude material to be sublimed is placed in the bottom of the vessel. Cold water is circulated through the inner vessel while the apparatus is evacuated and partially immersed in a hot liquid bath. The sublimate collects on the under surface of the cold vessel which is then removed, after breaking the vacuum. In Fig. 25 the substance, on a clock glass, is covered with a pin-pricked paper which is surmounted by an inverted funnel having a loose plug of glass wool in the stem—heating being applied via a sandbath.

When the substance is difficult to sublime, it may be heated in a crucible placed in a round hole in a piece of asbestos board. The crucible is covered with a large clock-glass and a small flame is used so that the heat is directed only on to the bottom of the crucible.

FILTRATION (see also p. 11)

Filtration by means of suction is generally employed where possible in the operations of organic chemistry, since more rapid and more complete separation of the mother liquor is in this way effected. For this purpose several types of apparatus are in use. The Buchner funnel or sintered glass funnel and flask (Figs. 26, 26A) connected by a rubber stopper or flat rubber ring, the latter serving for various sizes of flasks and funnels, is used. The filter paper is cut to cover the perforations and if it is attacked by the liquor, cloth, such as flannel or cotton, might be used instead. For highly corrosive liquids, a layer of fibrous asbestos should be employed as filtering medium ; this is prepared by boiling asbestos wool with hydrochloric acid, then pouring on to the Buchner funnel and washing thoroughly with water while suction is applied. If necessary, the asbestos is then dried by washing successively with alcohol and ether. In all cases, the filtering medium, paper, asbestos, cotton, glass wool, should be moistened with the solvent used, and well pressed down on the perforated plate.

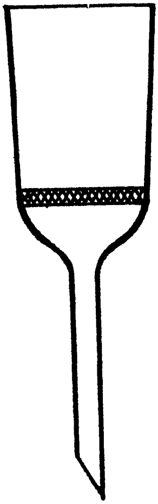


FIG. 26A.

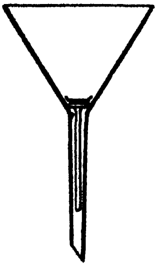


FIG. 27.

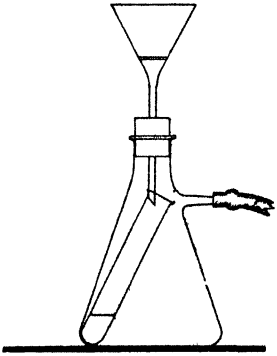


FIG. 28.

An ordinary funnel in which is placed a perforated disc (Fig. 28) may be used instead of the Buchner funnel, and this form is very convenient for separating small quantities of solids. The paper should be cut slightly larger than the disc, and should be carefully placed in position, and pressed down after moistening. Fig. 27 shows a similar arrangement in which a flattened glass rod is inserted through the stem of a glass filtering funnel.

For separating small quantities of liquid the apparatus (Fig. 28) is very suitable; the liquid is received in a test tube placed inside the Buchner flask.

The apparatus (Fig. 29) shows the most convenient arrangement when the filtrate is further required. It consists of a bell-jar cemented with vaseline to a ground-glass plate; the double-holed rubber stopper carries the filter funnel and a tube for connecting to a pump. The liquid is collected in a receiver placed inside the bell-jar. The great advantage of the apparatus is that any type of receiver may be employed. If the filter funnel has a long stem, it may be used in conjunction with a hot-water jacket (Fig. 3) or an ice jacket (Fig. 4).

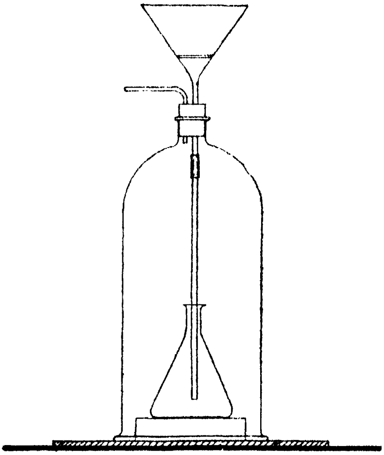


FIG. 29.

In order to separate as much liquid as possible from a large bulk of solid, the latter, after being filtered in the ordinary way by means of a Buchner funnel and well pressed, is removed from the funnel, placed in a stout piece of cloth and tightly wrapped. It is then placed in a press of the ledger type and pressure gradually applied.

DECOLOURISATION

It often happens that the compound prepared in a particular preparation is discoloured; various methods are used to remove traces of colouring and of tarry matter. The most common is to boil up the substance in solution with activated charcoal—added in the cold—and then to filter and recover the compound from the filtrate by crystallisation or distillation. Very little of good decolorising carbon is necessary as a rule, and that may be revivified by impregnating with a concentrated zinc chloride solution, igniting, and washing with acid. Decolourising carbon, which contains phosphates, should be boiled with hydrochloric acid, filtered, washed and dried before use. Sometimes a solution remains cloudy after filtration. As a rule this cloudiness can be removed by adding very small equivalent quantities of solutions of calcium chloride and sodium phosphate. The calcium phosphate precipitated usually brings down all gelatinous matter and may then be removed by filtration.

Discoloration is sometimes due to oxidation, and the colouring matter may often be removed by passing SO_2 gas through the solution, always provided that this has no action on the substance.

Filter-aids.—Neutral acid-washed diatomaceous earths (e.g. celite or supercel) can be used to remove turbidity, and to assist filtration.

Centrifuges.—High speed centrifuges (up to 4500 r.p.m.) are now available for laboratory use in clarifying solutions and breaking emulsions.

SALTING OUT

Some substances which are soluble in water are not soluble or only slightly soluble in solutions of certain salts, such as sodium chloride, calcium chloride, sodium acetate, sodium sulphate. The salt may be added in the solid form or as a saturated solution. By this means alcohol and acetone can be separated from their solutions in water.

The process is used very largely on the technical scale for the separation of dyestuffs (see pp. 387 to 400).

EXTRACTION OF SOLIDS

When it is required to separate a solid from an impurity, it is desirable to carry out the extraction in a Soxhlet apparatus a sketch of which is shown (Fig. 30). The substance to be extracted is placed in a paper thimble A which is set in position in the main Soxhlet tube, a loose plug of cotton wool being placed in the top of the thimble. The Soxhlet is attached to a flask B containing a small amount of a solvent; the solvent chosen should be such that either the desired substance or the impurity is insoluble, or nearly so. A condenser is attached to the Soxhlet tube; the ball condenser C shown in sketch is the most convenient.

When the solvent is boiled, the vapour passes through opening D to the condenser, from which liquid drops back to the thimble. When this liquid reaches the top of the side tube E, it automatically syphons back into the flask B with the extracted matter in solution. The process is continuous.

It is advisable to use a minimum quantity of solvent at the beginning and, if necessary, to add more solvent through the condenser. More rapid extraction can be brought about if the substance is intimately mixed with some inert substance, such as glass or sand.

When the extraction is judged to be complete, the Soxhlet is removed and the substance crystallised from the solution remaining in the flask. For modifications, see J. S. C. I., 43, 281 ; 50, 144.

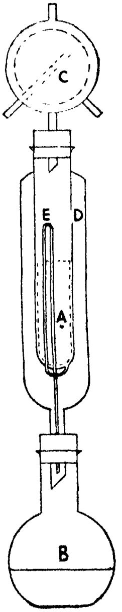


FIG. 30.

SEPARATION OF IMMISCIBLE LIQUIDS

Funnels of the types shown in Fig. 31 are used. The liquids to be separated are run into the funnel, and after standing for some time the stopper at the top is removed and the more dense liquid is run off through the tap at the bottom. If the upper layer is required, it is poured out through the top of the funnel after running off the bottom layer ; this is to prevent contamination with the liquid in the stem and tap of the funnel. In all cases a funnel of convenient size should be chosen.

If the volume of liquids is small, separation can be effected by the use of a small pipette, to which is attached a length of rubber tubing ; the rubber tubing is held in the mouth, gentle suction is applied, and the eye kept on a level with the common surface of the liquids. When separation is difficult due to emulsion formation a centrifuge may be helpful (see p. 38).

Separation by Extraction.—Separating funnels are again used for this purpose. The substance to be extracted is generally in solution or suspension in water. A solvent which is immiscible with water and in which the substance is soluble is added—in small quantities at first. The funnel is stoppered and agitated, holding the tap and stopper closed, after which it is set aside in a vertical position until the liquids separate. Separation is then effected as above. The solvent most commonly employed is ether, but benzene, chloroform, ligroin and amyl alcohol are used in special circumstances.

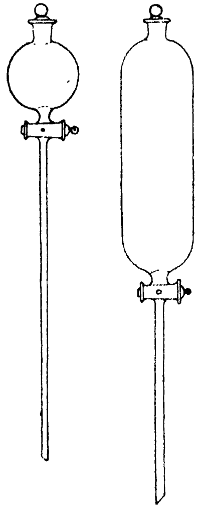


FIG. 31.

In all cases extraction should be carried out more than once, the extracts being added together. The amount of substance which goes into solution in ether, etc., depends on the distribution coefficient, that is, the ratio of the concentrations in the two solvents after equilibrium is attained. This ratio is constant for any given temperature, provided the molecular weight of the solute does not vary in either solvent. It follows then that extraction may have to be repeated several times, and also that it is more efficient to extract a number of times with successive small quantities of solvent rather than once with a large quantity.

When a quantity of the substance separates from the solution as an oil, this oil should be separated before extraction is attempted.

EXTRACTION WITH ETHER

In extraction with ether, the following points should be noticed :—

1. All burners in the immediate vicinity should be extinguished.
2. After shaking, the funnel should be inverted and the pressure released by gradually opening the stopcock.
3. If an emulsion persists after standing, this may frequently be destroyed by agitating the ethereal layer with a glass rod. Addition of a few drops of alcohol is sometimes effective. In special cases filtration may

be useful. If the funnel be held in a stream of warm water for a time, separation may be facilitated. See use of centrifuge, p. 38.

4. Extraction is complete when a sample of the ether layer evaporated to dryness leaves no residue.

5. Ether is soluble in water to the extent of 8%. If the aqueous volume to be extracted is large, it should be saturated with common salt, in which solution ether is much less soluble.

6. Water is soluble in ether to the extent of 1·5%. It follows, therefore, that the ether extract must be dried (see p. 41) before removing the ether by evaporation.

7. Ether is generally removed by distillation (*Caution*, see p. 21). A moderate-sized flask should be used and more solution added from time to time. The apparatus (Fig. 32) enables the additions to be made without interruption of the distillation. The flask is fitted with a two-holed stopper carrying a dropping funnel and a glass tube. By means of a piece of rubber tubing and a second short piece of glass tubing inserted through a cork, the top of the funnel is connected through the first piece of glass tubing with the interior of the flask; the rubber tubing on this connection carries a spring clip. The ethereal solution—a portion at a time—is placed in the funnel and the cork inserted in the neck of the funnel. The stopcock of the funnel and the spring clip are then opened simultaneously, and the ether flows into the flask without interruption, since the pressure above the ether in the funnel and the pressure inside the flask have been equalised by the opening of the spring clip. When the ether has run in, the tap and the clip are closed.

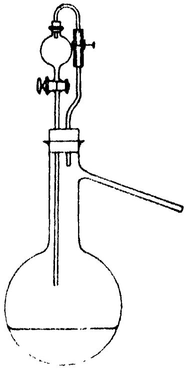


FIG. 32.

8. Salts are generally insoluble in ether. Ferric chloride, mercuric chloride, mercuric iodide, stannous chloride and chromic anhydride, however, are fairly soluble.

DRYING

Drying of Solids.—(*a*) *At Ordinary Temperature.*—When the solid is insoluble in a volatile solvent, such as ether or petroleum ether (40°–60°), and this solvent is miscible with the solvent from which the solid was crystallised, drying may be greatly facilitated by washing the substance while still on the filter with such a volatile solvent. The usual method of drying at ordinary temperature consists in spreading the solid on several layers of filter paper or on a porous plate, and leaving until dry. It is necessary, however, to protect the solid from dust contamination by covering with filter paper or watch-glass in such a manner that free access of air is permitted. The drying may be more quickly carried out by placing the solid on a porous tile in a vacuum desiccator.

Desiccators.—These are two types, the ordinary and the vacuum (see Fig. 33). The drying in the latter is generally 6–7 times quicker than in the former. The desiccator is charged, according to the nature of the substance to be absorbed, with one or other of the following substances.

Conc. sulphuric acid : to absorb water, basic substances.
(Acid containing 18 gms. barium sulphate per litre acts as its own indicator of unfitness for drying.)
Granular calcium chloride : to absorb water, alcohols, some basic substances.
Solid sodium or potassium hydroxide : to absorb water, acids, phenols, alcohols, esters.
Quicklime : to absorb water, acids.
Soda lime : to absorb water, acids.
Paraffin wax : to absorb carbon disulphide, ether, chloroform, benzene.
Absorbent cotton (previously dried in steam oven) : to absorb water.

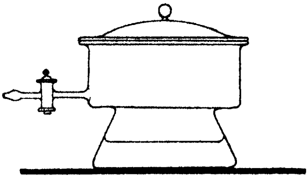


Fig. 33.

It is obvious from the foregoing list that impurities as well as solvent may be removed from a solution by exposure in a desiccator containing a suitable absorbent. It is essential that the absorbent does not react with the substance to be dried.

N.B.—A suction flask should always be inserted between a vacuum desiccator and a water pump when the latter is used, as slight variations in water pressure may result in water being sucked back into the desiccator. Desiccators when under vacuum should be kept in a box or wire cage to protect operator in case of implosion.

(*b*) *At Higher Temperature.*—If it is desired to dry a solid at a temperature higher than ordinary, a test should first be made with a small portion. This is necessary since many substances decompose at relatively low temperatures and *such temperatures should be noted.* Moreover, the presence of slight impurities or of solvent may considerably lower the melting point of the solid. Other changes—loss of solvent of crystallisation, etc.—may take place on heating, and these also should be noted.

For drying at temperatures up to 100°, the water bath or steam oven is generally used. For drying at higher temperatures the air oven is employed, but here a thermometer should be inserted and particular care taken that the substance is not over-heated. A very convenient form of drying apparatus is the toluene bath (p. 43).

The drying gun (Fig. 33A) is suitable for removing water or solvent from a solid under vacuum. The heating medium is the vapour of a liquid of suitable boiling point placed in flask (*a*) and kept refluxing under the condenser (*b*). The flask (*c*) contains the drying medium.

The addition of benzene, toluene, or xylene to a solid and subsequent distillation of the solvent is a useful method of removing and estimating moisture in a non-volatile solid. This procedure may be more efficient than storage over P_2O_5 in a desiccator. The absence of cloudiness in the distillate indicates absence of water.

Drying of Liquids.—(*a*) *At Ordinary Temperature.*—Liquids are usually dried by the addition of some solid dehydrating agent, such as granular calcium chloride, solid caustic potash or soda, anhydrous sodium sulphate, anhydrous potassium carbonate, anhydrous cupric sulphate, phosphorus pentoxide, metallic sodium. It is essential that the drying agent should have no action on the liquid, or on any substance dissolved in it, and great care should be exercised in the choice of a drying agent. For example, calcium chloride should not be used for drying alcohols or amines. Caustic potash or soda should not be employed for drying acids, phenols, esters, certain halides, etc. The minimum quantity of drying agent should be used, otherwise liquid is lost by absorption. After standing some time, the liquid is separated by decantation or filtration.

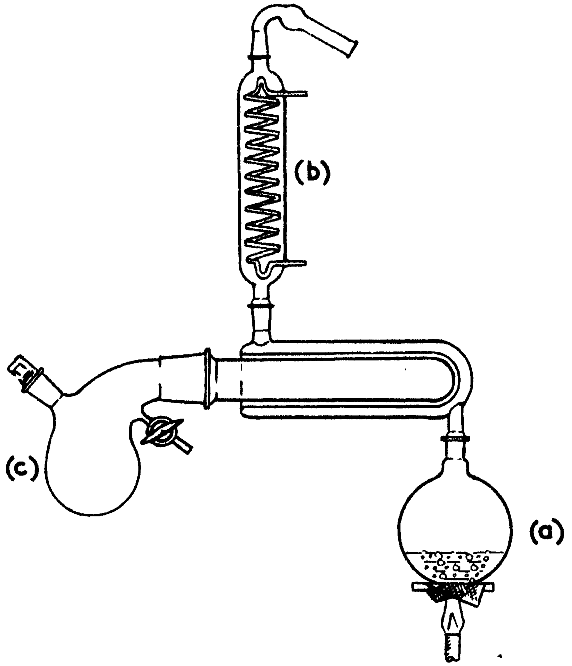


Fig. 33A.

The drying of ethereal solutions is an operation frequently met with. In most cases it is advisable to dry an ethereal extract before evaporating off the ether. Again, to dry a moist solid, it is often convenient to dissolve it in ether and to dry the ethereal solution with a dehydrating agent. The dry solid is then obtained by evaporation. For the drying of organic liquids by dialysis, see U.S.P., 1,885,393.

(*b*) *At Higher Temperatures.*—Dehydrating agents are seldom employed at elevated temperatures and are only effective when the liquid has a high boiling point and is not volatile in steam.

BATHS

Baths are used for heating, drying, etc.; the heating can thus be carried out more uniformly than is possible with a direct flame. A judicious selection of the type of bath required for any operation should be made—an air bath should not be used if a water bath suits the purpose. In all cases a means of ascertaining the temperature should be provided, either by taking the temperature of the bath, or of the substance heated on the bath.

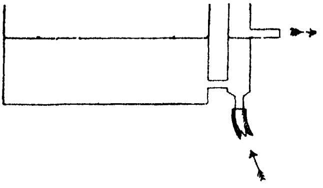


FIG. 34.

Water Bath.—This is employed for heating or drying up to 100°. For temperatures below 100° the vessel should be immersed in the water; for 100° the vessel should be so far immersed as to be largely surrounded by steam. When a water bath is to be used for many hours, a constant-level arrangement is attached (Fig. 34).

Salt Solutions.—Temperatures above 100° can be attained by the addition of salts to the water. The boiling points of a few saturated solutions are appended :

	B.P.
Sodium chloride	109°
Magnesium sulphate	108°
Potassium nitrate	116°
Sodium nitrate	121°
Calcium chloride	180°

Toluene Bath (Fig. 35).—This bath consists of a double-walled enclosure, access to which is obtained by a hinged door carrying a stout rubber joint. The door is fastened by thumb-screws. Any suitable liquid can be placed in the outer jacket to which is attached a condenser; the liquid, however, most generally used is toluene (B.P. 110°). The inner compartment is fitted with an exit tube carrying a vacuum gauge, and this may be attached to a vacuum pump. This offers a very convenient method of drying substances at a temperature slightly above 100° and under reduced pressure.

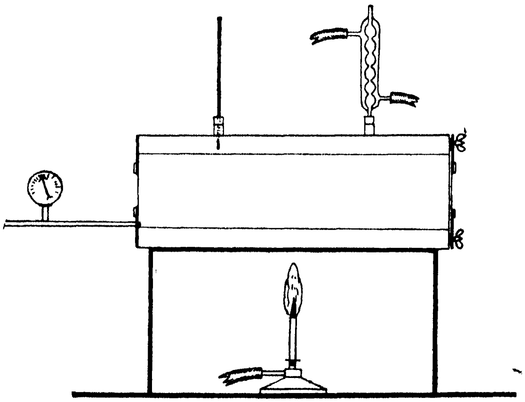


FIG. 35.

Air Bath.—A convenient form of air bath is made of sheet iron, and completely lined on the outside with asbestos. Air ovens are generally used for temperatures above 100°. In no case should the substance be placed on the lower shelf; the bulb of the thermometer should reach close to the shelf on which the substance is placed.

Sand Bath.—This form of bath is used for temperatures well above 100°. A thermometer should always be placed in the substance being heated. It is important that the layer of sand should only be just thick enough to protect the vessel from excessive heat. Hot plates and electric heaters are also available (see Fig. 35A).

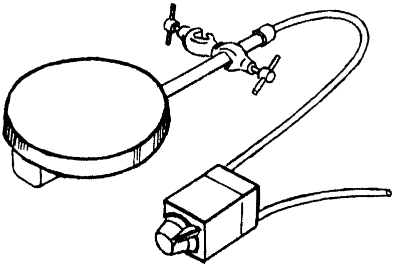


FIG. 35A.

Oil Bath.—Suitable oils may be used such as higher boiling paraffins, melted paraffin wax, glycerine, etc. The oil should not be heated to its flash point, and the surface of oil exposed should be as small as possible.

Graphite Baths.—These are sometimes used in place of oil baths.

Metal Bath.—This type of bath is the most suitable for heating to high temperatures. Before heating, the vessel should be held in a luminous flame until covered with a deposit of carbon which prevents the fused metal from adhering to the flask ; it also renders the vessel less liable to crack.

The following alloys may be used :—

Bi (4), **Cd** (1), **Pb** (2), **Sn** (1), M.P., 65° ; **Bi** (3), **Pb** (2), **Sn** (2), M.P., 95° ; **Pb** (37), **Sn** (63), M.P., 183°.

The last-mentioned alloy, which is the eutectic mixture of lead and tin, is very convenient for many operations (see p. 213). When used in a pot of the type shown on p. 214 oxidation of the metal—a drawback attending the use of metal baths—is largely overcome.

MECHANICAL AGITATION

The importance of mechanical agitation cannot be over-estimated. In some cases satisfactory yields cannot be obtained unless efficient agitation is provided ; mechanical agitation should be used, therefore, whenever continuous agitation is essential. A suitable vessel should first be chosen, and an agitator made, usually of glass rod, to suit this particular vessel. The relative densities of the substances to be mixed must be borne in mind ; obviously it will require much more vigorous agitation to sulphonate benzene, or to reduce nitrobenzene with, say, iron, than to fuse a sulphonic acid with caustic soda—due to the much greater differences in the specific gravities of the reacting substances. The propeller type of agitator is always serviceable provided the speed is high. The driving force may be electric or hydraulic, but various simple devices can be adopted depending on the nature of the chemical reaction. For example, air, steam or other suitable gas may be passed into the mixture.

Where active boiling is taking place in a mixture, mechanical agitation is usually unnecessary.

Fig. 36 shows a suitable direct-drive electrically-operated agitator, showing a mercury seal to prevent exit of vapours, and a type of glass agitator in common use.

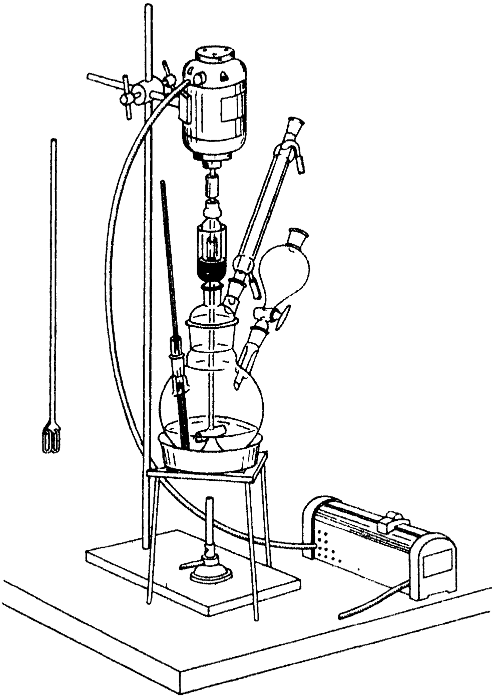


Fig. 36.

Sulphonation Pot.—The most satisfactory method, however, of using mechanical agitation is in conjunction with a specially-constructed piece of apparatus. Various types can now be procured, and some are very effective. Fig. 37 shows one such. It consists of a cast-iron pot with a lid carrying the brass bearing and gear wheels of the central shafts. The large driving pulley drives the outer shaft in one direction and the inner shaft in the opposite direction, a suitable form of " blade " being attached to each. The lid is attached to the pot by thumb-screws, suitable jointing matter being used, such as rubber. Openings are provided in the lid for reflux condenser, thermometer, and addition tube. The apparatus, which may be driven from an electric motor, is admirably suited for sulphonations, nitrations, and reductions. When such an apparatus cannot be obtained the apparatus (Fig. 38) in glass is recommended.

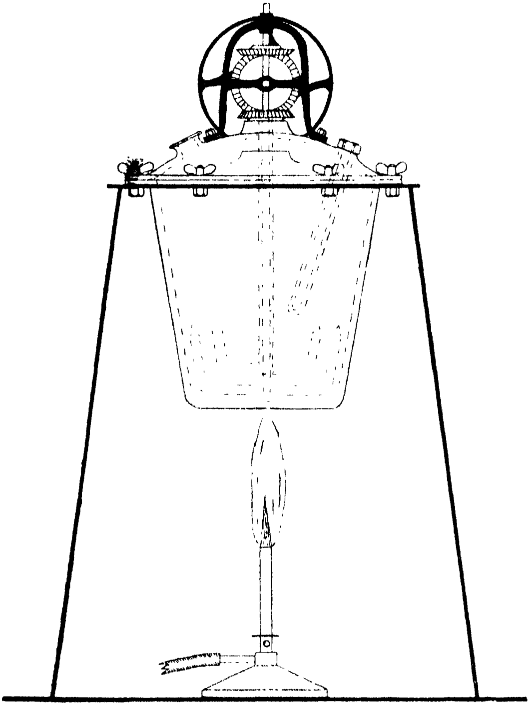


FIG. 37.

HEATING UNDER PRESSURE

When a mixture of substances is heated in an enclosed space no volatile matter can escape, and hence, at a certain period in the heating, pressure begins to develop. Substances or solutions may thus be heated to a temperature above the boiling point of any or all of them without incurring the loss of reacting substances or reaction products; and the method has the advantage that many reactions which cannot be brought about by boiling substances in open vessels can be easily brought about by heating under pressures above atmospheric. If it is desired to heat two substances under pressure, but not to a temperature above the boiling point of either, a third

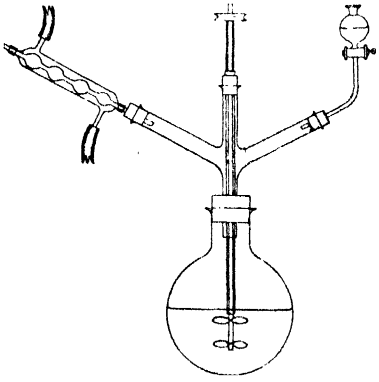


FIG. 38.

substance of lower boiling point which has no chemical action on either of them is introduced.

Heating under pressure is generally done in—(*a*) Sealed Tubes, or (*b*) Autoclaves.

(*a*) **Sealed Tubes.**—As only small quantities of substance can be dealt with, the method is only applicable for small scale experiments or quantitative work (e.g. Estimation of Halogens—p. 476). Generally, soft glass tubes bout 50 cms. along, 18–20 mms. outside diameter, and walls 2·5–3 mms. thick, are used, but if the contents attack soft glass, or if large quantities of gas are evolved on heating, or if the temperature of heating is high, tubes of difficultly fusible potash glass should be employed, since these are more resistant to chemical action and do not crack so readily. As glass deteriorates with age, a piece of new glass should be selected for sealed tube work. A suitable length is cut (see p. 50), thoroughly washed, and after being allowed to drain for some time is dried by warming with a moving flame while a current of air is blown through it.

To seal one end of the tube, about 2 inches of the tube at this end is heated by revolving it in the smoky flame of a blowpipe for a few minutes. The blast is then turned on slowly, and the tube, while held in one hand at an angle of 45°, heated at the end, until softening takes place, when a previously warmed glass rod held in the other hand is fused on to it. The blast flame is adjusted so that it will heat a zone of glass about as broad as the diameter of the tube to be sealed, and is directed at a point about 3 cms. from the end of the tube, which is slowly brought into the flame with constant rotation. When the glass begins to thicken the ends are slowly drawn out, care being taken not to extend the softened glass too much, but to allow the sides to fall together, as shown at A (Fig. 39). When this occurs, the narrow part is heated till it melts and the ends pulled asunder. The closed end should present the appearance shown at D. If a considerable mass of glass be left at *d*, it may be removed by heating it to redness, touching it with the pointed end of a cold glass tube, to which it will adhere, and by which it may be pulled away. Any blob of glass remaining is heated in a small blowpipe flame, and by gently blowing with the mouth into the open end of the tube, and re-heating and blowing again, the blob can be removed, and finally, by using a rather

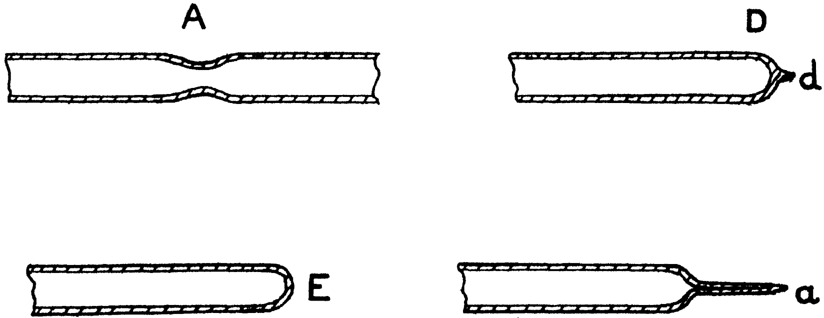


Fig. 39.

larger flame, heating and blowing alternately, the end is neatly rounded —shown at E. After cooling slightly the hot end of the tube is annealed by holding it for a few minutes in a luminous flame.

Hard glass is much more easily worked in the oxygen-coal gas flame, obtained by attaching a cylinder of oxygen in place of the air blast to the lamp.

Filling the Tube.—Since the tube is afterwards sealed at the open end, it is necessary when filling the tube to take care that none of the ingredients come into contact with it near that end. The tube should be clamped in a vertical position beside the working bench, and a funnel tube, having a stem as wide as the tube will admit, is inserted in the open end; through this the substances are added. In analytical work (see Estimation of Halogens) the weighed substance should be introduced in a container of its own. When fuming liquids are employed (see Preparation of Paranitrobenzyl Bromide) these should be placed in test tubes stoppered with glass wool or asbestos; obnoxious fumes during the sealing process are thus largely avoided. When withdrawing the funnel tube, care is taken to avoid bringing it into contact with the walls of the tube. The amount of substance which may be introduced depends on the conditions; the tube should never be more than half full, and if much gaseous product is formed, or if the temperature of heating be high, a lesser quantity should be introduced.

Sealing.—The tube is held at an angle of 45°, and in a manner already described; the open end is warmed in a smoky flame, then heated to softening, and a glass rod sealed on to it. Likewise, as described before, the tube is heated about 3 cms. from the end while rotating it in a blast flame. The glass is evenly heated and not drawn out, but when the apparent inside diameter of the tube is reduced to about 3 mms., the tube is quickly withdrawn from the flame and a capillary formed by slowly drawing out the thickened part (Fig. 39). In order to secure a thick end to the point of the capillary *a*, about 2 cms. of the tube at the shoulder is warmed a little at the moment of finally sealing it; the contraction of the air in the tube, in consequence of its cooling, ensures the glass at *a* running together to a solid end when it is melted in the flame. If it is desired to collect a gas produced during the chemical reaction, the capillary is made several inches long, and is bent into the form of a delivery tube. It is then possible to break the tip of this under a cylinder in a trough of liquid.

Sealing of Hard Glass.—For this a slightly different method of sealing is employed. As soon as the glass is sufficiently soft, it is not thickened, but is drawn out at once to a wide capillary. By directing the flame on the shoulder of the tube and continuing to draw out the capillary is then lengthened to about 3 cms. It is then thickened by revolving in the flame and finally sealed off. The sealing of hard glass requires at least a first-class blowpipe; and the sealing may be facilitated by placing a brick or tile near the flame in such a position that the heat is reflected on to the tube.

As soon as the tube is sealed and annealed, it is clamped in a vertical position, with capillary uppermost, and left to cool in a place where if it bursts no damage will accrue.

Tube Furnace or Bomb Furnace.—When cold, the tube is transferred to the removable metallic cylinder of the tube furnace (Fig. 40). The cap of the cylinder is screwed on and the latter placed in position in the furnace. Various forms of furnace are used: the common forms are heated by a series of pinhole gas-jets, and are easily regulated. The removable cylinder is not supplied with all furnaces, but it is advisable to have it for the following reasons: (*a*) The furnace may be approached without fear of glass splinters, and (*b*) in case the tube bursts, the glass fragments and contents (of the sealed tube) remaining in the cylinder can be easily removed.

When a removable cylinder with screw cap is not available, the sealed tube is placed in the fixed cylinder of the furnace, the capillary end pointing towards a wall of the furnace room so that no damage will accrue in case of an explosion.

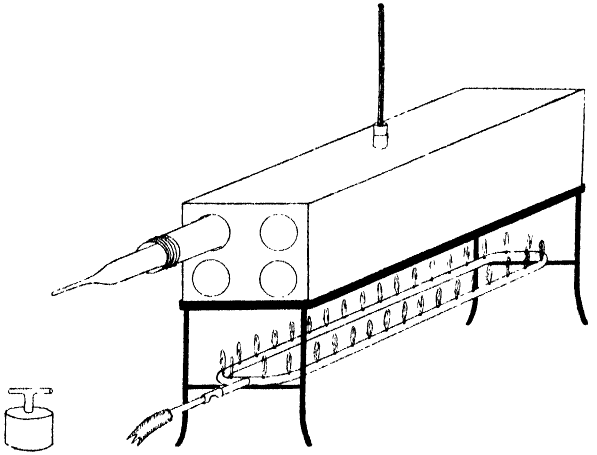


FIG. 40.

At the commencement of the heating, small flames are used and the temperature raised gradually to the desired point. The temperature is indicated by a thermometer, inserted through a cork in the opening at the top of the furnace, the bulb of the thermometer being placed level with the iron tube. The danger of the bursting of sealed tubes may be diminished in many cases by interrupting the heating after a certain length of time, opening the capillary when the tube has completely cooled, and allowing the generated gases to escape. The tube is then resealed and heated again. Or, to take an example of bromination, one-half the necessary quantity of bromine may be added at first, the tube sealed and heated to the desired temperature; the tube is then allowed to cool, after which the capillary is opened, the second instalment of bromine added through a long capillary tube, and the tube after being resealed is heated as before.

Opening Sealed Tubes.—The greatest possible care must be observed in handling an unopened tube. It must never be removed from its protecting case for examination or for any other purpose. It must not be opened until perfectly cold, and when being opened it is held in such a position that no one can be injured should it burst.

When cold, the protecting case of iron is withdrawn from the furnace and held in one hand. The cap (if present) is unscrewed, and while the iron tube is held in a slightly inclined position so that the capillary is somewhat higher than the other end, the capillary is made to project beyond the iron case by giving the cylinder a slight jerk. The part of the iron cylinder near the open end and which is gripped with the hand is wrapped round with a cloth. The extreme end of the capillary is then gradually heated in a Bunsen flame. If pressure exists inside, the end of the capillary is blown open on softening, provided there is no obstruction in the capillary. If there is obstruction it may be removed by heating.

Under certain conditions, as, for instance, when the tube contains an explosive mixture of gases (which sometimes happens when phosphorus and hydriodic acid are used) or when it is desired to collect the gaseous products, the end of the capillary is carefully broken off with pincers or tongs—in the latter case inside a piece of pressure tubing connected with a suitable gas receiver.

After the capillary is opened, the tube is removed from the iron case, and the conical end broken off in the following manner. A deep file mark is made round the tube about 1 cm. below the shoulder, and the scratch is touched with the pointed end of a drawn-out glass rod which has been previously heated to redness in a blowpipe flame. In the majority of cases a crack forms at the file mark, and this may be led round the tube by touching the glass immediately in front of the crack with the heated point of the glass rod. If the thick end of a glass rod is used in these operations, the crack may form longitudinally on the tube. A piece of wire, bent to the shape of the tube, and heated to redness, may be employed in place of the heated glass rod.

Another method which is not so liable to cause splintering at the cut is the following. The file mark is made as before. Two pieces of wet filter paper are rolled round the tube, one on each side of the file mark and about 0·5 cm. apart. The space between the papers is then heated by gradually bringing it transversely into a bat's-wing flame, the tube being rotated the while. If the tube does not sever at once, it is given a few turns in the flame, after which the heated portion is moistened with a few drops of water, when the breaking off follows with certainty. In analytical work great care should be taken in opening as it is important to avoid the mixing of fragments of glass with the contents of the tube. The tube is then emptied.

(*b*) **Autoclaves.**—These are closed vessels made of iron, bronze or copper. Those in common use are made from cast steel, and hence are capable of standing high pressure. Such vessels are not suited for heating mixtures of a resultant acid reaction, but may be used for mixtures which are of neutral or alkaline reaction. When acidic substances are being dealt with, autoclaves covered on the interior with a resistant enamel, or provided with an enamelled cast iron or resistant metal liner (e.g. Monel), for acid and alkali resistance, respectively, are used. Various alloy steels are available, those of the austenitic (stainless steel) type being specially suitable where resistance to hydrogen is also desired. A good steel for general purpose contains 2·25% Ni, 0·8% Mo, 0·4% Cr. Fig. 41 represents a form of autoclave which is commonly used for experimental purposes. The body B of the autoclave is immersed in an oil or metal bath. Along the flange of the body there runs a circular groove of rectangular section which is filled with lead (molten lead run in and allowed to solidify). On the lower surface of the flange of the lid there is a projecting ring which fits neatly into the lead-filled groove, and when the screws between the body and lid are tightened, a pressure-tight joint is formed at the lead ring. In order to secure a proper joint, judicious tightening of the screws (these should run easily at first) is necessary. To begin with, one nut is screwed home with the hand, the nut diametrically opposite is similarly treated, these are then alternately given a few turns with a wrench until they are moderately tight. The intervening nuts are then screwed home, each one a little at a time so as to maintain as far as possible a uniform pressure over the whole surface of the lead ring. This done, a further tightening—which may be repeated a few times—is given to all the nuts, going round them in circular fashion. During the heating, the nuts should be tested from time to time, and tightened if necessary. The lid of the

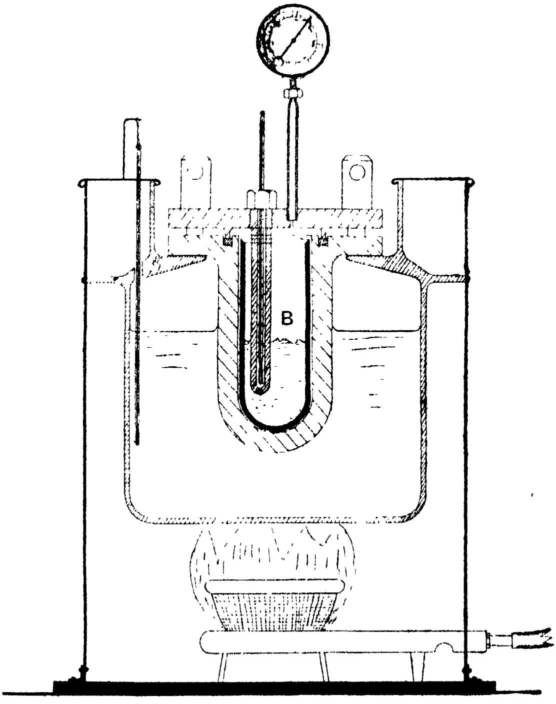


FIG. 41.

autoclave is provided with two openings—one for a thermometer tube, and another for a pressure gauge, each of which is fixed by a screw pressure-tight joint; sometimes there is a third opening for a safety valve, but with a tested autoclave bought from a reliable firm a safety valve is unnecessary, and often an encumbrance. Such autoclaves should, however, be frequently tested by engineers. A tube may be provided with suitable valve for releasing the internal pressure when required. If such a tube dips into the liquid in the autoclave, samples can be withdrawn by carefully opening the valve while the autoclave is under pressure. Autoclaves may be emptied after completion of a reaction by a similar arrangement, when the pressure has fallen to, say, 4 or 5 atmospheres.

During the operation of heating, oil or mercury sufficient to cover the bulb of a thermometer is placed in the thermometer tube. Autoclaves are made in various sizes with capacities ranging from half a litre up to a few thousand litres. Those which are provided with stirring gear are more efficient in operation, and details may be obtained from the catalogues of well-known manufacturers. Types in which agitation is provided by mechanical rocking or magnetically-operated plunger are also available. The usual limits of temperature and pressure are about 500° C. and 200 atmospheres, and the greatest charge should not be more than about 75% of the volume of the vessel. Temperature of the outer bath, in which a thermometer is kept immersed, should be about 30° higher than the internal temperature. The screws must not be loosened so long as there is any pressure indicated on the gauge. When a charge contains ammonia or develops ammonia on heating, a manometer or gauge fitted with an iron and not with a bronze tube must be used, since ammonia vapours rapidly destroy copper or bronze tubes.

Pressure Bottles.—Glass beer bottles are generally tested hydraulically to 500 lbs. pressure and therefore make suitable vessels in which to carry out reactions at moderate pressures and temperatures. If a cork is used it should be wired in position after inserting the reactants; if it is a screw-top stopper it is desirable to coat the rubber washer with graphite. The bottle may be placed in a bucket of water and covered with a duster. The water (or a solution of salt) may then be heated to the desired temperature.

DENSITY OF LIQUIDS

The density of a liquid is most easily determined by means of vessels known as pyknometers, the volume of which need not exceed 1 c.c. Perkin's modification (Fig. 42) of the Sprengel pyknometer is well adapted for small quantities of liquid and also for volatile liquids. The apparatus which usually has a volume of 2–10 c.cs. consists of a U-tube, the limbs of which are drawn out to capillaries, and bent as shown. On limb A a small bulb is blown, and below this a ring is etched round the capillary. The ends of the capillaries are fitted with loose glass caps.

The apparatus is cleaned and dried by washing successively with water, alcohol, and ether, and then drawing air through the tube. The apparatus is first weighed empty, being suspended from the beam of a balance by a piece of platinum wire. Liquid is then drawn into the vessel through B until the bulb on A is half full. The apparatus is immersed in a bath at constant temperature—ice and water serve for 0°, while a thermostat should be used for higher temperatures. After standing in the bath for some time, the apparatus is inclined until limb B assumes a horizontal position; a piece of filter paper applied to the end of this limb is allowed to absorb liquid until the meniscus on limb B sinks to the etched mark. The apparatus is then returned to a vertical position, the glass caps are replaced on the limbs, and after removing from the bath the whole is carefully dried with a clean cloth and weighed. Afterwards the apparatus is cleaned and dried, and the operation repeated, using distilled water.

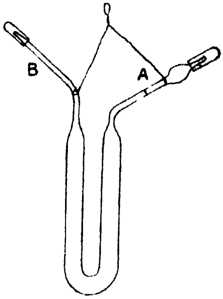


FIG. 42.

If both these operations are carried out at the same temperature—

$$\text{The approximate density} = \frac{W}{W_1}$$

where W = weight of liquid,

and W_1 = weight of water.

$$\text{The absolute density } \left(D_4^t\right) = \frac{W}{W_1} \times D,$$

where D = density of water at 4°,

and t = temperature of operations.

THE POLARIMETER

The polarimeter is used for determining the specific rotations of optically active substances and also for determining concentrations of solutions of optically active substances of known specific rotation.

The polarimeter consists of two Nicol prisms N and N_1 (Fig. 43) set at a distance from one another and on a common axis. N_1 is the polariser and N the analyser. The polarimeter tube T, containing a definite length —usually 10 or 20 cms.—of liquid is placed between the two Nicols. Monochromatic light must be used, generally that from a sodium flame or from a mercury vapour lamp being employed. The light from F when using a sodium flame passes first through a bichromate cell C in order to give the pure sodium D light, then through a lens to the polariser; when using a mercury arc, the light is passed through a filter so as to give the green line ($546{\cdot}1 m\mu$). The K.B.B. Atmospheric Burner (p. 56) fitted

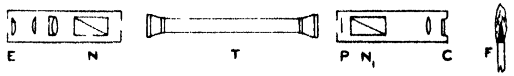


FIG. 43.

with a hood and filter is a suitable means of supplying mercury vapour light. In the Laurent polarimeter a thin quartz plate P is inserted to cover half the field. In the Lippich type a small Nicol prism or two Nicol prisms are used instead of a quartz plate to cover part of the field ; and this instrument possesses the advantage that it can be used with light of any wave length.

Light vibrating in only one plane passes through the polarimeter tube to the analyser N, which can be rotated about the main axis. The eyepiece at E consists of a system of lenses for focussing.

The flame produced from common salt or a sodium lamp is adjusted to give a maximum of light, the tube T being removed for the time being. The polariser N_1 is fixed in position. The illuminated split disc is then focussed from the eyepiece E, and the analyser rotated until the whole field is of uniform intensity. The reading as indicated on a circular disc fitted with a vernier attached to the eyepiece is taken as the zero reading. This reading should be determined before every experiment. The substance of which the specific rotation is to be determined is placed in a clean dry polarimeter tube in the form of liquid or of solution so as to completely fill the tube. The tube is then placed in position in the polarimeter ; the analyser is again turned until the intensity of illumination on each half of the disc is equal. The angle is again read on the scale, and this reading, minus the zero reading, gives the angle of rotation, α_D. The temperature at which the observation is made should be noted ; in some cases a jacketed polarimeter tube, through which water at a definite temperature is circulated, is used. The specific rotation—$\left[\alpha\right]_D^t$—at temperature t of a pure liquid is calculated from the formula :—

$$\left[\alpha\right]_D^t = \frac{\alpha}{ld}$$

α = angle of rotation for sodium D line.
l = length in decimetres of liquid in polarimeter tube.
d = density of liquid at $t°$.

The specific rotation of an optically active compound in a pure solvent may be calculated from the formula :

$$\left[\alpha\right]_D^t = \frac{100\alpha}{lc} \quad \text{or} \quad \frac{100\alpha}{ldp}.$$

c = gms. of active compound in 100 c.cs. of solution.
p = percentage of solute by weight.

If the substance turns the plane of polarisation to the right, i.e. clockwise, it is said to be dextro-rotatory, and if to the left, laevo-rotatory (see Findlay, *Practical Physical Chemistry*).

CATALYTIC REDUCTION

The apparatus (Fig. 44) supported by an iron frame (*fff*) on a baseboard (*b*) and connected by the system of stout glass tubing (*ggg*), consists of hydrogenation flask A (500–1000 c.cs.), graduated hydrogen reservoirs B, 500 c.cs. and C, 100 c.cs., manometer dipping into mercury reservoir (D) and system for inlet at (l) of hydrogen from a cylinder of this gas. The water reservoirs (E and F) serve for the expulsion of gas from B and C prior to filling these with hydrogen and also for the adjustment of levels before reading the volume of hydrogen consumed. The long-necked, round-bottomed flask (A) is connected by a ground-glass joint (lubricated with vaseline) and pressure rubber tubing with g and is supported in a frame coupled to a shaker having an eccentric mechanism. The hydrogen inlet (l) has an open branch (g) dipping just under mercury in G. A rotary vacuum pump is connected to tap 1.

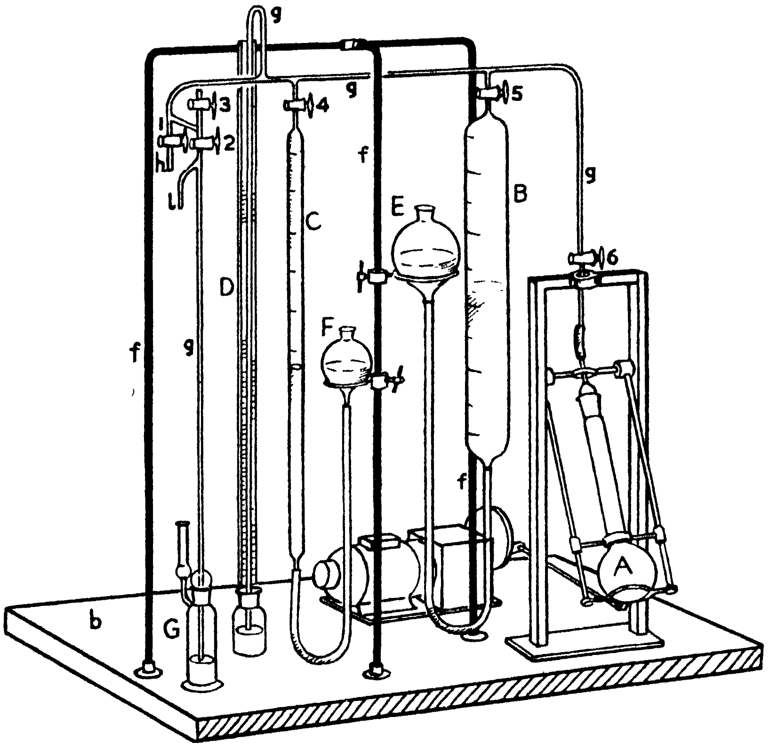


Fig. 44.

The apparatus can be used for purely preparative work (for details of procedure see Prep. 117) or for the determination of the amount of hydrogen taken up during a reaction (e.g. in the saturation of a double bond). A good general catalyst is Adams platinum oxide catalyst (C. V. I, 463), and it is usually employed in conjunction with a non-reactive solvent for the substrate.

Procedure.—The charge of substrate, solvent and catalyst having been inserted in A and this connected to g, tap 6 is opened and taps 4 and 5 closed after having expelled all gas from B and C by raising E and F.

To evacuate the system, the pump is started, taps 2 and 3 are closed and tap 1 opened. When the manometer registers at least 10 mm.—or when a low boiling solvent, if such is used, begins to boil—tap 1 is closed and the pump switched off.

The reducing valve of the hydrogen cylinder having been adjusted so that a brisk stream of gas issues through G, tap 2 is opened to admit hydrogen until the manometer registers atmospheric pressure. This attained, tap 2 is closed, the whole re-evacuated as before and then refilled with hydrogen while the reservoir (E) is lowered and tap 5 opened so that (B) is filled with hydrogen to its zero mark. Reservoir (C) used for small volumes of hydrogen, is seldom employed.

In the next stage, tap 2 is closed, the hydrogen cylinder turned off, the shaker started and hydrogenation allowed to proceed until no further reduction in the volume of hydrogen takes place. The volume absorbed may with advantage be read at intervals and plotted against time. Should the hydrogen in (B) become exhausted a second charge of the gas is introduced. From the volume of hydrogen absorbed the degree of unsaturation can be calculated.

When reduction is complete, shaking is stopped, tap 3 is opened, the water reservoir (E) is raised to expel gas from (B), taps 3, 4, and 5 are closed, tap 1 is opened and suction applied to remove hydrogen. After filling with air through tap 3, re-evacuating and finally admitting air, the flask A is removed and its contents worked up.

Cautions.—Wear goggles. Do not apply vacuum to B and C. Beware of hydrogen/air mixtures.

ADDITION TUBE

The Y-shaped tube (Fig. 45) is a most convenient apparatus through which to make additions to a mixture which is being heated under a reflux condenser. It is particularly useful for the addition of solids (for example, sodium—see p. 517). For the addition of liquids a dropping funnel is introduced through a cork in the upright limb.

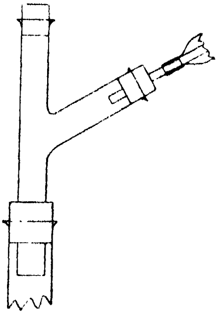


Fig. 45.

The K.B.B. Atmospheric Burner (Kelvin, Bottomley and Baird).—This lamp (Fig. 46) is a very convenient source of ultra-violet and monochromatic illumination. The quartz tube, which is not evacuated, is incompletely filled with air-free mercury. The current passes from the + electrode A to the – electrode B through the mercury, a small heating unit E being incorporated in the circuit. When the current is passed, this latter heats the mercury in the narrow tube at E to boiling, the mercury vapour thus formed displacing the mercury into the reservoir. An arc is then struck through the mercury vapour. A device is fixed which cuts out the heating unit when the pressure of mercury vapour increases to a certain level. The – electrode is kept from becoming too hot by the aluminium cooling fins D. When the lamp deteriorates, the glass stopper at C is removed and the mercury poured out and cleaned. If the quartz becomes discoloured, it can be heated in a blowpipe flame. (See Prep. 346 and Reactions LXXIV (*b*) and CLXVIII.)

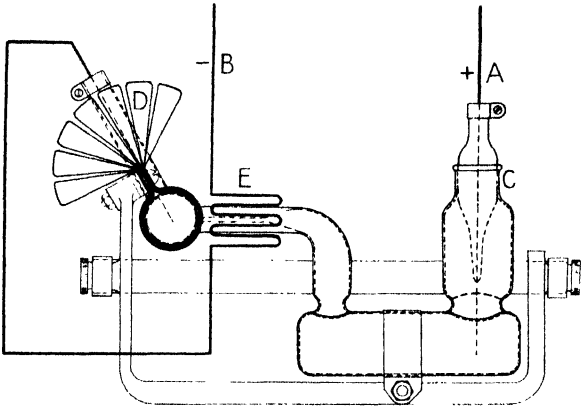


FIG. 46.

OZONISER

This consists of a jacketed tube constructed usually of glass (Fig. 47) through the annulus of which oxygen is passed. In the central compartment are placed dilute copper sulphate solution and centrally a copper rod immersed in the sulphate and attached to a terminal. The other electrode is of aluminium foil wrapped round the outside tube. Both electrodes are attached to a Tesla coil or preferably a high voltage transformer, e.g. a

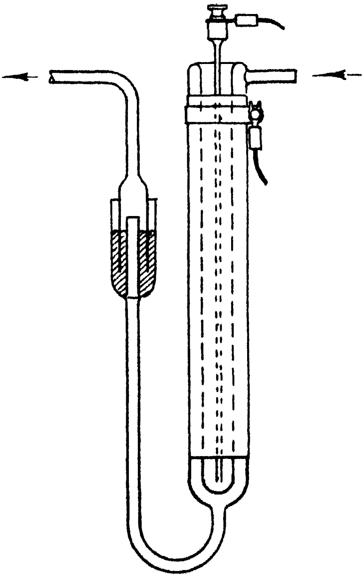


FIG. 47.

neon 7500v. transformer. The units may be connected in parallel if large throughputs are required. Rubber fittings must not be used on the ozone side ; junctions between tubes should consist of mercury seals as shown. Ozone concentrations of 3–5% are then obtained. See Prep. 477A.

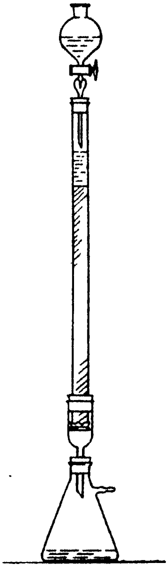


Fig. 47A.

Chromatography.—Chromatographic adsorption-analysis, the most delicate method of separation of closely related compounds, coloured or colourless, depends on the simultaneous adsorption and separation of mixtures of organic compounds, such as natural dyes, biochemical products, isomerides, hydrocarbons, etc., in suitable solvents such as petroleum, ether, chloroform, carbon disulphide and water.

The solution (hot or cold) is dropped through a funnel to the column of the absorbent, alumina, silica, magnesia, etc., usually specially prepared for the purpose, in a vertical tube to which gentle suction can be applied (Fig. 47A). Selective adsorption of the components of the mixture results in the formation of zones or bands sometimes coloured, sometimes colourless, and in some cases only visible under ultra-violet light. When the bands have been formed the solvent or a different solvent is similarly applied to the column to give sharper separation of the bands. This process is known as *developing*. The bands may then be separated by cutting the tube, by pressing out the chromatogram with a plunger, or by using different solvents, the latter process being known as *elution*. The operation can be conducted in the presence of an inert atmosphere where necessary by suitable alteration in the apparatus.

A simple experiment in which aqueous 2% commercial congo red is passed through a column of alumina will illustrate the principle.

In some cases colourless substances, e.g. aldehydes, ketones, etc., can be converted to coloured derivatives, e.g. 2–4–dinitrophenylhydrazones and regenerated after elution. In others qualitative tests on the eluate give an indication of adsorption.

The column may be packed mechanically by pressing with a glass rod, or by applying the absorbent in the form of a cream made up from a volatile solvent which can be removed by suction. The choice of absorbent is often a matter of trial and error. To some extent it is dependent on its basic or acidic properties, its porosity, etc. The selective adsorption depends on the molecular configuration of the organic component, its polarity, degree of unsaturation, etc.

References : Williams, *Introduction to Chromatography.*
Zechmeister and Cholnoky, *Principles of Chromatography.*
J. C. S., 1947, 1302, 1308, 1315, 1321. C. and I, 1949, 12, 25.

PART II

CHAPTER III

THE LINKING OF CARBON TO CARBON

HYDROGEN COMPOUNDS

In this section are described those preparations in which carbon atoms are caused to unite with one another.

Reaction I. Passage of the Vapour of certain Hydrocarbons through a red-hot Tube (A., 230, 5).—A large number of hydrocarbons condense to form hydrocarbons of higher molecular weight when their vapour is passed through a red-hot tube. The method, however, is only of theoretical importance, for the yield is in most cases small owing to incomplete conversion, and to the formation of a large number of by-products. Benzene has been obtained from acetylene in this way ; benzene itself, and diphenyl methane treated in a similar manner, give diphenyl and fluorene respectively.

$$R.H + H.R \xrightarrow{\text{Heat}} R.R + H_2,$$

where R.H is a hydrocarbon.

PREPARATION 1.—**Diphenyl** (*Phenylbenzene*).

$$C_6H_5.C_6H_5. \qquad C_{12}H_{10}. \qquad 154.$$

Method I.—In this experiment the apparatus shown in Fig. 48 is used. The flask, of about 1½ litres capacity, contains 500 gms. of benzene kept boiling by means of a water bath. The flask is provided with a cork having two perforations, through one of which the tube *a* passes while the second accommodates the tube *b*. This leads to the iron tube R (a wrought-iron gas pipe of 1 metre length, and 20 mms. internal diameter), which is filled with pieces of pumice, and heated by means of a combustion furnace to a bright red heat. From the flask the benzene vapour passes into the glowing tube, and is here partially converted into diphenyl, hydrogen, and other products. The unchanged benzene and the volatile diphenyl pass through the tube *e* into the condenser K and flow from it through *a* back into the flask. The tube *a* dips below the level of the liquid, and at *d* has a tube sealed on for the escape of the hydrogen. The operation is carried on for from 6 to 10 hours, the apparatus acting automatically. The flask now contains a fairly concentrated solution of diphenyl in benzene. The latter is removed on a water bath, and the residue is fractionated. The part passing over above 150° solidifies in the receiver, and consists of almost pure diphenyl. It may be purified by crystallisation from alcohol. The yield is greatly dependent on the temperature of the iron tube. With a low gas pressure the ordinary combustion furnace is almost useless ; in that case it is better to substitute a Fletcher's gas furnace or an electric furnace.

$$2C_6H_6 = C_6H_5.C_6H_5 + H_2.$$

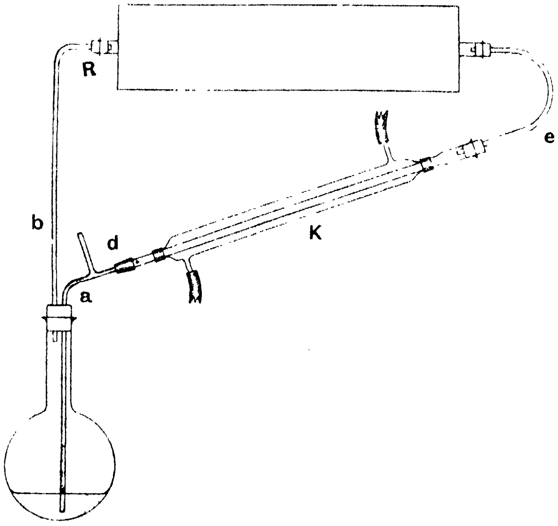


FIG. 48.

Yield.—Up to 20% theoretical (100 gms.). $D.^{82}_{4}$ 0·9845. (Z. Ch., 1866, 707 ; A., 230, 5 ; U.S.P., 1894283 ; E.P., 369613.)

This " thermal condensation " can also be brought about by exposing the vapour of benzene to the action of a wire or filament kept at red heat by an electric current.

Method II.—The apparatus is as follows : Two copper wires pass tight-fitting through the cork in the neck of a flask, and are connected together above the benzene in the flask by a coiled platinum wire, 25 cms. long and 0·2 mm. in diameter. A reflux condenser is fitted to the side tube of the flask. 50 gms. of benzene are boiled in the flask on a water bath. After fifteen minutes' boiling the air in the flask will have been expelled, and the current is switched on and regulated by means of a variable resistance so that the platinum spiral glows red (4–4·5 amps. ; 8–10 volts). A battery of accumulators can be used as a source of current, or the latter can be obtained from an alternating service supply at 110 or 220 volts, the necessary reduction in current and voltage being brought about by a rheostat or a bank of lamps. In the latter case it is more economical to use the thread of a carbon lamp instead of a platinum wire. After 5 hours a portion of the benzene will have been converted into diphenyl under the action of red heat. The unaltered benzene is removed on a water bath, and the residual liquid fractionated from a small flask, the portion 240°–270° being collected separately, and recrystallised from alcohol or from a mixture of benzene and petroleum ether :

$$2C_6H_6 = C_6H_5.C_6H_5 + 2H.$$

Yield.—22% theoretical (11 gms.). Colourless leaflets ; soluble in benzene ; M.P. 71° ; B.P. 254° ; $D.^{82}_{4}$ 0·9845. (Z. e., 7, 903.)

For similar preparations yielding 1·3-butadienes, see C. V., II, 102.

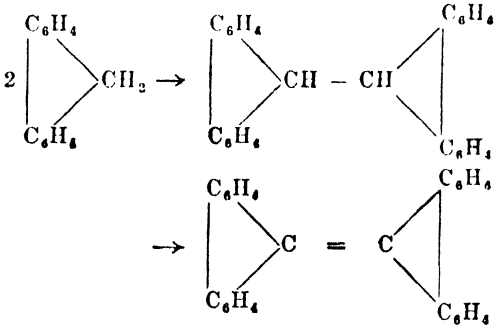
Reaction II. Reduction under certain Conditions of Aromatic Ketones. (A., 194, 310).—When aromatic ketones are reduced by zinc dust in the presence of glacial acetic acid pinacols are formed (see p. 77).

$$2C_6H_5.CO.C_6H_5 + 2H = (C_6H_5)_2C.(OH).C(OH).(C_6H_5)_2.$$

If hydrochloric acid is added the reduction goes to the corresponding hydrocarbon ; e.g. from benzophenone *s*-tetraphenylethane is obtained.

$$2C_6H_5.CO.C_6H_5 + 6H \longrightarrow (C_6H_5)_2.CH.CH.(C_6H_5)_2.$$

Reaction III. Oxidation under certain Conditions of Cyclic Hydrocarbons. (B., 32, 432)—In this reaction two molecules of a hydrocarbon are condensed, hydrogen being eliminated by the action of an oxidising agent. Two neutral oxidising agents, potassium persulphate and lead oxide, are especially useful in this type of reaction. The former is used in dilute aqueous solution, at a temperature of about 100° ; to obtain results with the latter much higher temperatures are necessary. The substance is mixed with the lead oxide and heated to over 250°, or it is distilled over heated lead oxide. The results obtained vary with the temperature and the amount of lead oxide used, e.g. fluorene can be oxidised to either bisdiphenylene-ethane or bisdiphenylene-ethylene. With potassium persulphate the first stage only is reached.



It is to be noted that to obtain practicable yields this reaction must be confined to aromatic hydrocarbons. In the aliphatic series it only takes place, in a few cases, and then gives a yield of the order of 1%.

PREPARATION 2.—*s*-**Diphenylethane** (*Dibenzyl*).

$$C_6H_5CH_2.CH_2.C_6H_5. \qquad C_{14}H_{14}. \qquad 182.$$

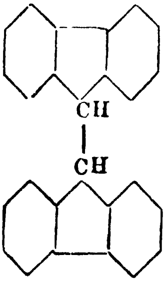
90 gms. potassium persulphate (1 mol.) are dissolved in a litre of water, and to this is added 60 gms. (2 mols.) of toluene. The mixture is heated on a water bath for 4 hours in a flask fitted with good agitation and a reflux condenser (see Fig. 38). The oily layer is then separated, dried over calcium chloride and fractionally distilled, the fraction 270°–280° con-

sisting of dibenzyl and benzoic acid being separately collected. The earlier fractions consist of toluene and benzaldehyde. The dibenzyl fraction is dissolved in ether and the benzoic acid removed by shaking with dilute caustic soda solution. The ether is then removed on the water bath, and the residue recrystallised from dilute alcohol.

$$4C_6H_5.CH_3 + O_2 \longrightarrow 2C_6H_5CH_2CH_2C_6H_5 + 2H_2O.$$

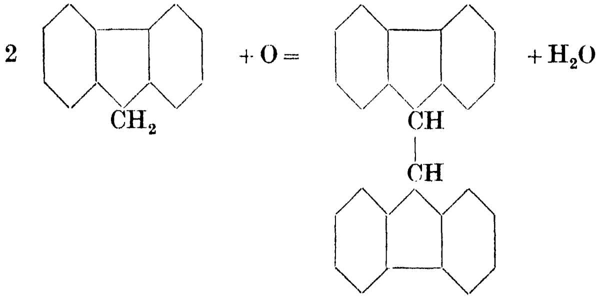
Yield.—15% theoretical (9 gms.). Colourless monoclinic needles; M.P. 51°–52°; B.P. 284°; $D.^{50}_{50}$ 0·9752. (B., 32, 432, 2531.)

PREPARATION 3.—**Bisdiphenylene-ethane.**



$C_{26}H_{18}$. 330.

10 gms. (2 mols.) of fluorene, and 15 gms. (excess) of litharge are thoroughly mixed and heated with slow stirring in a metal crucible in a bath till the temperature of the latter reaches 270°, where it is kept for 2 hours. The crucible is cooled to 150°, wiped, and partially immersed in cold water. The contents, which are by this means loosened, are ground up, extracted with boiling benzene, and the extract concentrated to small bulk. The crystals which separate are recrystallised from benzene, or glacial acetic acid. The mother liquors contain unaltered fluorene.



Yield.—50% theoretical (5 gms.). Colourless crystals; slightly soluble in alcohol and ether; soluble in hot benzene and glacial acetic acid; M.P. 246°. (A., 291, 6.)

Reaction IV. (*a*) **Action of Dehydrating Agents on a Mixture of certain Compounds.** (B., 6, 964).—Various dehydrating agents—concentrated sulphuric acid, zinc chloride, phosphorus pentoxide—can be used. Sulphuric acid, although perhaps the most convenient, has the disadvantage that it tends to sulphonate the aromatic substances employed. At a low temperature, however, diphenylmethane can be obtained from benzyl alcohol and benzene. At 140° phosphorus pentoxide condenses benzene and diphenylcarbinol to triphenylmethane (B., 7, 1204). Substituted benzyl alcohols, and mandelic acid can be brought within the scope of the reaction, while in place of benzene its nitro, amino or phenolic derivatives may be used.

Boron trifluoride and hydrogen fluoride have been shown to possess remarkable condensing properties in the preparation of diphenylmethane, etc. (Am. Soc., 59, 470 ; 62, 1623).

See also *Newer Methods of Preparative Organic Chemistry*, Kastner, p. 249 ; Weichert, p. 315.

$$RR_1CH\ \boxed{OH + H}\ R_{11} = RR_1CHR_{11} + H_2O.$$

A similar reaction between chloral and chlorobenzene with oleum as dehydrating agent yields *p-p'*-dichlorodiphenyl-trichloroethane (D.D.T.).

PREPARATION 4.—**Diphenylmethane** (*Benzylbenzene*).

$CH_2.(C_6H_5)_2$. $C_{13}H_{12}$. 168.

A mixture of equal weights of concentrated sulphuric acid and glacial acetic acid is run into a mixture of 10 gms. (1 mol.) of benzyl alcohol, 27 gms. (excess) benzene and 100 gms. glacial acetic acid until most of the benzene separates on the surface. After 12 hours, 500 gms. of concentrated sulphuric acid are added under constant cooling, and the mixture again allowed to stand for 6 hours. The mass is then poured into water, extracted with ether, the extract dried over calcium chloride, and the residue, after removing the ether on a water bath, fractionated under reduced pressure, the fraction 174°–176° at 30 mms. being separately collected.

$$C_6H_5.CH_2OH + C_6H_6 = C_6H_5.CH_2.C_6H_5 + H_2O.$$

Yield.—25% theoretical (4 gms.). Colourless oil ; on cooling solidifies to needle-shaped crystals ; orange-like odour ; M.P. 26° ; B.P. ^{760} 263° ; B.P. ^{30} 175° ; D. $^{25}_{25}$ 1·0056. (B., 6, 964.)

Reaction IV. (*b*) **Action of Dehydrating Agents on certain Ketones.** (J. pr., 15, 129.)—This is a reaction of historical interest, for it was by the preparation from acetone by distillation with fairly strong sulphuric acid that the symmetry of mesitylene was deduced, and hence the orientation of such compounds as *m*-xylene was established.

Besides its dehydrating action, the purely condensing capabilities of sulphuric acid should not be overlooked. Thus methyl acetylene condenses in the presence of sulphuric acid to mesitylene. (B., 29, 958, 2884 ; C. V., I, 341 ; cf. polymerisation of acetylene to benzene.)

$$3CH_3C{:}CH = C_6H_3(CH_3)_3.$$

Silica gel or alumina as catalyst serves in place of sulphuric acid (Am. Soc., 53, 330 ; C. A., 28, 5052).

PREPARATION 5.—**Mesitylene** (s-*Trimethylbenzene*).

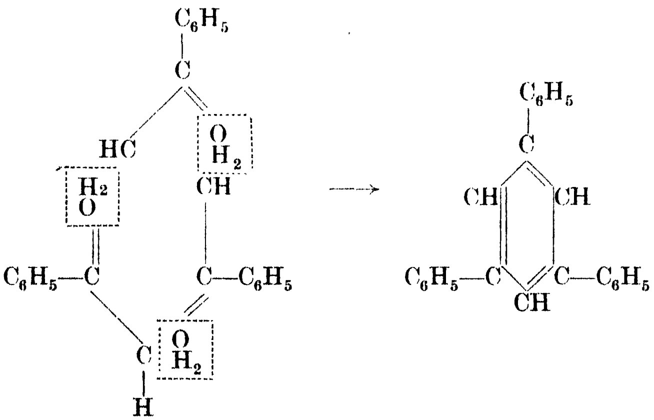
$C_6H_3(CH_3)_3[1:3:5]$. C_9H_{12}. 120.

400 gms. of clean dry sand are placed in a 2-litre retort connected with a condenser. 250 gms. (3 mols.) of acetone are added, and then a cooled mixture of 560 gms. of concentrated sulphuric acid and 150 gms. of water is run in, in a *slow* continuous stream, the retort being meantime cooled in cold water. After 24 hours' standing, the mixture is slowly distilled, directly or in steam. When oily drops appear in the neck of the retort, the receiver is changed, and the distillate collected until only very small quantities of the oil appear. The colour of the liquid (if directly distilled) changes to deep brown, and finally to black, sulphur dioxide is evolved, and the mass froths up considerably. The upper yellowish layer of the distillate is separated from the lower aqueous layer, washed with caustic soda and water, and dehydrated over calcium chloride. It is then fractionated, the fraction 100°–200° being redistilled four times over thin slices of metallic sodium, when about two-thirds of it is obtained as pure mesitylene coming over at 161°–166°.

$$3CH_3.CO.CH_3 = C_6H_3(CH_3)_3 + 3H_2O.$$

Yield.—Variable, about 25% theoretical (40 gms.). Colourless, strongly refracting liquid; B.P. ^{750} 163°; D. $^{10}_{4}$ 0·8694. (J. pr., 15, 129; A., 147, 143; 278, 260; Bl., 40, 267; Am. Soc., 15, 256; 20, 807; C. V., I, 341.)

Acetophenone condenses in a similar manner if it is heated with phosphorus pentoxide, or better if saturated with dry hydrogen chloride at ordinary temperatures. *s*-Triphenylbenzene is deposited after standing for several days in a warm place; by resaturating the mother liquors, yields up to 50% can be obtained.



Reaction V. Cinnamic Condensation and Decarboxylation. (Am. Soc. 1, 313.)—This is an extension of Perkin's reaction, and depends on the fact that when benzaldehyde and phenyl-acetic acid are condensed in the usual way, the unsaturated acid thus formed is unstable, and loses carbon dioxide, giving stilbene.

$$C_6H_5.CHO + H_2C.(C_6H_5)COOH \longrightarrow$$

$$C_6H_5CH : C(C_6H)_5COOH \longrightarrow C_6H_5CH : CH.C_6H_5.$$

Technically this method is of no importance, as the hydrocarbon is obtained from coal-tar.

Reaction VI. (*a*) **Action of certain Anhydrous Metallic Halides on a Mixture of an Aromatic Hydrocarbon and an Alkyl Halide.** (Friedel-Crafts.) (C. r., 1877, 1450.)—The "Friedel-Crafts" reaction, of which this illustrates one phase, is one of the most important condensing reactions known to organic chemistry. Applied to the production of aromatic hydrocarbons and their derivatives, the action consists in the catalytic use of anhydrous aluminium chloride for condensing an aromatic hydrocarbon or its derivatives with a chloro- or bromo-compound. Halogen acid is always evolved, and the product forms a complex with aluminium chloride which decomposes, yielding the required compound on addition of water. Not only does the reaction proceed without the use of heat in most cases, but frequently it must be moderated by using a large excess of the hydrocarbon, or better by diluting with some neutral solvent, such as ligroin, carbon disulphide or nitrobenzene. The two former diluents automatically keep down the temperature to their boiling points ; the latter has the especially useful property of dissolving anhydrous aluminium chloride. If a hydrocarbon derivative is used, coupling takes place in the *para* position or, if that is occupied, in the *ortho*, but the yield suffers. In place of aluminium chloride, aluminium bromide (D.R.P., 126421), aluminium foil and hydrogen chloride (B., 28, 1136), mercuric chloride (see Reaction VI (*b*)), ferric chloride, zinc chloride (B., 30, 1766), the aluminium-mercury couple (Reaction VI (*c*)), boron trifluoride and hydrogen fluoride, can be used in some cases. For other uses of this reaction, see pp. 92, 127). Chem. Rev., 17, 327. *Organic Reactions*, Adams, Vol. III.)

The methods employed vary but little. The aluminium chloride is slowly added to a mixture of the hydrocarbon and the alkyl halide, or the alkyl halide is added to a mixture of the other two. The latter process is mostly used with volatile halides which are led in gaseous form into the mixture of the other two components, for a time which varies as the number of alkyl groups it is desired to introduce.

$$RCl + AlCl_3 \longrightarrow R^+[AlCl_4]^-$$

$$R^+ + ArH \longrightarrow R.Ar + H^+$$

$$H^+ + [AlCl_4]^- \longrightarrow HCl + AlCl_3.$$

Note.—Bottles filled with aluminium chloride have frequently a high internal pressure and must, therefore, be opened with great care, being covered with a cloth during this operation.

For some anomalies in the behaviour of aluminium chloride as compared with that of aluminium bromide, see A., 225, 155.

PREPARATION 6.—**Triphenylmethane** (*Methenyltriphenyl*).

$CH(C_6H_5)_3$. $C_{19}H_{16}$. 224.

To a mixture of 30 gms. dry benzene and 12 gms. dry carbon tetrachloride in a 200 c.cs. flask provided with a reflux condenser fitted with a calcium chloride drying tube, 10 gms. anhydrous aluminium chloride in lump form are added. The flask is almost completely immersed at once in ice water the temperature of which is allowed to rise to that of the room during 24 hours. After this time 12 gms. dry ether are added dropwise during 10 minutes through the condenser with occasional shaking. After the mixture has stood for about 24 hours it is poured on to 65 gms. ice and 5 c.cs. conc. hydrochloric acid contained in a 500 c.cs. flask. About 100 c.cs. benzene (or less preferably 50 c.cs. carbon disulphide) are added and after boiling gently under reflux for 10 minutes, the mixture is cooled to about 50°, the benzene layer separated, washed with 80 c.cs. warm water containing 3 c.cs. conc. hydrochloric acid and distilled to remove benzene. The residue is distilled from a small flask under reduced pressure, the fraction boiling at 190°–215° at 10 m.ms. being collected and recrystallised from alcohol.

It will be noted that ether reduces the triphenylchloromethane formed in the Friedel-Crafts reaction :

$$CCl_4 + 3C_6H_6 \longrightarrow ClC(C_6H_5)_3 + 3HCl.$$

$$CCl(C_6H_5)_3 + (C_2H_5)_2O \longrightarrow CH(C_6H_5)_3 + CH_3CHO + C_2H_5Cl.$$

Yield.—65% theoretical (12 gms.). Colourless rhombic plates ; M.P. 92° ; B.P. ^{760} 350° ; D. $^{95}_{95}$ 1·0568. The compound with benzene has the formula $C_{19}H_{16}.C_6H_6$. (Am. Soc., 46, 2580.)

Note.—The aluminium chloride used must be recently made and of good quality, otherwise it must be resublimed from a retort, as it is essential it should be anhydrous. (C. r., 1877, 1450 ; B., 26, 1961 ; Bl., 37, 6 ; A., 197, 252 ; C. V., I, 548.)

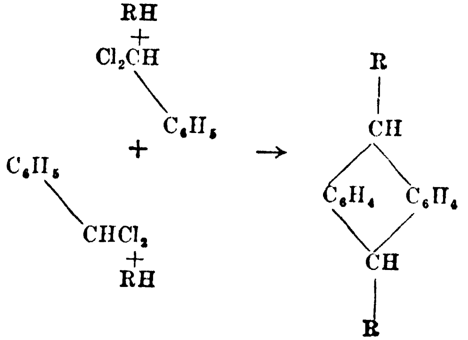
Reaction VI. (*b*) **Action of Aluminium and Mercuric Chloride on a Mixture of an Aromatic Hydrocarbon and an Alkyl Halide.** (J. C. S., 117, 1335).—This is a development of the Friedel-Crafts reaction which has yielded some very interesting results. As far back as 1895 an attempt to use a mixture of aluminium powder and mercuric chloride in the ordinary Friedel-Crafts reaction ended in failure (B., 28, 1139). Later (B., 37, 1560), it was proved that mercuric chloride and aluminium in benzene or toluene formed compounds of the type $C_6H_6.AlCl_3.HgCl$. It was by the use of these double compounds that the secondary reactions, which caused the failure of the earlier attempts, were avoided and some very interesting condensations brought about. In the formation of the catalyst the following reaction occurs :

$$C_6H_6 + Al + 2HgCl_2 \longrightarrow C_6H_6.AlCl_3.HgCl + Hg.$$

An excess of mercuric chloride must be used to prevent the mercury liberated amalgamating with the aluminium, for the couple so formed would act concurrently with, but in a different manner to, the double compound (see the next reaction).

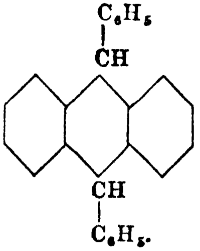
Applied to the synthesis of hydrocarbons the following results have been obtained by this new method. 9 : 10-Diphenyl-9 : 10-dihydroanthracene is formed by the condensation of benzene and chloroform, whilst in the ordinary Friedel-Crafts reaction (A., 194, 254 : 227, 107) triphenylmethane (Preparation 6) is the main product, traces of chlorarylmethanes and tetraphenylethane (B., 26, 1952) being also formed. The same compound is also obtained from benzal chloride and benzene. Carbon tetrachloride and benzene give 9 : 9 : 10 : 10-tetraphenyl-9 : 10-dihydroanthracene as do also benzyl chloride and benzene. In the earlier reaction triphenylchloromethane (p. 440) is the chief product.

Chloroform and toluene yield by this process dimethyl-9 : 10-ditolyl-9 : 10-dihydroanthracene ; using aluminium chloride, tetratolylethane is obtained (B., 14, 1530). Benzylidene chloride and toluene yield dimethyl-9 : 10-diphenyl-9 : 10-dihydroanthracene.



For other applications of this reaction see pp. 96,127 .

PREPARATION 7.—**9 : 10-Diphenyl-9 : 10-dihydroanthracene.**



$C_{26}H_{20}$. 332.

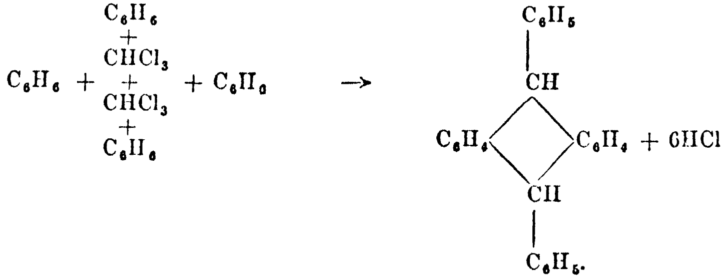
Preparation of Catalyst.—13 gms. (excess) of dry benzene and 20 gms. (excess) of mercuric chloride are treated, gradually, in a flask fitted with a reflux condenser, with 1 gm. of aluminium powder, the flask being meanwhile vigorously shaken and occasionally cooled in ice-water. A green crystalline mass separates, and the reaction is completed by immersing the flask in tepid water for half an hour. The mercury liberated in the reaction is removed, and the catalyst is then ready for use.

9 gms. (2 mols.) of chloroform are added drop by drop through the condenser, and the flask left at ordinary temperature for 2 hours, heated for an hour at 40° and then for an hour at 40°–50°. During the whole course

of the reaction the contents of the flask are well agitated by a mechanical stirrer (see the apparatus shown on p. 46).

On cooling, the product is decomposed with ice and filtered. From the filtrate a deep-red oil separates, from which all unchanged benzene is evaporated, and the residue extracted with boiling acetic acid containing a little water. The compound which separates on cooling is recrystallised from dilute alcohol, and then repeatedly from acetone.

The same compound can be prepared from 8 gms. (2 mols.) of benzal chloride, 13 gms. (excess) of benzene, and the above quantities of aluminium and mercuric chloride. The reaction is completed at 50°–55°. Otherwise the details are as already described.



Colourless crystals : soluble in alcohol ; M.P. 159° (J. C. S., *loc. cit.*) ; M.P. 164·2° (Am. Soc., 13, 556). Oxidised with chromium trioxide in glacial acetic acid solution, yields anthraquinone ; gives a diacetyl derivative on heating with acetic anhydride and pyridine (J. C. S., 117, 1335).

Reaction VI. (*c*) **Action of the Aluminium-Mercury Couple, or of certain finely-divided Metals on a Mixture of an Aromatic Hydrocarbon and an Alkyl Halide.** (J. C. S., 67, 826.)—The action of the couple is analogous to that of anhydrous aluminium chloride. Zinc dust or finely-divided copper can also be used.

PREPARATION 8.—**Diphenylmethane** (*Benzylbenzene*).

$C_6H_5.CH_2.C_6H_5$. $C_{13}H_{12}$. 168.

1 gm. freshly prepared aluminium-mercury couple (p. 67) is added to 65 gms. (excess) of *dry* benzene in a flask attached to an upright condenser, the whole being placed in a fume cupboard. 32 gms. (1 mol.) of benzyl chloride are slowly dropped in from a tap funnel, during an hour, through the top of the condenser. The flask is then heated on a water bath for 15 minutes, its contents shaken with a very dilute solution of caustic soda, and the benzene solution separated. The aqueous portion is again extracted with benzene, and the whole benzene solution dehydrated over calcium chloride, the benzene removed on a water bath, and the residue distilled under reduced pressure, the fraction, 174°–176° at 80 mms., being retained.

$$C_6H_5CH_2Cl + C_6H_6 + (Al/Hg) = C_6H_5.CH_2.C_6H_5 + HCl + (Al/Hg).$$

Yield.—33% theoretical (14 gms.). Properties (see p. 63). (J. C. S., 67, 826 ; O. S., XIV, 34.)

Reaction VI. (*d*) **Ethylation of Benzene and Naphthalene by means of Ethylene in presence of Anhydrous Aluminium Chloride.**—Ethyl chloride in presence of aluminium chloride reacts with benzene to give ethyl- and poly-ethyl-derivatives of benzene (Reaction VI (*a*)). Ethylene and hydrogen chloride may be used in place of ethyl chloride, but as hydrogen chloride is evolved in the reaction little of this is necessary (Bl., 31 (2), 539). Ethylene and aluminium chloride will also react, the latter probably containing traces of water, etc., sufficient to supply the hydrogen chloride to maintain the reaction. By this method good yields of ethyl benzene can be obtained, while naphthalene can be ethylated in presence of benzene, the alkyl group being transferred from the latter to naphthalene in presence of aluminium chloride. Higher alkylated derivatives are also formed in each case. High speed agitation is essential (Am. Soc., 44, 206).

PREPARATION 9.—**Ethyl Benzene.**

$C_2H_5.C_6H_5$. C_8H_{10}. 106.

Ethylene.—The apparatus consists of an ordinary combustion tube packed with bauxite which has been previously ignited to 850° and sifted through a 400 mesh sieve. The tube is heated in a suitable electric furnace at about 350°. To one end of this tube is attached by the side tube a small distilling flask heated on a metal bath at 95°–105°, while a dropping funnel of sufficient length to overcome back pressure is also fixed to the flask for the addition of alcohol. At the other end of the tube is attached a sloping condenser leading to a distilling flask, the side tube of which leads to a wash-bottle containing conc. sulphuric acid. The wash-bottle is connected to the flask (Fig. 49) fitted with efficient agitation, and heated on a water bath.

Absolute alcohol is placed in the funnel and the tap set to deliver 36 c.cs. per hour. This is vaporised on dropping into the hot flask, and passes to the bauxite. 50 gms. of ethylene are produced in 3 hours, unchanged alcohol being condensed in the distilling flask.

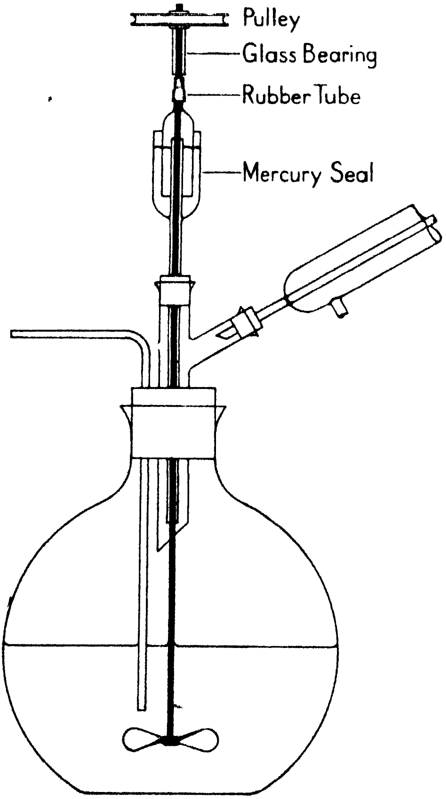


FIG. 49.

Ethyl Benzene.—116 gms. of pure benzene and 25 gms. anhydrous aluminium chloride are placed in the reaction flask and stirred at about 1,500 r.p.m., the temperature being maintained at 70°–75°. Ethylene is passed in for 3 hours, when on keeping the product separates into two layers, the upper almost colourless, the lower brown and viscous. The latter is discarded. The upper layer is washed with dilute hydrochloric acid, then with water, and dried with calcium chloride. It is then fractionated, the fractions 80°–100°, and 100°–150°, being collected (p. 23). These are then finally fractionated and the fraction 134°–136° collected.

Yield.—50% theoretical (74 gms.). Colourless liquid; B.P. 134°; D. 0·866. (Z. a., 41, 955.) See Preparation 10.

On dehydrogenation ethyl benzene gives styrene (phenylethylene).

Reaction VII. (*a*) **Action of Sodium on Halogen Compounds** (Würtz). (A., 131, 303; Am. Soc., 58, 1697)—The application of this reaction to the synthesis of paraffins by Wurtz was of great importance to chemical theory, as it afforded strong evidence of the chain linking of carbon atoms, and enabled the structure of many hydrocarbons to be determined.

Fittig applied the reaction to aromatic hydrocarbons. In this latter case a second side-chain may be introduced from a di-halogen derivative, simultaneously with the first or subsequently in a second reaction. Reaction may take place according to one or other or both of the schemes ·

(*a*) Involving free radicals :

$$2RX + 2Na \longrightarrow 2R^{\cdot} + 2NaX \longrightarrow R\text{-}R + 2NaX.$$

(*b*) Involving organoalkali compounds :

$$RX + 2Na \longrightarrow RNa + NaX.$$

$$RNa + RX \longrightarrow R\text{-}R + NaX.$$

The total in each instance being

$$2RX + 2Na \longrightarrow R\text{-}R + 2NaX.$$

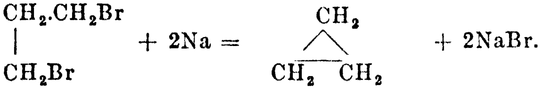
Phenylsodium is obtainable in high yield from sodium and chlorobenzene.

For the alkyl halides the order of reactivity is :

$$RI > RBr > RCl.$$

The reaction does not occur with the same readiness in all cases, the yields obtained varying greatly. In general, a basic group *para* to the halogen, and an acidic group *ortho* to the halogen, favour condensation. If the reaction is sluggish, it may be promoted in many cases by raising the temperature or by adding a little ethyl acetate (J. C. S., 67, 656). If the reaction is too vigorous, an inert solvent, e.g. toluene, ether, or ligroin, is added to moderate it. Since the discovery of the Friedel-Crafts reaction, its very wide and varied application has led to its supplanting the Fittig method, than which in most cases it gives better yields.

Freund applied the method to the synthesis of cycloparaffins. From trimethylenedibromide, trimethylene was prepared, whilst hexamethylene-dibromide, yielded hexamethylene in a similar manner. (M., 3, 626; A. Ch., [5], 14, 488.)



When nitro groups are present copper powder gives better results (Reaction VII (*b*)).

Preparation 10.—**Ethyl Benzene** (*Phenylethane*).

$$C_6H_5.C_2H_5. \qquad C_8H_{10}. \qquad 106.$$

30 gms. (excess) of metallic sodium in the form of small pieces of wire are slowly added to 120 c.cs. of anhydrous ether prepared from commercial ether as described on p. 219. The ether is contained in a round flask (1 litre) which when the evolution of hydrogen has ceased, is attached to an upright condenser and immersed in a vessel of ice-water. A mixture of 78 gms. (2 mols.) of bromobenzene and 70 gms. (excess) of ethyl bromide, both carefully dehydrated, is added, and the mixture left to stand overnight. The liquid is then decanted from the sodium bromide, which has a blue colour, and the latter washed twice with dry ether. The ether is removed on a water bath, and the residue fractionated from a small distilling flask, the fraction 132°–135°, being collected separately.

$$C_6H_5Br + C_2H_5Br + 2Na = C_6H_5.C_2H_5 + 2NaBr.$$

Yield.—60% theoretical (30 gms.). Colourless liquid; B.P. 134°; $D.\ ^{22\cdot5}_{4}\ 0{\cdot}8664$. (A., 131, 303.) See Preparation 9.

Note.—The residue in the flask contains unaltered sodium. This must be destroyed by adding the residue in small portions to alcohol, and allowing to stand till all action ceases.

Preparation 11.—**Dibenzyl** (s-*Diphenylethane*).

$$C_6H_5.CH_2.CH_2.C_6H_5. \qquad C_{14}H_{14}. \qquad 182.$$

12 gms. (slightly more than 2 mols.) of sodium wire are added to 50 gms. (2 mols.) of benzyl chloride, the whole refluxed on a water bath until no further change takes place, extracted with dry ether, and the extract fractionated, the fraction 244°–254° being retained, and recrystallised from alcohol. The reaction goes best in the absence of a solvent, but toluene can be added to lower the refluxing temperature.

$$2C_6H_5CH_2Cl + 2Na = C_6H_5.CH_2.CH_2.C_6H_5 + 2NaCl.$$

Colourless needles; soluble in benzene and in hot alcohol; M.P. 51°–52°; B.P. 248°; $D.\ ^{50}_{50}\ 0{\cdot}9752$. (A., 121, 250; 137, 258.)

Reaction VII. (*b*) **Action of Metals other than Sodium on Halogen Compounds.** (B., 34, 2176).—In the aliphatic series the iodo compound is heated, usually under pressure, with zinc, while in the aromatic series, the chloro-, bromo-, or iodo-compound may be heated above its melting point, or in presence of a solvent, such as nitrobenzene, with copper powder (Ullmann). The order of reactivity of the halogen is $I > Br > Cl$.

Good yields are obtained when the halogen is activated by the presence of a nitro group in the *ortho*-position (A., 332, 38 ; 350, 83). Amino-halogen compounds cannot be condensed in this way. These generalisations hold in the naphthalene series. (J. C. S., 1931, 3176 ; Chem. Rev., 38, 139.)

$$RI + 2Cu + IR \longrightarrow R.R + Cu_2I_2.$$

The reaction is only applicable for the preparation of symmetrical compounds from mono-halogen derivatives.

PREPARATION 12.—**Diphenyl** (*Phenylbenzene*).

$$C_6H_5.C_6H_5. \qquad C_{12}H_{10}. \qquad 154.$$

20 gms. (2 mols.) of iodobenzene are heated with 20 gms. (excess) of copper powder (p. 515) for 3 hours in a sealed tube (p. 47) to 230°. The contents of the tube are extracted with ether and the filtered extract fractionated, the ether being removed on a water bath and the fraction 245°-255° retained and recrystallised from alcohol.

$$2C_6H_5I + 2Cu = C_6H_5.C_6H_5 + Cu_2I_2.$$

Yield.—80% theoretical (6 gms.). Colourless leaflets ; soluble in hot alcohol ; M.P. 70°-71° ; B.P. 254° ; D. $^{82}_{4}$ 0·9845. (B., 34, 2176.)

Reaction VIII. Action of certain finely-divided Metals on Diazonium Compounds in Alcohol or Acetic Anhydride.—This reaction is limited to the preparation of *s*-biaryl compounds. Copper, zinc, or iron powder may be used, but the first is, on the whole, the most satisfactory, especially when it has been freshly prepared according to Gattermann (p. 515). As with other " finely-divided metal " reactions of this type there is a Sandmeyer analogue, but except in the case of nitro-compounds, the reaction for the most part takes a different course (see Reaction CLXVI).

The course of the reaction may be formulated as follows:

$$RNH_2 \longrightarrow RN_2SO_4H$$

$$2RN_2.SO_4H + Cu \longrightarrow RR + 2N_2 + CuSO_4 + H_2SO_4.$$

PREPARATION 13.—**Diphenyl** (*Phenylbenzene*).

$$C_6H_5.C_6H_5. \qquad C_{12}H_{10}. \qquad 154.$$

31 gms. (2 mols.) of aniline dissolved in 150 c.cs. of water and 40 gms. (slight excess) of concentrated sulphuric acid are diazotised in the usual way (see p. 380) with 23 gms. (2 mols.) of sodium nitrite in 10% solution. The diazonium solution is treated with 100 gms. of 98% alcohol and 50 gms. (excess) of copper powder (p. 515) are added while the whole is well stirred (see p. 44). A vigorous evolution of nitrogen occurs, and by the end of the reaction the temperature has risen to 30° or 40°. The stirring is continued for an hour, and then the mixture is steam distilled. The distillate at first consists chiefly of alcohol with small amounts of an oil insoluble in water. Small portions of it are tested from time to time by dilution with water. When a solid precipitate is thus obtained, the distillate is separately collected until no more solid comes over. The distillate is then heated to 71° to melt the solid diphenyl ; on cooling until solidification takes place, the still liquid portion is poured off. The product is almost pure, but may be recrystallised from alcohol.

100 gms. of zinc powder may be used instead of the copper. With it the best results are obtained by adding, first, 10 c.cs. of a cold saturated solution of copper sulphate, and then the zinc as above. Care must be taken in this case not to let the temperature rise above 30°–40°. Iron powder can also be employed.

Yield.—In each case 25% theoretical (6 gms.). Properties (see p. 72).

Diphenyl can also be obtained from diazobenzene sulphate by treating it with warm benzene (B., 26, 1997). The method is of importance for the preparation of unsymmetrical biaryls (*Organic Reactions*, Adams, Vol. II, 224).

Reaction IX. (*a*) **An alkyl or aryl halide treated with magnesium, usually in presence of absolute ether, forms a magnesium alkyl or aryl halide, known as a Grignard reagent.** This although a complex equilibrium mixture co-ordinated with the solvent employed may for ordinary purposes be designated as RMgX (Gilman, *Organic Chemistry*, Vol. I, 518).

$$2RMgX \rightleftharpoons R_2Mg + MgX_2.$$

The reagent is applicable to the preparation of a large variety of compounds under anhydrous conditions.

Thus with alkyl or aryl halide, hydrocarbons are formed.

$$RMgI + R_1I = RR_1 + MgI_2.$$

The same type of reaction occurs when magnesium acts on an excess of an alkyl or aryl halide in the presence of absolute ether. *n*-Hexyl bromide in this way yields *n*-dodecane ; similarly, cyclohexyl magnesium bromide and 2 : 3-dibromopropene yield cyclohexylbromopropene (C. V., I, 186).

$$C_6H_{13}.MgBr + C_6H_{13}Br = C_{12}H_{26} + MgBr_2.$$

$$C_6H_{11}MgBr + CH_2BrCBr:CH_2 = C_6H_{11}.CH_2CBr:CH_2.$$

Further applications of the Grignard reaction are given under Reactions XIV, XXII, XXXIV (*b*), XLIII, LX. See also Ann. Rep., 1932, 99.

Reaction IX. (*b*) **Action of Heat on the Compound formed by treating Magnesium Alkyl or Aryl Halide with a Ketone or Ester in absolute Ether** (Grignard). (B., 35, 2647).—When the Grignard reagent is treated with a ketone or ester, the following reaction occurs :—

$$RR_1CO + R_{11}MgI = RR_1R_{11}C.OMgI.$$

$$2RMgBr + R_1COOR_2 = R_1(R)_2COMgBr.$$

This latter compound when treated with water is hydrolysed to a tertiary alcohol $RR_1R_{11}COH$. If, however, the anhydrous reaction mixture be heated, an olefine is formed.

$$CH_3I + Mg = CH_3MgI.$$

$$CH_3MgI. + C_6H_5.CO.CH_3 = C_6H_5(CH_3)_2COMgI.$$

$$C_6H_5(CH_3)_2COMgI = C_6H_5(CH_3).C:CH_2 + Mg(OH)I.$$

Acetophenone and magnesium methyl iodide yield 2-phenyl-1-propene. As can be seen from the equation, one at least of the radicals R, R_1, R_{11}, must have a non-tertiary carbon linked in the intermediate compound to the "hydroxy-magnesium-iodide" carbon.

PREPARATION 14.—αα-**Diphenylmethylethylene** (αα-*Diphenylpropene*).

$(C_6H_5)_2C : CH.CH_3$. $C_{15}H_{14}$. 194.

The Grignard reagent is prepared from 6 gms. (2 mols.) of dry magnesium and 39 gms. (2 mols.) of ethyl iodide (redistilled), as described in Preparation 19, 120 c.cs. of anhydrous ether being used. 23 gms. (1 mol.) of dry, finely-divided benzophenone are added, the flask being cooled if the reaction becomes too vigorous. The mixture is then heated 6 hours on a water bath, treated with dilute acid, extracted with ether, the ether removed on a water bath, and the residue fractionated under reduced pressure, the fraction 169°–170° at 18 mms. being separately collected and recrystallised from petroleum ether.

$$C_2H_5.Mg.I + (C_6H_5)_2CO \longrightarrow (C_6H_5)_2C(OMgI)CH_2CH_3.$$

$$(C_6H_5)_2C(OMgI)CH_2CH_3 \longrightarrow (C_6H_5)_2C{=}CH.CH_3 + Mg(OH)I.$$

Colourless crystals; M.P. 52°; B.P.^{18} 169°–170°. (B., 35, 2647.)

C. V., I, 226; II, 606, give similar preparations of diphenyl- and triphenyl-ethylene.

Reaction IX. (*c*) **Action of Dialkyl Sulphates on Magnesium Alkyl or Aryl Halide** (Grignard).—When a Grignard compound is treated with dialkyl sulphate, alkylation of the alkyl or aryl group takes place, the metal-halogen residue being split off. (B., 36, 2116. See also O. S., XI, 66.)

$$R.Mg.Br + (CH_3)_2SO_4 = R.CH_3 + Br.Mg.(CH_3)SO_4.$$

It will be noted that in the Grignard reactions so far described, only bromo- or iodo-compounds are mentioned. Chlorine compounds do not enter so readily into this reaction; to induce them to react it is usually necessary to add a crystal of iodine (B., 38, 2759), or mercuric chloride (C., 1907, I, 872), or a previously prepared magnesium solution (B., 38, 1746; C., 1907, I, 455), or a small amount of Gilman's catalyst (C. V., II, 361), which is prepared by heating an alloy of Mg containing 12·75% of Cu with about 20% iodine by weight *in vacuo*.

By the method above outlined, toluene has been prepared from bromobenzene, *p*-xylene from *p*-bromotoluene and isodurene from bromomesitylene (C. V., II, 380).

PREPARATION 15.—*p*-**Xylene** (1 : 4-*Dimethylbenzene*).

C_8H_{10}. 106.

The Grignard reagent is prepared, as in Preparation 19. by heating 67 gms. (1 mol.) *p*-bromotoluene, 10 gms. (1 mol.) of dry magnesium and 200 c.cs. of anhydrous ether. When almost all the magnesium has disappeared a solution of 50 gms. (1 mol.) of dimethyl sulphate (caution!) in anhydrous ether is added. A vigorous reaction takes place, and after it subsides the reaction product is poured on to ice. The ether is removed by distillation, and the residue is steam distilled. The oil is separated from the distillate and fractionated, the fraction 136°–140°, being collected.

$$CH_3C_6H_4Br \longrightarrow CH_3C_6H_4MgBr \longrightarrow CH_3.C_6H_4.CH_3.$$

Yield.—75% theoretical (30 gms.). Colourless oil: characteristic odour; B.P. 138°; D. $^{20}_{4}$ 0·869. (B., 36, 2166.)

Owing to the closeness of the boiling points of the three xylenes they cannot be readily separated by ordinary distillation. A method such as the above, by which one isomer can be obtained free from the others, in a good yield, is of importance. For some details on magnesium aryl halides, see B., 36, 2898, and O. S., X, 4.

Note.—Dialkyl sulphates are extremely poisonous; on no account must their vapour be inhaled. Work with them should be carried out in a good fume cupboard; they should be added to mixtures from a tap funnel, for if spilled on the hands they are absorbed through the skin. Should any fall on the clothes, these must be changed at once. See also p. 2 and 266.

Reaction X. (*a*) **Action of Zinc Alkyl on Alkyl Halides to form Hydrocarbons.**—The action of zinc alkyl on various types of compounds is much the same as that of magnesium alkyl or aryl halide. Before the discovery of the latter, zinc alkyl was widely used as a general synthetic reagent, but its spontaneous inflammability led to its replacement by the more conveniently prepared Grignard reagent; it does not form aryl compounds; even in alkyl syntheses it is not nearly so widely applicable, though it reacts more smoothly in certain instances.

$$Zn(CH_3)_2 + 2CH_3I = ZnI_2 + 2C_2H_6.$$

Lithium alkyls obtainable from lithium and alkyl bromides in nitrogen react similarly to Grignard reagents and are useful in syntheses in which these reagents fail or are not formed (Am. Soc., 54, 1957). See also *Newer Methods of Preparative Organic Chemistry*, Wittig, p. 571.

An interesting extension of the Friedel-Crafts' reaction, by which paraffins are converted into cyclo-paraffins, is described in B., 66, 1892. The reaction is summarised in A., 510, 269.

Reaction X. (*b*) **Catalytic Conversion of Simple Hydrocarbons into more Complex Hydrocarbons.**—These reactions are usually accomplished at high temperatures in presence of catalysts. Acetylene, propylene and even methane can be converted into benzene and other complex hydrocarbons. (E.P., 374,422; 369,351; 366,394.)

Within recent years important industrial developments have taken place in the petroleum industry in which simple gaseous hydrocarbons (usually olefines from cracking processes) are converted catalytically into liquid hydrocarbons for special purposes or into polymerised products such as synthetic rubber. In presence of sulphuric acid isobutene is dimerised to di-isobutylene or iso-octene which on hydrogenation yield iso-octane (2 : 2 : 4-trimethyl pentane). The same compound is obtained from a mixture of isobutene and isobutane, the latter being derived by isomerisation of *n*-butane, catalytically, or by action of heat.

$$(CH_3)_2C{=}CH_2 \longrightarrow (CH_3)_3C.CH_2{-}C(CH_3){=}CH_2 \quad \text{iso-octene.}$$

$$(CH_3)_2C{=}CH_2 + (CH_3)_3CH \longrightarrow (CH_3)_3C.CH_2{-}CH(CH_3)_2 \quad \text{iso-octane.}$$

$$n(CH_2CH{=}CHCH_2) \longrightarrow (CH_2CH{=}CH.CH_2)_n \quad \text{buna rubber.}$$

The Fischer-Tropsch reaction consists of treating a mixture of carbon monoxide and hydrogen (from water gas) at 200° in presence of catalysts

(Ni/ThO_2). Hydrocarbons ranging from methane to high melting waxes are obtained at or near atmospheric pressure.

$$nCO + 2nH_2 \longrightarrow C_nH_{2n} + nH_2O.$$

$$nCO + (2n + 1)H_2 \longrightarrow C_nH_{2n+2} + nH_2O.$$

See also J. Eng., 1938, 58 ; 1940, 528. Am. Soc., 1946, 1615.

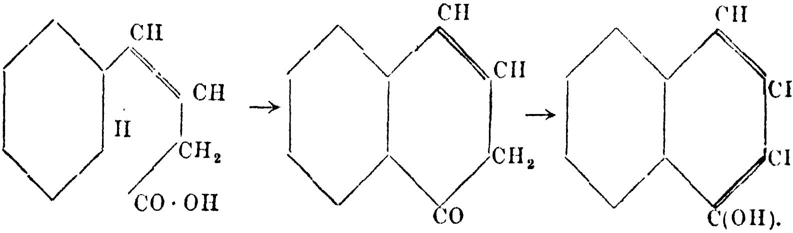
CHAPTER IV

CARBON TO CARBON

HYDROXY COMPOUNDS

The condensations now to be considered include all those in which the reaction is such that there is a hydroxyl group in the final product.

Reaction XI. Intramolecular Elimination of Water from certain Molecules. (A., 227, 242.)—When β-benzalpropionic acid is heated, water is eliminated and α-naphthol is formed. This synthesis, which is of theoretical interest, was discovered by Fittig. It is one of the proofs of the structure of naphthalene. Compare Reaction XVIII.



Reaction XII. Reduction of Aldehydes and Ketones to Pinacols. (B., 27, 456.)—When ketones are reduced to secondary alcohols, some intermolecular condensation usually occurs, and pinacols are formed.

$$2RR_1CO + 2H = RR_1C(OH).C(OH).RR_1.$$

This side reaction cannot be avoided when reducing aliphatic ketones, but in the aromatic series either product can be obtained by varying the conditions of the reduction. An alkaline reduction favours alcohol production ; pinacols are formed when acid reducing agents are employed (see Preparation 16).

Pinacols can also be obtained by using suitable electrolytic reductions. Aldehydes, too, have been brought within the scope of the reaction. Thus hydrobenzoin [*s*-diphenyl-ethan-diol] has been prepared from benzaldehyde by an acid reduction.

$$2C_6H_5.CHO \longrightarrow C_6H_5.CH(OH).CH(OH).C_6H_5.$$

Acetone gives the simplest pinacol (see C. V., I, 459).

$$2(CH_3)_2CO \longrightarrow (CH_3)_2C(OH)C(OH)(CH_3)_2.$$

The pinacols formed from acetophenone, benzophenone, and many other ketones are similar in structure (C., 1096, II, 148 ; B., 27, 454 ; C., 1900, II, 794 ; C., 1903, II, 23).

Preparation 16.—Benzpinacol (*αβ-Dihydroxy-tetraphenylethane*).

$$(C_6H_5)_2.C(OH).C(OH).(C_6H_5)_2. \qquad C_{26}H_{22}O_2. \qquad 366.$$

5 gms. (2 mols.) of benzophenone are boiled for ¼ hour with 50 gms. of 85% acetic acid and 10 gms. of zinc foil, the whole being well shaken throughout. The liquid is decanted from the zinc residues, cooled, and filtered ; the filtrate is again boiled up with zinc, and this process repeated a third time, the same filter being used each time. The benzpinacol remaining on the filter is then washed with 85% acetic acid, and recrystallised from 13 parts of boiling glacial acetic acid.

Yield.—90% theoretical (4·5 gms.). Colourless crystals ; M.P. (with decomposition) 168°. (C., 1881, 150 ; A., 133, 26 ; B., 10, 1473.)

For photochemical reduction of benzophenone to benzpinacol by means of isopropyl alcohol, see O. S., XIV, 8.

For the " pinacolone transformation " see p. 86.

Reaction XIII. Condensation of a Phenol with Formaldehyde (Lederer-Manasse). (B., 27, 2411.)—This reaction can take three different courses according to conditions.

(i) With the more powerful condensing agents, e.g. caustic alkalis or hydrochloric acid, a diphenylmethane compound is usually formed.

$$2C_6H_5OH \ + \ H.CHO \ = \ HO.C_6H_4.CH_2.C_6H_4OH + H_2O.$$

(ii) The less powerful condensing agents, e.g. alkali carbonates, alkaline earth oxides, lead oxide, or dilute acids or alkalis, give a benzyl alcohol or sometimes a di-(hydroxy-methyl) compound.

$$C_6H_5OH \ + \ H.CHO \ = \ OH.C_6H_4.CH_2OH$$

$$C_6H_4(CH_3)(OH)[1:4] + 2H.CHO = C_6H_2(CH_3)(OH)(CH_2OH)_2[1:4:3:5].$$

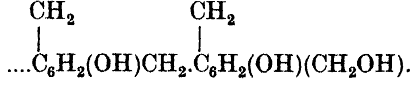
(iii) Hydrochloric acid sometimes gives a benzyl chloride derivative, the benzyl alcohol first formed being chlorinated by the acid. Such chlorides are easily hydrolysed to the alcohol (see Preparation 126).

$$OHC_6H_4.Cl[1:2] \ + \ H.CHO \longrightarrow C_6H_3(OH)(Cl)(CH_2OH)[1:2:4]$$

$$\longrightarrow C_6H_3(OH)(Cl)(CH_2Cl)[1:2:4].$$

In all three cases the *para*-position to the hydroxyl group is preferred ; if it is occupied, condensation takes place, but less readily, in the *ortho*-. The methylol compounds readily polymerise on suitable treatment to give thermoplastic and thermosetting resins (Novolak Bakelite).

$$....C_6H_2(OH)(CH_2OH)CH_2.C_6H_2(OH)(CH_2OH)$$



$$\begin{array}{l} ....C_6H_2(OH)CH_2.C_6H_2(OH)(CH_2OH) \\ \quad\;\, | \qquad\qquad\qquad\; | \\ \quad CH_2 \qquad\qquad\;\; CH_2 \\ \quad\;\, | \qquad\qquad\qquad\; | \\ ....C_6H_2(OH)CH_2.C_6H_2(OH)(CH_2OH). \end{array}$$

Similar condensation and polymerisation can take place with phenol sulphonic acids to give synthetic tanning agents (Syntans).

For other formaldehyde condensations, see Reactions XIX (*b*), XXXIII (*a*).

Preparation 17.—*o*- and *p*-**Hydroxybenzyl Alcohols** (1 : 2- and 1 : 4-*Methylolhydroxybenzenes*).

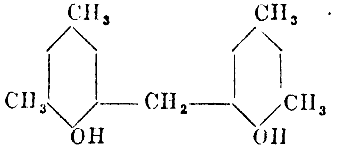
$C_6H_4.(OH)(CH_2OH)$. $C_7H_8O_2$. 124.

30 gms. (1 mol.) of phenol are dissolved in 150 c.c. (slight excess) of 10% caustic soda ; 35 gms. (excess) of 40% formaldehyde solution are added, and the whole allowed to remain at room temperature for 6 days. It is neutralised with hydrochloric acid, extracted repeatedly with ether, and the latter removed on a water bath. If necessary the residue is steam distilled to remove unchanged phenol, and the benzyl alcohols which are left are then shaken for some time with cold benzene until nothing further dissolves. The *ortho*-compound, which is much the more soluble, is thus separated from the *para*-.

$$C_6H_5(OH) + H.CHO = OH.C_6H_4.CH_2OH.$$

Yield.—Including both compounds, 80% theoretical (32 gms.). *o*-Hydroxybenzyl alcohol (saligenin) forms colourless crystals ; M.P. 82° ; the *para*-compound melts at 112°. (B., 27, 2411.)

Preparation 18.—3 : 5 : 3′ : 5′-**Tetramethyl-2 : 2′-Dihydroxydiphenylmethane.**



$C_{17}H_{20}O_2$. 256.

10 gms. (2 mols.) of xylenol (1 : 3-dimethyl-4-hydroxybenzene) are dissolved in 300 c.cs. (excess) of 1·5% caustic soda solution ; 5 gms. (excess) of 40% formaldehyde solution are added, and the mixture allowed to stand for 4 days. It is then acidified with acetic acid and extracted with ether, the solvent removed on a water bath, and the residual oil left in a vacuum over sulphuric acid until at length it becomes almost a solid. The latter is recrystallised several times from ligroin.

$$2C_6H_3(CH_3)_2(OH)[1:3:4] + CH_2O = [3:5:6]C_6H_2(CH_3)_2(OH).CH_2.C_6H_2\text{—}(CH_3)_2(OH)[3':5':6'] + H_2O.$$

Long colourless needles ; easily soluble in alcohol, ether, chloroform, acetic acid, benzene ; sparingly soluble in cold ligroin ; M.P. 145°–146° ; when boiled for 1 hour with acetic anhydride a diacetate is obtained which when recrystallised from dilute alcohol forms fine needles, M.P. 86°. (B., 40, 2526.)

Reaction XIV. (*a*) **Action of Magnesium Alkyl or Aryl Halide on Aldehydes and Ketones** (Grignard). (B., 31, 1003.)—This phase of the Grignard reaction can be utilised for the preparation of all types of alcohols (C., 1901, I, 725 ; II, 622 ; 1902, I, 414).

(i) Primary alcohols can be obtained from formaldehyde, or rather from its polymer trioxymethylene, which has to be used in place of the usual aqueous solution. Magnesium phenyl iodide and trioxymethylene yield benzyl alcohol for example, the usual Grignard intermediate compound being formed.

$$C_6H_5MgI + CH_2O \longrightarrow H_2C(C_6H_5)OMgI \longrightarrow C_6H_5CH_2OH.$$

(ii) Other aldehydes yield in the same way secondary alcohols.

Acetaldehyde with methyl iodide or isopropyl bromide give isopropyl alcohol or methyl isopropyl carbinol (C. V., II, 406).

$$CH_3CHO + MgCH_3I \longrightarrow (CH_3)CH(CH_3)OMgI \longrightarrow (CH_3)_2CHOH.$$

Benzaldehyde and magnesium phenyl bromide or iodide give diphenyl carbinol.

$$C_6H_5CHO + MgC_6H_5I \longrightarrow (C_6H_5)_2CHOMgI \longrightarrow (C_6H_5)_2CHOH.$$

(iii) Tertiary alcohols are formed from ketones.

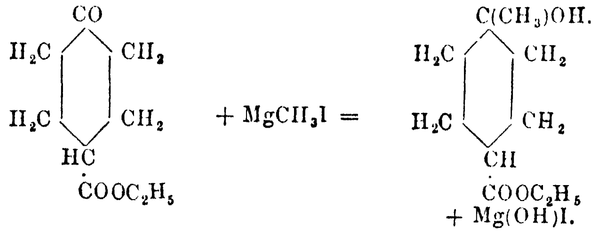
The simplest tertiary alcohol is prepared from acetone and magnesium methyl iodide.

$$Mg(CH_3)I + (CH_3)_2CO \longrightarrow (CH_3)_2C(CH_3)OMgI \longrightarrow (CH_3)_3C(OH).$$

Methyl ethyl ketone and methyl iodide give tertiary amyl alcohol.

$$CH_3COC_2H_5 + CH_3MgI = (CH_3)_2C(OH)C_2H_5 + Mg(OH)I.$$

In the aromatic series, acetophenone and methyl iodide, for example, yield phenyldimethylcarbinol. An important step in the synthesis of *i*-terpineol is the preparation of ethyl-δ-hydroxy-hexahydro-*p*-toluate from ethyl-δ-ketohexahydrobenzoate and magnesium methyl iodide.



The usual precautions must be taken in all these reactions, to guard against the possibility of moisture being present.

PREPARATION 19.—**Phenylmethylcarbinol** (1-*Phenyl*-1-*ethanol*).

$$HC(CH_3)(C_6H_5)OH. \qquad C_8H_{10}O. \qquad 122.$$

All reagents used must be thoroughly dry.

(1) 36 gms. (1 mol.) of methyl iodide which have been allowed to stand for 12 hours over calcium chloride and then redistilled, are mixed with 50 c.cs. of ether purified and dried as described on p. 216. 20 c.cs. of this mixture are run into a flask fitted with a dropping funnel and long reflux condenser. The flask contains 6 gms. magnesium turnings available commercially for Grignard preparations, or alternatively, 6 gms. ribbon, which has been cleaned with emery paper, washed with ether, and dried in an air oven at 110°. If necessary, the reaction is started by adding a

crystal of iodine. When the first reaction has subsided, 70 c.cs. of dry ether are added, and the remainder of the mixture of alkyl iodide and ether run in drop by drop from the tap funnel. The contents of the flask are then boiled on the water bath until all (or nearly all) of the magnesium has dissolved. E.P., 398561 describes preparation without ether.

(2) The flask is now disconnected, and under cooling by ice-water, 26 gms. (1 mol.) of freshly-distilled benzaldehyde mixed with an equal volume of dry ether are dropped in from a tap funnel with constant shaking, and the whole allowed to stand for 12 hours.

(3) Just sufficient hydrochloric acid to dissolve the precipitate is added with constant shaking and cooling. The aqueous layer is separated, and the ether washed first with sodium bicarbonate solution, then with sodium bisulphite (to remove free iodine) and again with sodium bicarbonate. The extract is dried over potassium carbonate and the ether removed on a water bath. The carbinol which remains is fractionated under reduced pressure.

(1) $CH_3I + Mg = CH_3MgI$.

(2) $C_6H_5CHO + CH_3MgI = C_6H_5(CH_3)CH(OMgI)$.

(3) $(C_6H_5)(CH_3)CH(OMgI) + H_2O = (C_6H_5)(CH_3)CHOH + (OH)MgI$.

Yield.—56% theoretical (20 gms.). Colourless liquid ; insoluble in water ; B.P. ^{15} 100° ; B.P. ^{28} 110°–111° ; B.P. ^{40} 118° ; B.P. ^{760} 203° ; D. $^{15}_{4}$ 1·013. (C. r., 130, 1322 ; B., 31, 1003.)

The same method may be used for phenylethyl carbinol taking 39 gms. (1 mol.) of ethyl iodide. The compound is obtained as a colourless liquid ; B.P. ^{760} 221° ; D. $^{15}_{4}$ 0·9900.

PREPARATION 20.—*tert.*-**Butyl Alcohol** (*Trimethylcarbinol*).

$(CH_3)_3C(OH)$. $C_4H_{10}O$. 74.

The Grignard compound is prepared as described in Preparation 19 from 36 gms. (1 mol.) of dry methyl iodide, 120 c.cs. of sodium-dried ether, and 6 gms. (1 mol.) of dry magnesium ribbon or powder. 14 gms. (1 mol.) of *dry* acetone dissolved in 30 c.cs. of *dry* ether are slowly added from a tap funnel with constant shaking and under cooling by ice-water. A white bulky precipitate of the magnesium compound separates. After standing overnight, just sufficient dilute sulphuric acid to dissolve the precipitate is added with constant shaking and cooling. The ether solution of the alcohol separates and is withdrawn and distilled.

$$(CH_3)_2CO + Mg.CH_3.I = (CH_3)_2C(CH_3).OMgI.$$

$$(CH_3)_3C(OMgI) + H_2O = (CH_3)_3C(OH) + Mg(OH)I.$$

Colourless crystals ; soluble in water ; M.P. 25° ; B.P. 83° ; D. $^{30}_{4}$ 0·7788.

In a similar manner dimethylethylcarbinol may be prepared from ethyl iodide. It is obtained as a colourless liquid, soluble in water ; B.P. ^{760} 102° ; D. $^{15}_{4}$ 0·8144. See also C. V., II, 602.

The following shows the method of preparing and using magnesium aryl halides in this synthesis.

PREPARATION 21.—**Triphenylcarbinol** (*Triphenylmethanol*).

$(C_6H_5)_3C(OH)$. $C_{19}H_{16}O$. 260.

1·2 gms. (1 mol.) of bright magnesium is dried in the air oven at 110°, and treated in a well-dried, round-bottomed, 300-c.c. flask with 8 gms. (1 mol.) of freshly-distilled bromobenzene in 40 gms. of sodium-dried ether to which a crystal of iodine is added. The flask is warmed on a water bath, under a reflux condenser with $CaCl_2$ tube attached in a current of dry hydrogen (caution! no flame must approach the end of the condenser). Light flocculae appear due to unavoidable moisture, but they soon disappear, and then the magnesium begins to dissolve. When the magnesium has completely dissolved, except for traces of impurities—this should not take more than 2 hours—the heating is stopped, and the liquid is treated at ordinary temperature with 9·1 gms. (1 mol.) of benzophenone dissolved in 25 gms. of sodium-dried ether. The liquid becomes red, then a thick tough precipitate separates, which, when the heating is renewed, reacts vigorously, and solidifies in the course of half an hour. The reaction mixture is then allowed to cool, and treated with pieces of ice and sulphuric acid. When decomposition is complete, steam is passed through until the distillate is clear. This removes ether and all by-products (benzene, diphenyl); almost pure triphenylcarbinol remains, and is recrystallised from benzene.

$$C_6H_5.Br + Mg = C_6H_5.Mg.Br.$$
$$C_6H_5.MgBr + C_6H_5.CO.C_6H_5 = (C_6H_5)_2C(C_6H_5)OMgBr.$$
$$(C_6H_5)_2C(C_6H_5)(OMgBr) + H_2O = (C_6H_5)_3C.OH + OH.Mg.Br.$$

Yield.—75% theoretical (10 gms.). Colourless crystals; soluble in ether and hot benzene; gives a deep red solution in strong sulphuric acid; in glacial acetic acid it is colourless, but addition of a drop of conc. hydrochloric acid gives a deep yellow coloration; M.P. 159°. (B., 37, 2755.)

Diphenylmethylcarbinol is prepared in the same way from acetophenone.

Reaction XIV. (*b*) **Action of Magnesium Alkyl or Aryl Halide on Esters, Acyl Chlorides, and Acid Anhydrides.** (C., 1901, I, 725; II, 622; 1902, I, 1414.)—Tertiary alcohols are obtained, except in the case of formic esters when secondary alcohols are formed. The reaction has wide application.

$$RCOOC_2H_5 + 2MgR_1Br \longrightarrow R(R_1)_2COMgBr + Mg(OC_2H_5)Br.$$
$$RC(R_1)_2OMgBr + H_2O \longrightarrow R(R_1)_2C(OH) + Mg(OH)Br.$$
$$RCOCl + 2MgR_1Br \longrightarrow RC(R_1)_2OMgBr + MgBrCl.$$
$$(RCO)_2O + 4MgR_1Br \longrightarrow 2R(R_1)_2COMgBr + (MgBr)_2O.$$
$$2R(R_1)_2COMgBr + H_2O \longrightarrow 2R(R_1)_2C(OH) + (MgBr)_2O.$$

The addition of anhydrous cadmium chloride to a Grignard reagent yields alkyl cadmium halide which combines with acid chlorides to give ketones without further reaction to form tertiary alcohols :—

$$RCdX + R_1COCl \longrightarrow RCOR_1 + CdXCl.$$

The yields are in most cases good, and the reactions smooth. A great advantage of the Grignard reaction is that it can be applied to complicated derivatives of the reacting substances. This renders it valuable in the synthesis of substances such as, e.g. terpenes. The following list should give some idea of the scope of the reaction :—

(i) Ethyl formate and magnesium ethyl iodide give diethyl carbinol.

(ii) Methyl acetate and magnesium methyl iodide give tertiary butyl alcohol (cf. Reaction XIV (*a*) (iii)).

(iii) Ethyl Δ'-tetrahydro-*p*-toluate, see p. 80, and magnesium methyl iodide give *i*-terpineol.

(iv) Ethyl chloroacetate and magnesium phenyl bromide give diphenylchlorohydrin.

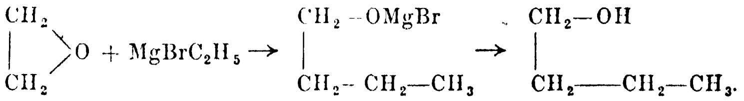
(v) Methyl benzoate and magnesium phenyl bromide give triphenyl carbinol.

(vi) Ethyl carbonate and magnesium alkyl halides give tertiary alcohols (C. V., II, 602).

(vii) Acetyl chloride and magnesium methyl iodide give trimethyl carbinol.

(viii) Acetic anhydride and magnesium ethyl iodide give diethylmethyl carbinol.

It may be mentioned that the " Grignard " reactions can also be applied to the production of primary alcohols by the interaction of ethylene oxide and magnesium alkyl halide.



PREPARATION 22.—**Triphenylcarbinol** (*Triphenylmethanol*).

$(C_6H_5)_3C(OH)$. $C_{19}H_{16}O$. 260.

(It is imperative that not only the reagents but also the apparatus and corks should be thoroughly dry.)

2·5 gms. (1 mol.) of bright magnesium previously dried in a steam oven, 3 gms. (1 mol.) of bromobenzene previously dried over calcium chloride and 7 c.cs. ether previously dried first over calcium chloride and then over sodium are warmed gently without shaking, under a reflux condenser provided with a calcium chloride tube until reaction becomes rapid. If the reaction is not initiated by heating, a small crystal of iodine may be added. When reaction has commenced, 13 gms. bromobenzene in 40 c.cs. dry ether are added from a tap funnel inserted through a second hole in the stopper at such a rate as to cause vigorous refluxing without the application of external heat. When addition is complete and reaction slackens, the mixture is gently warmed on a steam bath for 30 minutes when the magnesium almost completely dissolves.

The flask and contents are cooled in ice-water, 6 gms. ethyl benzoate in 6 c.cs. dry ether slowly added with shaking and the mixture kept at room temperature for 30 minutes. The contents are poured into a mixture of 50 gms. ice, 100 c.cs. water and 6 c.cs. conc. sulphuric acid, thoroughly shaken ; then 80 c.cs. ordinary grade ether added to ensure solution of the carbinol and the upper layer separated in a funnel. This is washed twice with dil. sulphuric acid, once with water and then steam distilled until no more organic material (diphenyl, unchanged bromobenzene and ether) distils. The non-volatile triphenylcarbinol is collected, pressed, and recrystallised from the minimum of alcohol.

$$C_6H_5COOC_2H_5 + 2C_6H_5MgBr \longrightarrow (C_6H_5)_3COMgBr \longrightarrow (C_6H_5)_3C(OH).$$

Yield.—75% theoretical (18 gms.). See p. 82. (O. S., XXIII, 98.)

Reaction XV. Action of Zinc Alkyl on Aldehydes, on certain Ketones, or on Acyl Chlorides. (A., 223, 162.)—As with other "zinc alkyl" reactions the corresponding Grignard reaction described in Reaction XIV has replaced it almost completely, so that the following is mainly of historical interest:

(*a*) With *all* aldehydes, except formaldehyde, secondary alcohols are formed (A., 213, 369; B., 14, 2557).

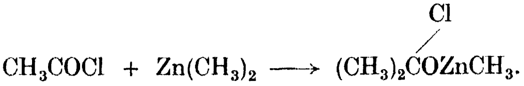
$$CH_3CHO \longrightarrow (CH_3)_2CHOZnCH_3 \xrightarrow{H_2O} (CH_3)_2CHOH.$$

This reaction only occurs with zinc methyl and zinc ethyl.

(*b*) In general ketones do not react with zinc alkyl. Exceptions are certain ketones with no methyl group attached directly to the carbonyl group, e.g. diethyl ketone and ethylpropyl ketone give tertiary alcohols (B., 19, 60; 21, R., 55).

$$(C_2H_5)_2CO \longrightarrow (C_2H_5)_3COZnC_2H_5 \xrightarrow{H_2O} (C_2H_5)_3C(OH).$$

(*c*) Acid chlorides also give tertiary alcohols.



$$CH_3COCl + Zn(CH_3)_2 \longrightarrow (CH_3)_2\overset{Cl}{C}OZnCH_3.$$

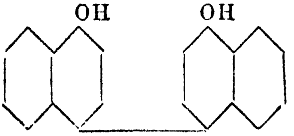
$$(CH_3)_2C(Cl)(OZnCH_3) + Zn(CH_3)_2 \longrightarrow (CH_3)_3COZnCH_3 + Zn(CH_3)(Cl).$$

$$(CH_3)_3C(O.Zn.CH_3) \xrightarrow{H_2O} (CH_3)_3C(OH).$$

The preparation of zinc diethyl is given in C. V., II, 184.

Reaction XVI. Action of certain Oxidising Agents on α- and β-Naphthols. (J. R. C. S., 6, 183.)—If to an aqueous solution of a naphthol a few drops of a neutral aqueous solution of ferric chloride be added, a green coloration is produced, and, after a time, a flocculent precipitate of dinaphthol. Performed in this way on the "test tube" scale, the reaction is very useful for identification purposes.

Preparation 23.—**αα-Dinaphthol** (4 : 4′-*Dihydroxy*-1 : 1′-*dinaphthyl*).



$C_{20}H_{14}O_2$. 286.

10 gms. (2 mols.) of α-naphthol are dissolved in the minimum quantity of boiling water, and ferric chloride solution is gradually added on cooling,

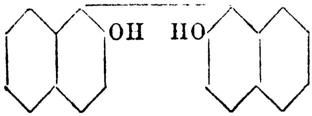
until the precipitate formed is a bright reddish-violet. The latter is filtered off, and is boiled once with water, and twice with benzene. The residue is recrystallised from alcohol.

$$2C_{10}H_7OH + O = OH.C_{10}H_6.C_{10}H_6.OH + H_2O.$$

Yield.—35–40% theoretical (7–8 gms.). Shining rhombic crystals; insoluble in water; soluble in alcohol and ether; slightly soluble in chloroform and benzene; M.P. 300°. (J. R. C. S., 6, 183.)

A solution of α-naphthol in very dilute alcohol can also be used in the above preparation.

PREPARATION 24.—*ββ*-**Dinaphthol** (2 : 2'-*Dihydroxy*-1 : 1'-*dinaphthyl*).



$C_{20}H_{14}O_2$. 286.

10 gms. (2 mols.) of β-naphthol are dissolved in an excess of ether, and 16 gms. (excess) of anhydrous ferric chloride are gradually added to the solution in a flask fitted with a reflux condenser. Much heat is evolved during this operation. The mixture is then refluxed on a water bath until most of the naphthol is oxidised. (To test this a small portion of the ethereal solution is treated with an excess of dilute hydrochloric acid, and the ether evaporated. The dinaphthol separates out even in the warm as an oil whilst β-naphthol crystallises out on cooling.) When this is the case, the ether is removed on a water bath, water and powdered calcium carbonate are added to the residue, and the whole well shaken. Excess caustic soda is then added, the solution is filtered and precipitated with dilute sulphuric acid. The precipitate is washed with boiling water or boiling ligroin, and recrystallised from benzene.

$$2C_{10}H_7OH + 2FeCl_3 = OH.C_{10}H_6.C_{10}H_6.OH + 2FeCl_2 + 2HCl.$$

Yield.—40% theoretical (8 gms.). Colourless needles from alcohol, prisms from a mixture of carbon disulphide and alcohol; insoluble in water; slightly soluble in chloroform; soluble in alcohol and ether; M.P. 216°; M.P. (corr.) 218°; Forms a picrate. (J. R. C. S., 6, 187; B., 15, 2166.) See also Abs. A., 1938, 11.

CHAPTER V

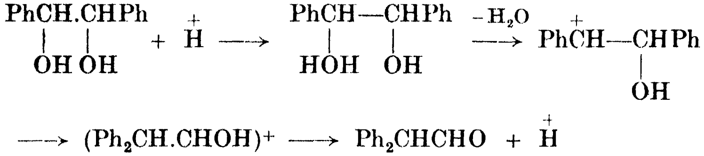
CARBON TO CARBON

OXY COMPOUNDS

In the following section are discussed the more important of those condensations which give rise to oxy compounds—aldehydes, ketones, and quinones. The reactions in this section may be divided into two classes—those in which the product is an oxy compound, because oxy compounds only undergo the reaction, e.g. Reaction XX (*b*); and those in which an oxy compound is actually formed during the action from non-oxy starting substances, e.g. Reaction XVII.

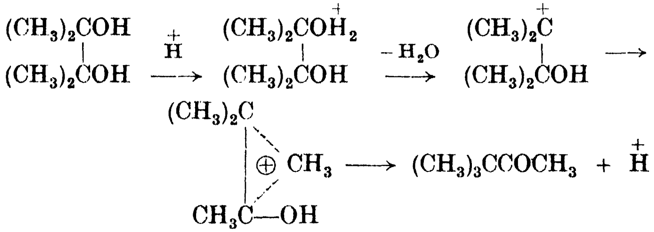
Owing to the peculiar activating properties of the oxy group, the former reaction is more important than those discussed in the previous section.

Reaction XVII. Intramolecular Rearrangement of the Glycols (Pinacolone Transformation). (B., 36, 2016.)—Di-primary, primary-secondary, primary-tertiary, and di-secondary glycols yield aldehydes when heated with hydrochloric or sulphuric acid, or with certain dehydrating agents. (Ann. Rep., 1939, 195; Am. Soc., 1932, 3274.) Hydrobenzoin yields diphenylacetaldehyde; and di-tertiary glycols (pinacols) undergo this reaction with great readiness yielding pinacolones (see C. V., I, 462).



$$\begin{array}{ccccc}
\mathrm{PhCH.CHPh} & & \mathrm{PhCH{-}CHPh} & -\mathrm{H_2O} & \\
\vert \quad \vert & +\ \overset{+}{\mathrm{H}} \longrightarrow & \vert \quad \vert & \longrightarrow & \mathrm{Ph\overset{+}{C}H{-}CHPh} \\
\mathrm{OH\,OH} & & \mathrm{HOH\quad OH} & & \qquad \vert \\
 & & & & \qquad \mathrm{OH}
\end{array}$$

$$\longrightarrow (\mathrm{Ph_2CH.CHOH})^+ \longrightarrow \mathrm{Ph_2CHCHO} + \overset{+}{\mathrm{H}}$$



$$\begin{array}{cccccc}
\mathrm{(CH_3)_2COH} & + & \mathrm{(CH_3)_2CO\overset{+}{H}_2} & & \mathrm{(CH_3)_2\overset{+}{C}} & \\
\vert & \mathrm{H} & \vert & -\mathrm{H_2O} & \vert & \longrightarrow \\
\mathrm{(CH_3)_2COH} & \longrightarrow & \mathrm{(CH_3)_2COH} & \longrightarrow & \mathrm{(CH_3)_2COH} &
\end{array}$$

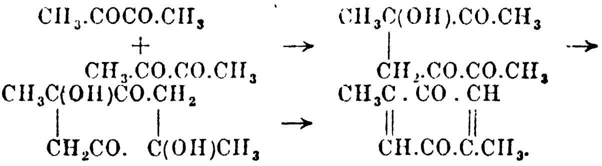
$$\begin{array}{l}
\mathrm{(CH_3)_2C} \\
\vert \\
\vert\ \oplus\ \mathrm{CH_3} \longrightarrow \mathrm{(CH_3)_3CCOCH_3} + \overset{+}{\mathrm{H}} \\
\vert \\
\mathrm{CH_3C{-}OH}
\end{array}$$

It is considered that the removal of hydroxyl by a proton leaves a sextet only of electrons around a carbon atom to which a radical migrates forming a new, but unstable, structure from which a proton is finally eliminated.

Ethers of glyclos behave similarly, in some cases with particular ease (B., 39, 2288; A., Ch. (8), 9, 484). For a corresponding reaction among ketones, see p. 118.

Reaction XVIII. Ring Formation by Elimination of Water or Halogen Hydride.—Many important syntheses of ring compounds come under this heading. Only a few can be mentioned.

(i) 1 : 2-Diketones containing a CH_2 group together with the CO group can be condensed to quinone derivatives—diacetyl, for example, readily yields dimethyl quinone—under the action of alkalis ; ketols are intermediately formed.

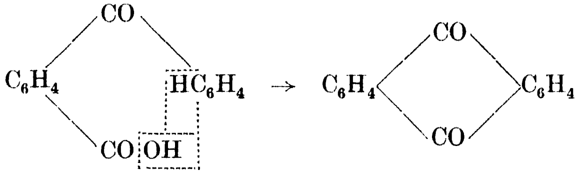


$$\begin{array}{l} CH_3.COCO.CH_3 \\ \qquad + \\ \qquad CH_3.CO.CO.CH_3 \end{array} \rightarrow \begin{array}{l} CH_3C(OH).CO.CH_3 \\ \quad | \\ CH_2.CO.CO.CH_3 \end{array} \rightarrow$$

$$\begin{array}{l} CH_3C(OH)CO.CH_2 \\ \;|\qquad\qquad | \\ CH_2CO.\ C(OH)CH_3 \end{array} \rightarrow \begin{array}{l} CH_3C\,.\,CO\,.\,CH \\ \quad \|\qquad\quad \| \\ \quad CH.CO.C.CH_3. \end{array}$$

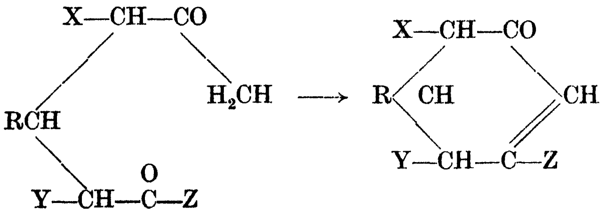
(B., 22, 2215 ; 28, 1845.)

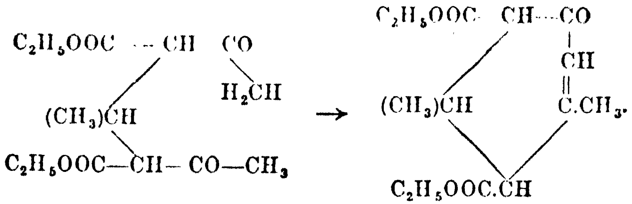
(ii) The *o*-benzoylbenzoic acids give anthraquinone derivatives on heating with dehydrating agents such as sulphuric acid or phosphorus pentoxide. Cf. synthesis of α-naphthol from β-benzalpropionic acid (Reaction XI). (Z. a., 19, 669.)



o-Benzoylbenzoic acid (Reaction XXXV (*a*)) itself yields anthraquinone, and 2-*p*-toluoylbenzoic acid gives 2-methyl-anthraquinone. These syntheses are of theoretical interest in throwing light on the structure of anthraquinone and hence of anthracene, and many of them are of considerable industrial importance (see Reaction XX (*a*), also Preparation 25).

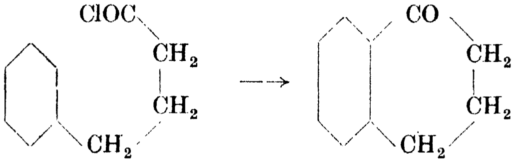
(iii) When ethylidene bisacetoacetic ester is refluxed with conc. sulphuric acid, simultaneous condensation to a ring compound, hydrolysis, and elimination of carbon dioxide take place, and a cyclic ketone is obtained. All compounds which, like ethylidene bisacetoacetic ester, contain 1 : 5-carbonyl groups and in addition a methyl group attached to one of them, undergo the same condensation with acids or alkalis, so that there exists here a very general method of passing from open-chain to ring compounds.





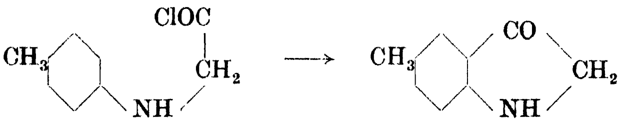
A further reaction then takes place in this particular instance (see Preparation 26), but in the general case the reaction goes no further. The compounds so obtained are all derivatives of cyclohexenone. These latter compounds may be transformed by various reactions into cycloparaffins on the one hand, and aromatic compounds on the other. This affords a method of passing from simple aliphatic to aromatic compounds (see Preparation 446). (A., 281, 25.)

(iv) General methods for effecting ring closure are by the Friedel and Crafts reaction on acid chlorides, or anhydrous hydrogen fluoride on free acids.



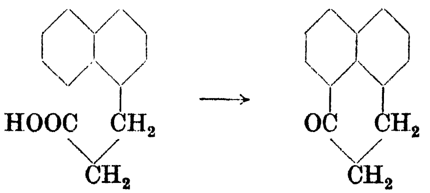
γ-phenylbutyrylchloride tetralone

Aluminium chloride or stannic chloride brings about intermolecular condensation of aryl substituted acyl chlorides, the ease of ring closure being determined by the size of ring formed and the effect of substituents.



chloroacetyl *p*- toluidine methyl oxindol

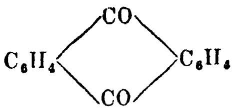
Anhydrous liquid hydrogen fluoride readily effects ring closure of aryl substituted aliphatic acids.



naphthylpropionic acid peri-naphthanone

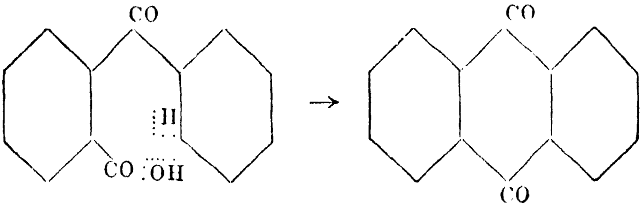
See *Organic Reactions*, Adams, Vol. II, 114.

Preparation 25.—Anthraquinone.



$C_{14}H_8O_2$. 208.

10 gms. (1 mol.) of *o*-benzoylbenzoic acid are mixed with 60 gms. of conc. sulphuric acid, heated to 150° for 1 hour, cooled and poured on to ice. The precipitated anthraquinone is collected and thoroughly washed, first with hot water, then with warm dilute (5 N) caustic soda and finally with warm water. It is dried in a steam oven, and completely purified by sublimation, at 250° (see p. 35).

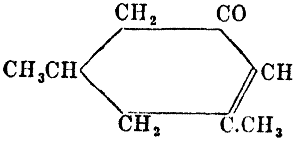


Yield.—Theoretical (9 gms.). Yellow needles; insoluble in water; somewhat soluble in benzene and the usual organic solvents; soluble in glacial acetic acid; M.P. 277°; sublimes at 250°; B.P. 382°. (Z. a., 19, 669.)

In the above preparation phosphorus pentoxide can equally well be used instead of sulphuric acid.

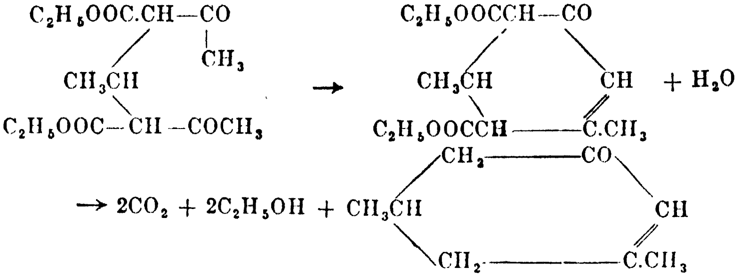
2-Methylanthraquinone can be prepared by heating 2-*p*-toluoylbenzoic acid with about 9 times its weight of oleum containing 20% SO_3. On precipitation with water, and recrystallising from dilute acetic acid, pale yellow needles are obtained, M.P. 177°. (B., 41, 3632; J. pr. [ii], 33, 318; A., 311, 178.)

Preparation 26.—1 : 3-Dimethyl-Δ^6-cyclohexen-5-one.



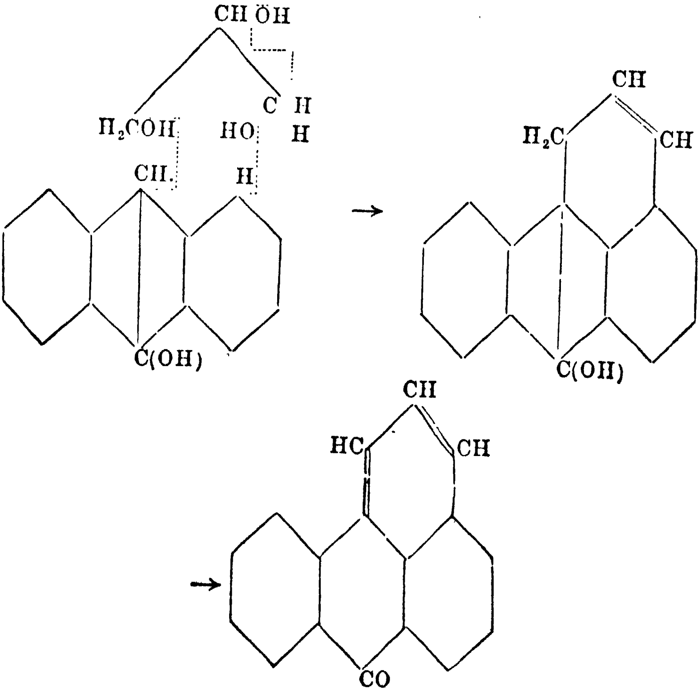
$C_8H_{12}O$. 124.

Crude ethylidinebisacetoacetic ester as prepared in Preparation 74 is melted on the water bath and poured into 500 c.cs. 20% sulphuric acid in a round-bottomed flask attached to a reflux condenser. A few pieces of porcelain chips are added, and the whole vigorously boiled for 7 hours. It is then steam distilled until the distillate measures about 100 c.cs. The distillate is then set aside in a well-stoppered bottle. The residue is again refluxed for 7 hours and again steam distilled, 100 c.cs. of distillate being again collected. The process is repeated a third time, and then steam is blown into the mixture until no oil, or only a trace, separates from a test portion when treated with solid caustic potash. To the three united distillates solid caustic potash is carefully added until the solution is saturated. A reddish-brown oil separates, and is removed by means of a separating funnel. The alcohol is distilled off, using a column, and the residue dried over anhydrous sodium sulphate. The dimethylcyclohexenone is then recovered from the residue by fractional distillation, the fraction 200°–215° being retained.



Yield.—75–90% theoretical (15–18 gms.). Colourless liquid, B.P. 211°. (A., 281, 111.)

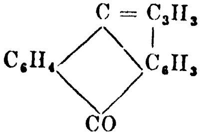
Reaction XIX. (*a*) **Condensation of Anthranol Derivatives with Glycerol.** (B., 44, 1666.)—This condensation gives rise to the benzanthrones which are used as intermediates in the dye industry. The reaction may be assumed to go as follows :



Benzanthrone.

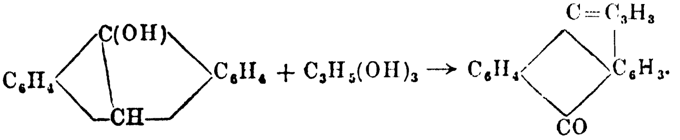
Sulphuric acid is the condensing agent used. The reaction might be compared with the preceding reaction and with Skraup's quinoline synthesis (see p. 170).

Preparation 27.—**Benzanthrone.**



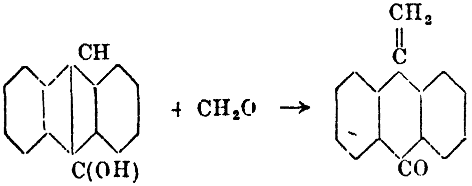
$C_{17}H_{10}O$. 230.

10 gms. (1 mol.) of anthranol are dissolved or suspended in 150 gms. of sulphuric acid (80%), and 10 gms. (excess) of glycerol are added. The mixture is carefully heated to 120°, when SO_2 is evolved, and kept there till the reaction is complete (4 hours). The cooled mass is poured into water, and the product which separates is collected, washed, boiled for 30 minutes with 13 parts by weight of 1% sodium hydroxide solution, pressed and dried. It is recrystallised from alcohol.

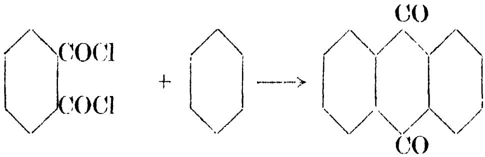


Pale yellow needles ; insoluble in cold alcohol and in dilute acids and alkalis ; soluble in conc. sulphuric acid with a reddish-brown colour and deep orange fluorescence ; M.P. 170°. (D.R.P., 176018 ; see also B., 44, 1666 ; O. S., XIV, 4 ; U.S.P., 1791309.)

Reaction XIX. (*b*) **Condensation of Anthranol Derivatives with Formaldehyde.** (A., 420, 134.)—The anthranols can also give rise to other intermediates by condensation with formaldehyde. Methylene anthraquinone is thus obtained from anthranol.



Reaction XX. (*a*) **Action of Metallic Zinc on a Mixture of an Aromatic Hydrocarbon and a Derivative of Phthalyl Chloride.**—This is a method of synthesising anthraquinone and its derivatives, and hence a method of elucidating their structure, and also the structure of anthracene. Otherwise the method is not of importance, but it may be in the future, since anthraquinone is in great and increasing demand for the production of vat-dyestuffs, such as indanthrene ; phthalyl chloride can be obtained readily from naphthalene. (See also Reaction XX (*b*) (vi).)



The action of zinc in this case resembles that of anhydrous aluminium chloride in the Friedel-Crafts reaction. Phthalyl chloride here reacts in the *s-* form (cf. Reaction XX (*b*) (vi)). Both forms have been prepared (A., 392, 245 ; M., 40, 81). The *s-* form melts at 15°–16°, the *as-* at 88°–89°, while both boil at 275° at 720 mms. The *s-* form is converted into the *as-* by the action of aluminium chloride, whilst the reverse change is effected by the action of heat or of hydrogen chloride. For preparation of phthalyl chloride, see C. V., 2, 528.

Reaction XX. (*b*) **Action of certain Anhydrous Metallic Halides (Aluminium Chloride, Aluminium Bromide, Aluminium and Hydrogen Chloride, Ferric Chloride) on a mixture of an Aromatic Hydrocarbon or certain Derivatives, and an Acyl Halide.** (Friedel-Crafts.) (A. Ch., [6], 1, 518.)—This is an even more important application of the Friedel-Crafts synthesis than the methods of synthesising hydrocarbons (pp. 65, 66). The reactions involved, using the same solvents and conditions as in Reaction VI, are more readily controlled since the products, in presence of aluminium chloride, do not undergo further condensations. (Ann. Rep., 1937, 251 ; *Aluminium Chloride*, Thomas.)

The reaction is represented electronically :

$$\begin{aligned} RCOX + AlCl_3 &\rightleftharpoons RCOCl.AlCl_3 \rightleftharpoons (RCO)^+(AlCl_4)^- \\ ArH + (RCO)^+ &\longrightarrow ArCOR + H^+ \\ H^+ + (AlCl_4)^- &\longrightarrow HCl + AlCl_3 \end{aligned}$$

and in summary :

$$ArH + RCOX \xrightarrow{AlCl_3} ArCOR + HX.$$

(i) Both aliphatic and aromatic acyl chlorides can be used.

$$\begin{aligned} C_6H_6 + CH_3COCl &= C_6H_5.CO.CH_3 + HCl. \\ C_6H_6 + C_6H_5COCl &= C_6H_5.CO.C_6H_5 + HCl. \end{aligned}$$

(ii) Homologues of both the reacting substances may be employed.

$$\begin{aligned} C_6H_6 + CH_3CH_2COCl &= C_6H_5.CO.CH_2.CH_3 + HCl. \\ C_6H_6 + C_6H_5CH_2COCl &= C_6H_5.CO.CH_2.C_6H_5 + HCl. \\ C_6H_5CH_3 + C_6H_5COCl &= p\text{-}CH_3C_6H_4COC_6H_5 + HCl. \end{aligned}$$

(iii) The acyl group enters mainly the *para*-position to the alkyl radical ; if that is occupied, it goes to the *ortho-*. A little of the *ortho-*compound is formed along with the *para-* in all cases, so that in preparing for instance, phenyl-*p*-tolyl-ketone, benzene and *p*-toluoyl chloride are used. (A., 189, 84 ; B., 12, 2299.)

$$C_6H_6 + p\text{-}CH_3C_6H_4COCl = p\text{-}CH_3C_6H_4COC_6H_5 + HCl.$$

The pure *o*- and *m*-compounds can be prepared in a similar manner.

(iv) Instead of the hydrocarbons the phenol ethers which react with great ease can be employed ; the same rules as to position apply.

$$C_6H_5.O.CH_3 + C_6H_5.CO.Cl = p\text{-}CH_3O.C_6H_4.COC_6H_5 + HCl.$$

(v) Substituted acid chlorides may be used to obtain substituted ketones.

$$C_6H_6 + p\text{-}Br.C_6H_4.COCl = p\text{-}BrC_6H_4COC_6H_5 + HCl.$$

$$C_6H_6 + p\text{-}NO_2C_6H_4COCl = p\text{-}NO_2C_6H_4COC_6H_5 + HCl.$$

(vi) The chlorides of the dibasic acids react in two ways : (*a*) With 1 mol. of hydrocarbon they give acid chlorides. (*b*) With 2 mols. of hydrocarbon di-ketones are formed, except in the case of phosgene.

$$COCl_2 + 2C_6H_6 = CO.(C_6H_5)_2 + 2HCl.$$

(B., 10, 1854.) See also E.P., 388734.

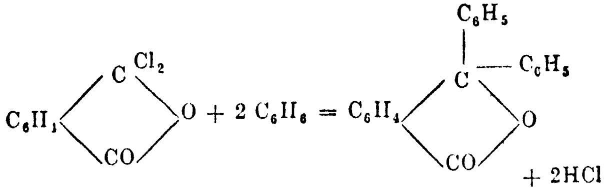
$$COCl_2 + 2C_6H_5CH_3 = CO.(C_6H_4.CH_3)_2[4:4'] + 2HCl.$$

(A., 312, 92 ; B., 7, 1183 ; 10, 2173 ; J. pr., [2], 35, 466.)

$$COCl_2 + C_6H_5N(CH_3)_2 = CO(C_6H_4N(CH_3)_2)_2[4:4'] + 2HCl.$$

(B., 19, 109 ; B., 24, 3198.)

The last compound 4 : 4′-tetramethyl-di-amino-benzophenone is also known as " Michler's ketone ", and is an important intermediate in the preparation of dyestuffs of the fuchsine series, e.g. crystal violet. For the preparation of this ketone by treatment of dimethylaniline with carbon dioxide in presence of aluminium chloride, see E.P., 353464.



With phthalyl chloride " diphenylphthalide ", important on account of its relation to the fluorescein dyes, is formed (B., 14, 1865).

Comparing with Reaction XX (*a*) it will be seen that phthalyl chloride is tautomeric. Succinyl chloride is also considered to be similarly tautomeric, a number of facts supporting this view. Unlike phthalyl chloride, however, it reacts in the symmetrical form.

(vii) Naphthalene reacts in a manner similar to benzene,

$$C_{10}H_8 + C_6H_5COCl = \alpha\text{-}C_{10}H_7COC_6H_5 + HCl.$$

It will be noted in the following examples that the quantities of aluminium chloride used are larger than in the case of the hydrocarbons synthesised by this reaction. This is necessary owing to the stability of the addition compounds of aluminium chloride with the product. So stable are those compounds that the aluminium chloride is unable to exert its catalytic action, and molecular quantities of the condensing agent have to be taken. (J. C. S., 83, 1470.)

PREPARATION 28.—**Acetophenone** (*Phenyl methyl ketone*).

$C_6H_5.CO.CH_3$. C_8H_8O.   120.

Into a three-necked 500 c.cs. flask fitted with reflux condenser with calcium chloride tube, a dropping funnel and agitator, are placed 100 c.cs. of sodium dried benzene and 80 gms. fresh aluminium chloride. 25 gms. acetic anhydride are then added over 30 minutes from dropping funnel with vigorous agitation. Brisk evolution of hydrogen chloride takes place. The mixture is boiled for 30 minutes with continuous stirring, and poured on to ice. The precipitated aluminium hydroxide is dissolved by adding conc. hydrochloric acid. Ether is added and after shaking, the ether-benzene layer is separated, shaken with sodium hydroxide solution, again separated and dried over calcium chloride. The solvents are evaporated and the acetophenone distilled, the fraction B.P. 199°–202° being collected.

$$C_6H_6 + (CH_3CO)_2O \xrightarrow{AlCl_3} C_6H_5COCH_3 + CH_3COOH.$$

Yield.—80% theoretical (24 gms.). Colourless plates ; sweetish odour ; insoluble in water ; soluble in benzene ; M.P. 20° ; B.P. 202° ; D. $^{0}_{4}$ 1·032. (A. Ch., [6], 1, 507 ; 14, 455.) See also C. V., I, 111.

Note.—In all these experiments the aluminium chloride must be weighed out in a dry stoppered bottle.

PREPARATION 29.—**Benzophenone** (*Diphenyl ketone*).

$C_6H_5.CO.C_6H_5$. $C_{13}H_{10}O$.   182.

30 gms. (excess) of *dry* benzene, 30 gms. (1 mol.) of pure benzoyl chloride, and 130 gms. of *dry* carbon disulphide are placed in a dry flask and 29 gms. (1 mol.) of finely-powdered, anhydrous aluminium chloride (p. 514) are added. (Caution, p. 65.)

The flask is then connected with a long reflux condenser, and heated on a water bath kept at 50°, until only small amounts of hydrogen chloride are evolved (about 2½ hours). The carbon disulphide is then distilled off on a water bath (caution) and the still warm residue is carefully poured into a large flask containing 300 c.cs. of ice-water. The reaction flask is then washed out into the ice-water flask with 100 c.cs. of water, 10 c.cs. of conc. hydrochloric acid are added, and the whole steam distilled for 15 minutes. The cold residue is extracted with ether, the ethereal solution is repeatedly washed with water, filtered, and three times washed with dilute caustic soda solution. It is dehydrated over calcium chloride, filtered and distilled from a " high boiling point " distilling flask (see p. 20), the fraction 290°–305° being retained.

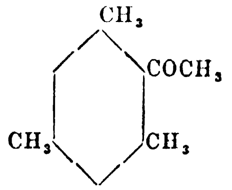
$$C_6H_6 + C_6H_5COCl + AlCl_3 = C_6H_5.CO.C_6H_5[AlCl_3] + HCl.$$

$$C_6H_5COC_6H_5[AlCl_3] + 3H_2O = C_6H_5.CO.C_6H_5 + Al(OH)_3 + 3HCl.$$

Yield.—80% theoretical (30 gms.). Colourless crystals; insoluble in water; soluble in benzene; M.P. 48°; B.P.^{760} 307°; B.P.^{12} 162°; a labile modification (M.P. 26°) also exists; it transforms to the stable modification on boiling, or on seeding with a little of the latter. (B., 26, R., 380; A. Ch., [6], 1, 518; Am. Soc., 50, 571; C. V., I, 95.)

The effect of carbon disulphide on the velocity and yield should be noted by comparing the above preparations. For preparation from benzene and carbon tetrachloride, see C. V. I, 95.

Preparation 30.—**Acetylmesitylene** (1 : 3 : 5-*Trimethyl-2-acetyl-benzene*).



$C_{11}H_{14}O$ 162.

25 gms. (1 mol.) of mesitylene (see p. 64), 75 gms. of carbon disulphide and 30 gms. (excess) of freshly-distilled acetyl chloride are placed in a flask provided with a reflux condenser, and 33 gms. (1¼ mols.) of finely-powdered, freshly-prepared, anhydrous aluminium chloride are added gradually. The mixture is finally warmed for 15 minutes on a water bath and poured on to ice, 10 c.cs. of conc. hydrochloric acid are added, and the whole is steam distilled until no more oily drops pass over. The distillate is extracted with benzene and the extract washed with dilute caustic soda solution and with water, dried over calcium chloride and distilled, the fraction 230°–240° being retained.

$C_6H_3(CH_3)_3[1:3:5] + CH_3.CO.Cl = C_6H_2(CH_3)_3(CO.CH_3)[1:3:5:2] + HCl.$

Yield.—60% theoretical (20 gms.). Colourless liquid; B.P. 235°. For preparation of acetyl-*p*-cymene, see C. V., II, 3.

Preparation 31.—**4 : 4′-Dimethylbenzophenone.**

$[4]CH_3.C_6H_4.CO.C_6H_4CH_3[4'].$ $C_{15}H_{14}O.$ 210.

This preparation must be conducted in a good draught cupboard.

100 gms. of toluene, containing 20% of carbonyl chloride (see p. 520) are placed in a flask to which is attached by a two-holed stopper a reflux condenser and a wide-stemmed glass filtering funnel. To the end of the condenser is attached a delivery tube leading to a fume duct. The flask is surrounded by a freezing mixture, and 50 gms. of finely-powdered anhydrous aluminium chloride are gradually added through the funnel during 4 hours, the funnel being closed by a cork after each addition. When all has been added, the flask is very gently warmed for a short time, and the contents slowly poured into ice-water (caution). It is then steam distilled until no further oil passes over. The aqueous layer of the distillate is removed and a 1% solution of hydrochloric acid added to the solid matter, which is again steam distilled for about 30 minutes.

The solid matter in the distillate is filtered off, washed and recrystallised several times from dilute alcohol.

$$2C_6H_5CH_3 + COCl_2 \longrightarrow CO(C_6H_4.CH_3[4])_2 + 2HCl.$$

Yield.—50% theoretical (45 gms.). Colourless needles; insoluble in water; soluble in benzene and alcohol; M.P. 95°; B.P. 333°. (B., 10, 2173; A., 312, 92; J. pr., [2], 35, 466.)

Note.—Carbonyl chloride (phosgene) is extremely poisonous, and special care must be taken in its use.

Reaction XX. (*c*) **Action of a Mixture of Aluminium and Mercuric Chloride on a Mixture of an Aromatic Hydrocarbon and an Acyl Halide.** (J. C. S., 117, 1330.)—This modification of the Friedel-Crafts condensation has been fully dealt with under its application to the synthesis of hydrocarbons. In the case of ketones the results obtained are more in accordance with the results of the earlier method than those discussed in the first hydrocarbon section.

PREPARATION 32.—**Acetophenone** (*Methyl phenyl ketone*).

$C_6H_5.CO.CH_3$. C_8H_8O. 120.

20 gms. (1 mol.) of *dry* benzene, and 20 gms. of mercuric chloride are placed in a flask fitted with a reflux condenser and 1 gm. of aluminium powder is added, gradually, and with vigorous shaking, the ensuing reaction being moderated by occasional cooling in an ice bath. A green, crystalline mass separates, and the reaction is completed by immersing the flask in tepid water for half an hour. The mercury liberated in the reaction is removed, and the preparation of the catalyst is complete. 20 gms. (1 mol.) of acetyl chloride are added in small quantities through the condenser, the reaction mixture being well agitated by a mechanical stirrer. (For a suitable apparatus, see Fig. 38.) The whole is allowed to stand for 2 hours, and then heated to 40° for 1 hour. On cooling, water is added to decompose the product, and the liberated oil extracted with benzene. The extract is dried over calcium chloride and fractionated, the fraction 195°–205° being retained.

$$C_6H_6 + Al + 2HgCl_2 = C_6H_6.AlCl_3.HgCl + Hg.$$

$$C_6H_6.AlCl_3.HgCl + CH_3COCl = CH_3.CO.C_6H_5.AlCl_3.HgCl + HCl.$$

$$2CH_3COC_6H_5.AlCl_3.HgCl + 6H_2O = 2CH_3COC_6H_5 + 2Al(OH)_3 + Hg_2Cl_2 + 6HCl.$$

Yield.—60% theoretical (18 gms.). Colourless plates; sweetish odour; soluble in benzene; insoluble in water; M.P. 20°; B.P. 202°; D. $^{0}_{4}$ 1·032, (J. C. S., 117, 1330.)

This yield of acetophenone is 10% better than that obtained in the ordinary Friedel-Crafts reaction. A similar method can be applied to the preparation of *p*-tolyl-methyl-ketone, 20 gms. (1 mol.) of dry toluene, 2 gms. of aluminium powder, 35 gms. of mercuric chloride, and 17 gms. (1 mol.) of acetyl chloride being used. The yield is 45% theoretical (13 gms.). The ketone is obtained as a low-melting solid, B.P. 224°.

Reaction XX. (*d*) **Combined Action of Carbon Monoxide and Hydrogen Chloride on an Aromatic Hydrocarbon in presence of a Mixture of Anhy-**

drous Aluminium and Cuprous Chlorides (Gattermann-Koch). (B., 30, 1622 ; Ann. Rep., 1937, 258.)—Since a mixture of carbon monoxide and hydrogen chloride behaves as the unknown formyl chloride, it is possible to utilise the Friedel-Crafts method in the synthesis of aldehydes. The isolation and use of the addition compound $CO.HCl.AlCl_3$ are described in E.P., 445554. See Chem. Rev., 38, 228.

$$HCl + CO[Cu_2Cl_2] = H.CO.Cl.[Cu_2Cl_2].$$

$$CH_3.C_6H_5 + H.CO.Cl[AlCl_3] = CH_3.C_6H_4.CHO.[Al.Cl_3] + HCl.$$

$$CH_3.C_6H_4.CHO.[AlCl_3] + 3H_2O = CH_3.C_6H_4.CHO + Al(OH)_3 + 3HCl.$$

Benzene itself does not react—unless hydrobromic acid is used—and can on that account be used as a solvent (D.R.P., 126421).

Many other hydrocarbons, *o*- and *m*-xylene, mesitylene, ethylbenzene, diphenyl, etc., can all be employed to give the corresponding aldehydes. The CHO group enters the *para*-position to the alkyl residue just as in the ketonic synthesis. Thus *o*-xylene gives 3 : 4-di-methyl-benzaldehyde.

Since the Friedel-Crafts reaction when applied to the phenol ethers yields the corresponding ketones far more easily than the same reaction applied to hydrocarbons (see Reaction XX (*b*) (iv)), it is noteworthy that the above reaction does not apply to the phenol ethers. To obtain aldehydes from them or from phenols, a modified method must be used (see pp. 111, 112).

PREPARATION 33.—*p*-**Tolylaldehyde** (1 : 4-*Methylbenzaldehyde*).

$$CH_3.C_6H_4.CHO[1:4]. \qquad C_8H_8O. \qquad 120.$$

To 30 gms. (1 mol.) of freshly-distilled toluene (B.P. 110°) contained in a wide-necked vessel cooled with water, 45 gms. of pulverised, freshly-prepared aluminium chloride and 5 gms. of pure cuprous chloride are added. The vessel is closed by a three-holed cork, in the middle hole of which is inserted a glass tube which carries an efficient stirrer ; the other holes are used for the inlet and outlet tubes. After the apparatus has been firmly fastened in a clamp, it is immersed in a jar containing water at 20°. A current, not too rapid, of carbon monoxide and hydrogen chloride is led in through a prong-shaped tube while the stirrer is set in motion. The gases are dried by bubbling each through conc. sulphuric acid, their rates of entry being so regulated that the volume of carbon monoxide is about twice that of the hydrogen chloride passing in. The escaping gas is led directly to the hood opening of a draught chamber. In the course of an hour, when about 1–2 litres of carbon monoxide have been passed into the mixture, the temperature rises to 25°–30° ; the remainder of the gas is passed in during 4–5 hours. Should the reaction mixture become so viscous before the lapse of this time that the stirrer revolves only with difficulty, the reaction may be stopped. The viscid product is then poured into a large flask containing crushed ice ; the aldehyde formed and any unattacked toluene are distilled over with steam. The distillate —oil and water—is then shaken up with a sodium bisulphite solution (see p. 517) for a long time, and the toluene which does not dissolve is separated in a funnel. If the aldehyde-bisulphite compound should crystallise out, water is added till it dissolves. The filtered aqueous solution is then treated with anhydrous sodium carbonate until it shows a decided alkaline reaction, the aldehyde distilled off in steam, extracted with ether, the extract dried over anhydrous calcium chloride, and the ether removed on a water bath.

$$\mathrm{CH_3.C_6H_4.H + Cl.CO.H = CH_3.C_6H_4.CHO + HCl.}$$

Yield.—60% theoretical (22 gms.). Colourless liquid ; B.P. 204°. (B., 31, 1149 ; A., 347, 347 ; J. C. S., 1932, 2793 ; O. S., XII, 80.)

Reaction XX. (*e*) **Action of Aliphatic or Aromatic Carboxylic Acids or their Chlorides or Anhydrides on Phenolic Compounds in presence of Zinc Chloride to yield Phenolic Ketones** (Nencki).

$$\mathrm{R.COOH + C_6H_{(6-\mathit{x})}(OH)_\mathit{x} \longrightarrow R.CO.C_6H_{(5-\mathit{x})}(OH)_\mathit{x} + H_2O.}$$

Thus acetic and higher fatty acids combine with resorcinol (U.S.P., 219,922 (1923)) ; propionyl chloride with phenol (J. C. S., 55, 546) ; fatty acids with pyrogallol, hydroquinone or α-naphthol (J. pr., 23, 546 ; 43, 86) ; benzoic acid with pyrogallol (D.R.P., 49149 (1889)). See also B., 63 (B), 2740 ; and O. S., XIV, 40.

The reaction is also of importance as a first stage in the preparation of certain higher phenols (p. 183).

PREPARATION 34.—**Resacetophenone** (1-*acetyl*-2 : 4-*dihydroxybenzene*).

$$\mathrm{CH_3CO.C_6H_3(OH)_2.} \qquad \mathrm{C_8H_8O_3.} \qquad 152.$$

30 gms. of fused zinc chloride are dissolved in 30 gms. of hot glacial acetic acid and 20 gms. of resorcinol added. Heating is continued in an open flask on a sand bath until (about 145°–150°) the liquid begins to boil vigorously, when the flame is removed, and the reaction left to complete itself on the hot sand bath. The temperature should not exceed 150°, nor should it remain at 150° for too long a time as resinous by-products are thus formed—indicated by the reaction mixture becoming deep red. After cooling, the product is thoroughly mixed with 200 c.cs. of 2% aqueous hydrochloric acid to dissolve the zinc chloride, and the undissolved portion collected by filtration. This dark brown lustrous product is dissolved in caustic soda solution, boiled with decolourising carbon and filtered. As resacetophenone is difficultly soluble in water it is precipitated from the filtrate by acidification with hydrochloric acid. It may, if necessary, be purified by a repetition of this treatment or by recrystallisation from 2% hydrochloric acid.

$$\mathrm{CH_3COOH + C_6H_4(OH)_2 \longrightarrow C_6H_3(OH)_2.COCH_3 + H_2O.}$$

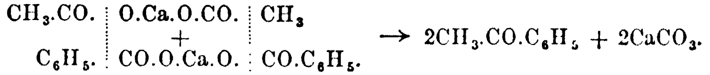
Yield.—40% theoretical (11 gms.). Needles, M.P. 142°. Decomposes on distillation even at reduced pressure. (See also O. S., XXI, 103.)

Reaction XXI. (*a*) **Dry Distillation of the Barium or Calcium Salt of a Fatty Acid with Barium or Calcium Formate.**—This is one of the methods by which aldehydes may be obtained from acids. Like most dry distillations, the yields are poor, and the method is seldom used.

$$\begin{array}{r|c|l} \mathrm{CH_3—} & \mathrm{CO.O.Ca.O.} & \mathrm{CO—CH_3} \\ \mathrm{H.CO.} & \mathrm{O.Ca.O.CO} & \mathrm{H} \end{array} \quad = \quad \mathrm{2CH_3.CHO} \; + \; \mathrm{2CaCO_3.}$$

Reaction XXI. (*b*) **Dry Distillation of the Barium or Calcium Salts of Fatty Acids.** (Z. Ch., 19, 1755.)—This early method of preparing ketones is still used. Originally calcium salts were employed, but barium salts have been found to give better yields. Mixed ketones can be prepared by distilling an intimate mixture of the salts of two acids, but the symmetrical ketones from the single acids are also formed at the same time. The method is closely analogous to that given above for aldehydes. Almost all of the fatty acids give this reaction, but it is better to distil under reduced pressure when working with the higher members of the series. If the salt of a dibasic acid be used, since the two carboxyls are already linked together, distillation produces a ring compound. Thus, adipic acid (ii) gives cyclopentanone (C. V., I, 192). The following examples will give an idea of the scope of the reaction :

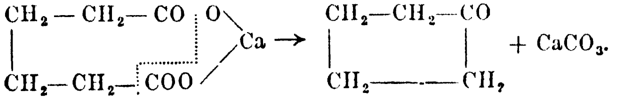
(i.)



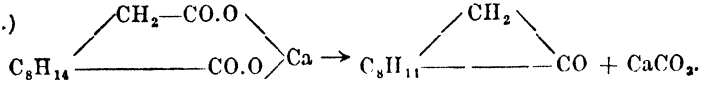
$$\begin{array}{l:l:l} \mathrm{CH_3.CO.} & \mathrm{O.Ca.O.CO.} & \mathrm{CH_3} \\ & \quad + & \\ \mathrm{C_6H_5.} & \mathrm{CO.O.Ca.O.} & \mathrm{CO.C_6H_5.} \end{array} \rightarrow \mathrm{2CH_3.CO.C_6H_5 + 2CaCO_3.}$$

Some $(CH_3)_2CO$ and $(C_6H_5)_2CO$ are also formed.

(ii.)



(iii.)



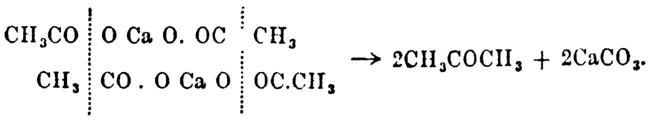
(iii) represents the last step in the synthesis of camphor by heating calcium homo-camphorate in a current of carbon dioxide (Z. Ch., 19, 1755).

Ketones containing up to 34 C-atoms in the ring have been prepared from the corresponding thorium dicarboxylates. By the Clemmensen reduction (Reaction LVIII (*c*)) the ketones have been converted into cyclic hydrocarbons. These large ring compounds are remarkably stable. (H. Acta, 11, 496, 670 ; 13, 1152 ; 17, 78.)

PREPARATION 35.—**Acetone** (*Dimethyl ketone*).

CH_3COCH_3. C_3H_6O. 58.

100 gms. (2 mols.) of anhydrous calcium or barium acetate are distilled from a metal retort attached to a long condenser, some dry iron turnings being previously mixed with the salt to distribute the heat. When no more liquid distils, the distillate is shaken for 5 hours with three volumes of saturated sodium bisulphite solution (see p. 517). The crystalline compound is filtered off, dissolved in the minimum quantity of water. Anhydrous sodium carbonate is added until the solution is alkaline, and the acetone then distilled from a water bath. The distillate is dried over calcium chloride and redistilled, the fraction 55°–59° being retained.



$$\begin{array}{r:l:l} \mathrm{CH_3CO} & \mathrm{O\ Ca\ O.\ OC} & \mathrm{CH_3} \\ \mathrm{CH_3} & \mathrm{CO\ .\ O\ Ca\ O} & \mathrm{OC.CH_3} \end{array} \rightarrow \mathrm{2CH_3COCH_3 + 2CaCO_3.}$$

Yield.—20% theoretical (12 gms.) from calcium acetate; 25% theoretical (10 gms.) from barium acetate. Colourless mobile liquid; B.P. 56·3°; D. $^{15}_{4}$ 0·742; soluble in water. (E.P., 392652.)

The distillate may also be purified by adding an equal volume of water to dissolve the acetone, dehydrating for several hours over quicklime under a reflux, distilling, and dehydrating further over anhydrous potassium carbonate followed by a further treatment with phosphorus pentoxide, if a very dry product is required (O. S., XX, 7).

PREPARATION 36.—**Benzophenone** (*Diphenyl ketone*).

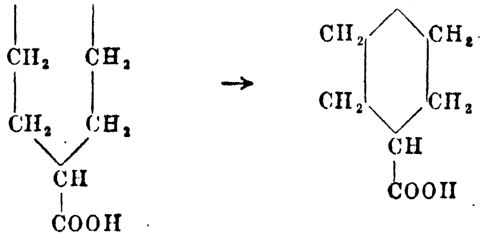
$C_6H_5.CO.C_6H_5$. $C_{13}H_{10}O$. 182.

10 gms. (2 mols.) of benzoic acid are heated to boiling with 25 gms. (excess) of slaked lime and ten times the weight of water, until the acid is completely dissolved and the liquid reacts alkaline. It is then filtered hot from the excess of slaked lime. On cooling most of the calcium benzoate separates out from the filtrate in white needles. The remainder is obtained on evaporating the mother liquor. The salt is filtered as dry as possible at the pump, pressed in cloth (p. 37) and completely dried in metal dishes over a free flame.

The mass is now introduced into a metal retort (made of iron or copper), which is connected with a long condenser tube. The retort must not be filled more than two-thirds full. It is heated over a powerful gas burner, so that the dry distillation of the salt proceeds as quickly as possible. A pale-brownish coloured mixture of benzene, benzophenone and aromatic products first distils over. The distillation is stopped when the distillate becomes brown and viscous. The distillate is dried with calcium chloride, and then fractionated. The fraction 250°–310° contains the benzophenone. The product sometimes solidifies quickly, but more frequently remains syrupy for days. Crystallisation begins, however, at once, when a small quantity of solid benzophenone is added. The crystals are freed from the oily mother liquor by pressing between filter paper, or by spreading on a porous tile, and are recrystallised from ligroin.

Yield.—30% theoretical (2 gms.) (see p. 95).

Reaction XXI. (*c*) **Action of Acetic Anhydride on Carboxylic Acids and subsequent Distillation.**—This method of preparing ketones is worthy of note because it was used to obtain δ-ketohexahydrobenzoic acid from δ-carboxypimelic acid.



δ-Ketohexahydrobenzoic acid is important, because it is the starting point in one of the methods of synthesising terpenes (see p. 80).

Reaction XXI. (*d*) **Catalytic Action of the Manganese Salt of a Fatty Acid on the Acid.**—When acetic acid vapour is passed over heated manganese acetate, acetone is formed. The process is continuous and the method gives better yields than the older distillation method. The cycle of changes which takes place in the action may be formulated :

$$Mn.(O.OC.CH_3)_2 = (CH_3)_2CO + MnCO_3.$$

$$MnCO_3 + 2CH_3COOH = Mn.(O.OC.CH_3)_2 + CO_2 + H_2O.$$

The principle of this method has been utilised on the industrial scale, and with success for the preparation of acetone. The acetic acid may be prepared from acetylene *via* acetaldehyde (see p. 442), thus providing a commercial synthesis of acetone from coke.

PREPARATION 37.—**Acetone** (*Propanon*).

$$CH_3.CO.CH_3 \qquad C_3H_6O. \qquad 58.$$

About 20 gms. of manganous carbonate are made into a thick paste with water in a basin. This is stirred with an equal bulk of pumice in small pieces, and then placed in an air oven at 110°–120° until quite dry. When dry it is loosely packed into a combustion tube, sufficient being taken to fill rather more than half (40 cms.) the length of the tube ; two asbestos plugs are used to keep the layer in position.

The combustion tube is placed in a cylindrical air bath (see Fig. 44) or electric furnace (J. C. S., 1940, 172). The side tube of a flask containing acetic acid is inserted through a cork in one end of the combustion tube. The other end of the combustion tube may be bent and drawn out after the fashion of an adapter, or it may be fitted with a cork and delivery tube ; in either case it is connected to an apparatus for condensing the mixture of acetone and acetic acid which passes over (see p. 50 for condenser arrangement). The air bath is heated to 120°–130° and maintained at this while the combustion tube is filled with the vapour of acetic acid by boiling the acetic acid in the distilling flask for a few minutes. The air bath is then raised to 400°–450°, i.e. until the bottom of the air bath is at a good red heat (N.B.—a nitrogen filled thermometer or thermocouple should be used). Shields of thick asbestos paper should be placed over the air bath to conserve heat. The distillate which collects in the receivers (the second receiver should be cooled in ice) consists of acetic acid, acetone and water. If this distillate is passed a second or third time over the catalyst, the yield of acetone is increased. In this way excellent yields may be obtained. The final distillate is distilled from an apparatus on a water bath, using a thermometer and efficient condenser, collecting what distils up to 80° ; this is dried in contact with solid potassium carbonate and fractionally distilled.

$$CH_3COOH + HOOC.CH_3 = CH_3.CO.CH_3 + CO_2 + H_2O.$$

(See p. 100.) (E.P., 392652. See also J. Eng., 26, 388, 1014.)

Reaction XXII. (*a*) **Action of Magnesium Alkyl or Aryl Halide on (i) excess of Ethyl Formate, (ii) Ethyl Orthoformate, (iii) di-substituted Formamide and other Derivatives of Formic Acid** (Grignard).—This is the

Grignard method of preparing aldehydes. The same remarks apply to this reaction as to the other "Grignards" already described.

(i) $$H.COOC_2H_5 + C_6H_5MgI \longrightarrow C_6H_5CHO + C_2H_5O.Mg.I.$$

(ii) $$H.C(OC_2H_5)_3 + C_6H_5MgI + H_2O. \longrightarrow C_6H_5CHO + C_2H_5OMgI + 2C_2H_5OH.$$

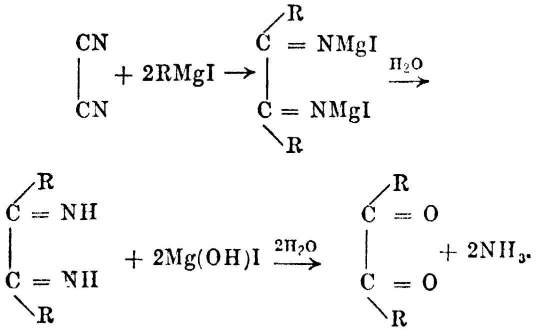
(iii) $$H.CO.N(CH_3)_2 + C_6H_5MgI \longrightarrow HC(C_6H_5)(OMgI)N(CH_3)_2 \longrightarrow C_6H_5CHO + (CH_3)_2NH + Mg(OH)I.$$

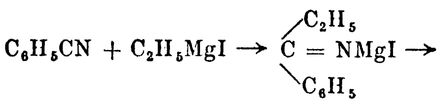
For preparation of *n*-hexylaldehyde, see C. V., II, 323.

The course of the above reaction is somewhat different from Grignard reactions previously discussed.

Reaction XXII. (*b*) **Action of Magnesium Alkyl or Aryl Halides on (i) Nitriles, and (ii) Amides** (Grignard).—This is the analogous reaction to the foregoing, ketones being obtained in place of aldehydes by using derivatives of acids other than formic.

(i.)





$$C_6H_5CN + C_2H_5MgI \rightarrow C(C_2H_5)(C_6H_5){=}NMgI \rightarrow$$

$$C_6H_5.CO.C_2H_5 + NH_3 + Mg(OH)I.$$

(ii.) $$C_6H_5CONH_2 + CH_3MgI \rightarrow C_6H_5C(CH_3)(OMgI)NH_2 \rightarrow C_6H_5.CO.CH_3 + Mg(OH)I + NH_3.$$

Reaction XXII. (*c*) **Action of Zinc Alkyl on Acyl Chlorides.**—The preparation of alcohols by this method has already been discussed (Reaction XV). By using only 1 mol. of zinc alkyl to 2 mols. of acid chloride, the reaction can be stopped at the intermediate ketone stage. In the Grignard reaction with acid chlorides, it is necessary to add cadmium chloride to arrest the reaction at the ketone stage (p. 82).

$$2CH_3.CO.Cl + Zn(CH_3)_2 = 2CH_3COCH_3 + ZnCl_2.$$

Reaction XXIII. (*a*) **Condensation of Ethyl Formate with certain Keto-Compounds under the influence of Sodium Ethoxide** (Claisen). (A., 283, 306.)—This condensation which is undergone generally by carbonyl compounds containing the $—CH_2CO—$ group, follows the course of other ester-ketone reactions—a mechanism of reaction for which is suggested on p. 104—and may be summarised in the equations :

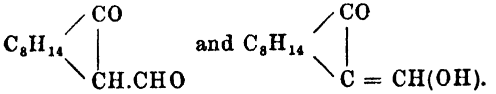
$$\mathrm{RCOCH_2R + EtOOCH \xrightarrow{NaOEt} RCO.CHRCHO + EtOH}$$

$$\mathrm{RCOCHRCHO \rightleftharpoons RCOCR{=}CHOH.}$$

The compounds so formed were at first thought to be aldehyde derivatives, thus the compound derived from acetophenone was thought to have the formula —C_6H_5.CO.CH_2.CHO. Support was lent to this view by the fact that the compound gave an oxime, C_6H_5.CO.CH_2.CH : NOH. On the other hand, in many reactions it behaved as if it had the formula C_6H_5.CO.CH : CH(OH). It gave a sodium salt, being obtained as such in its preparation ; and a chloro compound, C_6H_5.CO.CH : CHCl, when treated with PCl_5. The view now held is that these " hydroxymethylene " compounds are tautomeric ; both keto and enol forms being present. The enol form is of special interest on account of the great reactivity of the hydroxyl group. The double bond seems to have the same activating effect as the keto group in carboxyl compounds, the hydroxyl group behaving more as an acidic hydroxyl than an alcoholic. The chloride derived from it is nearly as reactive as an acid chloride ; and the corresponding amino compound behaves rather as an amide than as an amine.

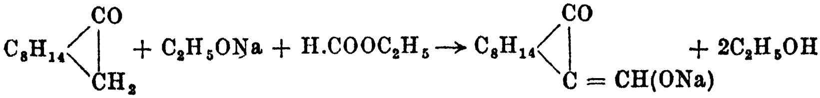
The compounds separate from the condensation as sodium salts. From the simple ketones, the compound formed is not stable and undergoes change on precipitation from its sodium salt. The formation of a hydroxymethylene compound is used as proof of the presence of the group —CH_2—CO—in camphor. The following preparation shows the details of the method.

Preparation 38.—**Camphoraldehyde** (*Hydroxymethylenecamphor*).



$C_{11}H_{16}O_2$. 180.

90 gms. (excess) of camphor are dissolved in toluene which has been freed from water by standing over calcium chloride, and to this solution are added 6 gms. of sodium wire. To the well-cooled mixture 19 gms. (1 mol.) ethyl formate are added, when it is set aside in an ice chest for 24 hours. It is then poured into ice-water, and after vigorous shaking the aqueous layer removed. After acidifying with acetic acid, and then extracting with ether, the ethereal extract is dried over calcium chloride. The ether is removed by distillation, and the residue, after being placed in a basin, is allowed to evaporate slowly at ordinary temperature. The oil which remains solidifies on standing to colourless crystals. These may be purified by steam distillation and crystallisation from dilute acetic acid.



Yield.—Theoretical (46 gms.). Soluble in ether ; M.P. 80°–81°. (A., 283, 306.)

Reaction XXIII. (*b*) **Condensation of Esters other than Ethyl Formate, with certain Ketones under the influence of Sodium Ethylate, Metallic Sodium, or Sodamide** (Claisen). (B., 22, 1009; 23, R., 40; 38, 695.)—This is a similar reaction to that discussed above, and is part of a general condensation undergone by esters with carbonyl compounds, other phases of which are discussed on pp. 148–154.

The reaction may be summarised :

$$RCOOEt + HR^{I}R^{II}C.COCR_3^{III} \xrightarrow{NaOEt} RCOCR^{I}R^{II}COCR_3^{III} + EtOH$$

where the Rs may be hydrogen or an alkyl or aryl group. Only those ketones containing the group CH.CO undergo the reaction, the products being 1 : 3-diketones. Sodamide is the most, and sodium ethylate the least effective, condensing agent.

The reaction probably involves an ionic mechanism :

The ethoxide ion (derived from sodium ethoxide or from sodium and traces of alcohol in the ester) or the NH_2 ion in the case of sodamide abstracts a proton from the α-carbon of the CH—CO group of the carbonyl compound : for example, with acetophenone.

$$PhCOCH_3 + \bar{O}Et \longrightarrow PhCO\bar{C}H_2 + HOEt.$$

The anion then condenses with the carbonyl group of the ester component in the reaction :

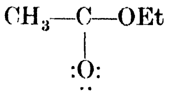
$$CH_3C(\ddot{\underset{..}{O}}:)OEt + \bar{C}H_2COPh \longrightarrow CH_3C(\ddot{\underset{..}{\bar{O}}}:)(OEt)CH_2COPh$$

$$\longrightarrow CH_3COCH_2COPh + \bar{O}Et.$$

Note.—In formulae representing the forms of the carbonyl group here and elsewhere in this book (pp. 149–153)

$$\underset{:O:}{\overset{|}{\text{—C—}}}\ \text{(double bond)} \longrightarrow \underset{:\underset{..}{O}:}{\overset{}{\text{—C—}}}$$

the latter structure is given as $\overset{|}{—C}(\ddot{\underset{..}{O}}:)$ written horizontally in formulae, e.g.



$$CH_3\text{—}\underset{:\underset{..}{O}:}{\underset{|}{C}}\text{—}OEt$$

as $CH_3C(\ddot{\underset{..}{O}}:)OEt.$

Preparation 39.—**Benzoylacetone** (1-*Phenyl*-1 : 3-*butandione*).

$C_6H_5.CO.CH_2.CO.CH_3$. $C_{10}H_{10}O_2$. 162.

Method I.—6 gms. (1 mol.) of fresh dry sodium ethylate (see p. 516) are added to 20 gms. (excess) of *dry* ethyl acetate under cooling by water. After 15 minutes, 10 gms. (1 mol.) of acetophenone are added ; the separation of the sodium salt of benzoyl acetone immediately begins. A little *dry* ether is added, and in 4 hours the sodium compound is filtered off, washed with ether, air-dried, dissolved in cold water, and the solution acidified with acetic acid. Benzoyl acetone separates.

Yield.—66% theoretical (10 gms.). Colourless crystals; insoluble in water; M.P. 61°; gives a deep violet coloration with ferric chloride and a bluish-green crystalline precipitate of copper benzoyl acetone with alcoholic copper acetate. This shows the compound to be tautomeric, a little of the enol form being present at ordinary temperatures. The acidity of the hydroxyl group in the enol form is not so marked as it is in the case of the hydroxymethylene compounds; nevertheless, the metallic salts of benzoyl acetone and such di-ketones are remarkably stable, and on account of their great crystallising power have been used for the determination of the valency and atomic weight of the rare elements. They are also of importance in the modern theory of co-ordination. (C., 1900, I, 588; B., 34, 2584.)

Method II.—25 gms. (excess) of ethyl acetate and 30 gms. of acetophenone (1 mol.) are dissolved in 200 c.cs. of anhydrous ether. To this is slowly added with gentle cooling 20 gms. (excess) of powdered sodamide. It is then set aside for 24 hours, when the sodium salt separates, and is poured on to a mixture of ice and water sufficient to dissolve it completely. The aqueous layer is separated, and the ether removed from it by passing air through. Acetic acid is then added until the solution is acid, the precipitated benzoylacetone being filtered off and washed with water.

$$CH_3COOEt + CH_3COC_6H_5 \xrightarrow[NaNH_2]{NaOEt} C_6H_5COCH_2COCH_3.$$

Yield.—75% theoretical (30 gms.). Colourless crystals; M.P. 61°; insoluble in water. (B., 36, 695.)

Thus the yield is improved by using ether as a solvent, and by replacing sodium ethylate by sodamide.

Reaction XXIV. The Aldol Condensation of certain Carbonyl Compounds followed by loss of Water. (A., 223, 139; Ann. Rep., 1938, 211).—Aldol addition is undoubtedly the first step in a number of important reactions of carbonyl compounds (see Reactions XXXIII (*b*) and (*c*).

It may be brought about by acid or base catalysis, and in the following instances is summarised by the equations:

$$CH_3CHO + CH_3CHO \longrightarrow CH_3CHOHCH_2CHO.$$

$$PhCHO + CH_3CHO \longrightarrow PhCHOHCH_2CHO.$$

$$(CH_3)_2CO + CH_3COCH_3 \longrightarrow (CH_3)_2C(OH)CH_2COCH_3.$$

$$(CH_3)_2CO + CHCl_3 \longrightarrow (CH_3)_2C(OH)CCl_3,$$

the carbonyl group of the first molecule undergoing proton addition at its oxygen atom and carbanion (K, below) addition at its carbon atom. The second molecule must contain at least one reactive hydrogen atom (activated by carbonyl or other electron-withdrawal group in an α-position). Effective base catalysts (represented by B) include organic bases as well as ethoxide, hydroxide, acetate or other anion, and the suggested ionic mechanism of reaction is :

$$B + CH_2R^1R^{11} \rightleftharpoons \overset{+}{B}H + \overset{-}{C}HR^1R^{11}(K),$$

(R^1 and/or R^{11} being activating groups, and K a carbanion),

$$RC(\underset{\cdot\cdot}{\ddot{O}}:)R_1 + \overset{-}{C}HR'R'' \longrightarrow RCR_1(\underset{\cdot\cdot}{\ddot{O}}:)CHR'R'' \text{ (see p. 104).}$$

$$RCR_1(\underset{\cdot\cdot}{\ddot{O}}:)CHR'R'' + \overset{+}{B}H \longrightarrow RCR_1(OH)CHR'R'' + B,$$

and in summary : (see Note, p. 104).

$$RCOR_1 + CH_2R'R'' \longrightarrow RCR_1(OH)CHR'R''$$

Those aldols which carry one or two hydrogen atoms on the carbon atom in the position α to the C(OH) group lose water readily under the influence of even weak base catalysts in some instances—but more readily under the influence of acid reagents since these catalyse the conversion of alcohols to olefines—yielding $\alpha\beta$-olefinic aldehydes or ketones. Thus (i) acetaldol yields crotonaldehyde ; (ii) cinnamic aldehyde is obtained by the action of hydrogen chloride, sodium hydrate or sodium ethylate on a mixture of acetaldehyde and benzaldehyde (B., 17, 2117) ; (iii) acetone when saturated with hydrogen chloride yields mesityl oxide *via* diacetone-alcohol (C. V., I, 345 ; C. V., II, 199) and a third molecule continues the sequence of steps yielding phorone ; (iv) citral and acetone yield pseudo-ionone (B., 27, R, 768). Other instances are given in Preparations 40 and 41.

(i) $CH_3CHO + CH_3CHO \rightarrow CH_3CH(OH)CH_2CHO \rightarrow CH_3CH : CHCHO.$

(ii) $PhCHO + CH_3CHO \rightarrow PhCHOHCH_2CHO \rightarrow PhCH : CHCHO.$

(iii) $2(CH_3)_2CO \rightarrow CH_3COCH_2C(OH)(CH_3)_2 \rightarrow CH_3COCH : C(CH_3)_2$

$(CH_3)_2CO + CH_3COCH : (CH_3)_2 \rightarrow (CH_3)_2C : CHCOCH : C(CH_3)_2.$

(iv) $(CH_3)_2C : CHCH_2CH_2C(CH_3) : CHCHO + CH_3COCH_3$

$\rightarrow (CH_3)_2C : CHCH_2CH_2C(CH_3) : CHCH : CHCOCH_3.$

PREPARATION 40.—**Styryl Methyl Ketone** (*Benzylideneacetone*).

$C_6H_5CH : CH.CO.CH_3.$ $C_{10}H_{10}O.$ 146.

2 gms. (1 mol.) of benzaldehyde and 3·5 gms. (excess) of acetone are heated with 20 c.cs. of 10% caustic soda solution on a water bath for 1 hour. The crystals which separate on cooling are filtered off and re-crystallised from a little alcohol.

$$C_6H_5.CHO + CH_3.CO.CH_3 = C_6H_5CH : CH.CO.CH_3 + H_2O.$$

***Yield.*—Theoretical (3 gms.). Colourless crystals ; dissolve with an orange-red colour in sulphuric acid ; M.P. 42° ; B.P. 262°. (C. V., I, 77.)**

For preparation of dibenzalacetone, see C. V., II, 167.

***o*- and *p*-nitrobenzylidene acetones can be prepared from *o*- and *p*-nitrobenzaldehydes respectively.**

PEPARATION 41.—**Phenyl Styryl Ketone** (*Benzylideneacetophenone*).

$$C_6H_5.CH : CH.CO.C_6H_5. \qquad C_{15}H_{12}O. \qquad 208.$$

2·1 gms. (1 mol.) of benzaldehyde and 2·4 gms. (1 mol.) of acetophenone are dissolved in 20 gms. of alcohol, 2 gms. of 10% caustic soda solution are added, and the whole allowed to stand for 24 hours. The precipitate is recrystallised from ligroin.

$$C_6H_5CHO + CH_3COC_6H_5 = C_5H_5CH : CH.CO.C_6H_5 + H_2O.$$

Yield.—Theoretical (4 gms.). Colourless crystals; M.P. 57°–58°; B.P. 346°. (C. V., I, 78.)

Reaction XXV. Action of Alkyl Halides on the Sodio-derivatives of certain Ketones. (B., 21, 1297; 23, 2072.)—The activating influence of a carbonyl and a phenyl group is shown in the case of deoxybenzoin, one of the methylene hydrogens in this being replaceable by sodium, and the same kind of synthesis may be effected as with sodioethylacetoacetate.

$$\mathrm{PhCOCH_2Ph} + \mathrm{Na} \longrightarrow [\mathrm{PhC}(\underset{\cdot\cdot}{\ddot{\mathrm{O}}}:):\mathrm{CHPh} \longleftrightarrow \mathrm{PhCOCHPh}]^- + \overset{+}{\mathrm{Na}}$$

$$\xrightarrow{\mathrm{EtI}} \mathrm{PhCOCHEtPh} + \mathrm{NaI}. \quad \text{(See Note, p. 104).}$$

Deoxy-*p*-toluoin $CH_3.C_6H_4.CH_2.CO.C_6H_4.CH_3$ and deoxy-*p*-anisoin $CH_3O.C_6H_4.CH_2CO.C_6H_4OCH_3$ behave similarly, as do all the phenyl-benzyl ketones.

CHAPTER VI

CARBON TO CARBON

HYDROXY-OXY COMPOUNDS

The reactions below are those in which carbon atoms are linked together to give compounds containing both a hydroxyl and an oxy (carbonyl) group. In the aliphatic series there are three main divisions of such compounds :

(*a*) The carbonyl group is linked to a terminal carbon, and the hydroxyl group to another carbon—aldols.

(*b*) The carbonyl group is linked to a non-terminal carbon, and the hydroxyl group to another—ketols.

(*c*) The carbonyl group is linked to the same carbon (necessarily terminal) as the hydroxyl group—acids.

The above only applies to the simplest hydroxy-oxy compounds ; acid-ketols, ketaldols, and acid ketaldols also exist.

The terms aldol and ketol are not usually applied in the aromatic series.

Reaction XXVI. (*a*) **Condensing Action of Potassium Cyanide, Potassium Carbonate, or other substances on Aliphatic** (Claisen) **and Aromatic Aldehydes** (Liebig). (J. C. S., 117, 324.)—With aliphatic and aromatic aldehydes this condensation follows very different lines. In the former the condensation takes place between the aldehydic carbon of one molecule and the α-carbon of another molecule. The same or different aldehydes may be used.

$$2R_1RCH.CHO = RR_1CH.CH(OH).C(RR_1).CHO.$$

$$R.CH_2.CHO + R_1CHO = R_1CH(OH).CH(R.)CHO.$$

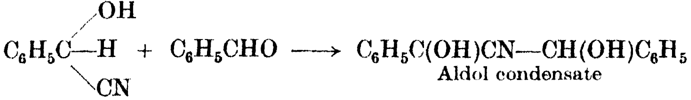
It will be seen that only an aldehyde with at least one α-hydrogen can condense with itself or with another aldehyde. Condensing agents stronger than those mentioned above eliminate water where structurally possible, after condensation. Two α-hydrogen atoms in an aldehyde are necessary for this change (see Reaction XXIV).

It is worth noting that if the aldol condensation takes place in the presence of magnesium amalgam, the aldehydic group is simultaneously reduced and a 1 : 3-dihydric alcohol is formed.

When aromatic aldehydes are heated with potassium cyanide in aqueous alcoholic solution, the aldehydic groups condense to form a ketol. The reaction was discovered by Liebig for benzaldehyde (A., 3, 276), but was later applied to other aromatic aldehydes (B., 25, 293 ; 26, 60), and heterocyclic aldehydes. (B., 28, R, 992 ; Ann. Rep., 1939, 210.)

Theoretically the reaction is supposed to take place as follows :

$$C_5H_5.CHO + KCN + H_2O \longrightarrow \underset{\text{Cyanohydrin}}{C_6H_5CH(OH)CN} + KOH.$$



$$C_6H_5C\begin{matrix}\diagup OH\\ -H\\ \diagdown CN\end{matrix} + C_6H_5CHO \longrightarrow \underset{\text{Aldol condensate}}{C_6H_5C(OH)CN{-}CH(OH)C_6H_5}$$

$$\longrightarrow \underset{\text{Benzoin}}{C_6H_5.CO.CH(OH)C_6H_5} + HCN.$$

The action of the potassium cyanide is catalytic.

For the preparation of aliphatic acyloins from esters, see O. S., XIII, 24.

PREPARATION 42.—**Aldol** (*β-Hydroxybutaldehyde*).

$CH_3.CHOH.CH_2.CHO.$ $C_4H_8O_2.$ 88.

200 c.cs. of ice-cold water are placed in the apparatus (Fig. 50) which is immersed in a cooling bath. 100 gms. of freshly-distilled acetaldehyde, in portions at a time, are introduced while the cork is momentarily withdrawn, the bottle being agitated slightly during the addition, and great care being taken that the temperature of the contents does not rise above 0°. A suitable cooling bath for this stage consists of ice, water and a little hydrochloric acid. When all the aldehyde is added, the cooling bath is replaced by one of ice and hydrochloric acid, and when the temperature of the contents of the bottle has fallen to −12°, 100 c.cs. of a 2·5% solution of potassium cyanide are slowly dropped in while the bottle is rotated ; the temperature must be kept below −8°. After the cyanide is added, the mixture is kept for 2 hours below −8°, the freezing mixture being renewed if necessary, and then for 30 hours in an ice chest at 0°. The resulting syrupy solution of pale yellow colour is saturated in the cold with common salt, and then quickly extracted four times with a moderately large volume of ether. The ethereal extracts are dried over anhydrous sodium sulphate, the ether distilled off, and the residue distilled under reduced pressure. Aldol passes over at 80°–90° and 20 mms. pressure. A suction flask containing conc. sulphuric acid should be placed between the receiver and the pump to absorb aldehyde vapours, which would otherwise prevent a high vacuum being obtained.

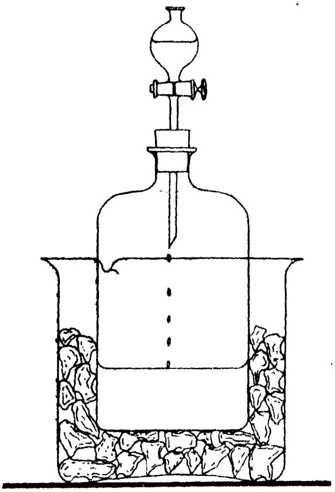


FIG. 50.

$$CH_3.CHO + CH_3CHO \longrightarrow CH.CHOH.CH_2.CHO.$$

Yield.—50% theoretical (50 gms.). Colourless, odourless liquid ; D. $^{0}_{4}$ 1·12 ; B.P. ^{20} 75°. On distilling at atmospheric pressure forms acetaldehyde and much crotonaldehyde. (A., 306, 323; C., 1907, I, 1400; J. C. S., 117, 324.)

PREPARATION 43.—**Benzoin** (*α-Hydroxy-β-keto-αβ-diphenylethane*).

$$C_6H_5.CO.CH(OH).C_6H_5. \quad C_{14}H_{12}O_2. \quad 212.$$

21 gms. (2 mols.) of *pure* benzaldehyde and 2 gms. of 95% potassium cyanide dissolved in 80 c.cs. of 50% alcohol are refluxed for an hour on a water bath. The crystals of benzoin which separate on cooling are filtered off; 2 gms. of potassium cyanide are added to the filtrate and a second yield of benzoin obtained after boiling as before. The whole is recrystallised from hot alcohol.

$$2C_6H_5CHO \longrightarrow C_6H_5CO.CH(OH).C_6H_5.$$

Yield.—90% theoretical (18 gms.). Colourless prisms; slightly soluble in water; soluble in alcohol and ether; M.P. 137°. (A., 198, 151; Am. Soc., 50, 2762; O. S., I, 33. See also J. C. S., 1928, 2483.)

Reaction XXVI. (*b*) **Condensing Action of Potassium Cyanide on a Mixture of an Aliphatic Aldehyde and a Ketone.** (A., 306, 324.)—This is a reaction similar to the previous, a ketone and an aldehyde being condensed to give a 1 : 3-ketol.

$$R.CO.CH_2R_1 + R_{11}CHO \longrightarrow R.CO.CHR_1.CH(OH)R_{11}.$$

The ketone undergoing condensation must have at least one H attached to the α-C. If it has two, then, on heating, these ketols eliminate water to give olefinic ketones. It is to be noted that no condensation takes place at the oxy-carbon of the ketone. An excess of the ketone must always be used to minimise the condensation of two molecules of the aldehyde to an aldol compound. If the reaction is carried out at a high temperature, and with more powerful condensing agents, the unsaturated ketone is directly obtained (see Reaction XXIV). (B., 25, 3165; C., 1905, II., 752.)

PREPARATION 44.—**Hydracetylacetone** (*δ-Hydroxy-β-keto-pentane*).

$$CH_3CH(OH)CH_2COCH_3. \quad C_5H_{10}O_2. \quad 102.$$

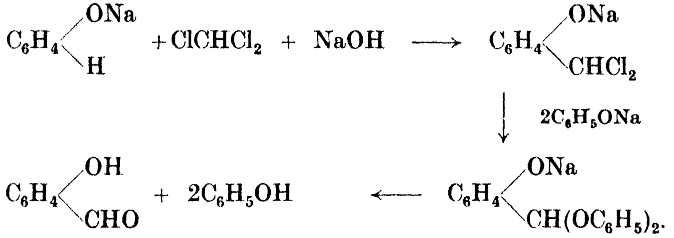
116 gms. (2 mols., excess) of *pure* acetone are cooled to −12° (see p. 12) and treated with a 30% solution of 5 gms. of potassium cyanide. The mixture is then slowly stirred by mechanical means, and 44 gms. (1 mol.) of freshly-prepared acetaldehyde dropped in, the temperature being kept below −5°. The whole is allowed to stand for half an hour in the freezing mixture and 8 hours in an ice chest. 1½ vols. of alcohol-free ether are added, and the lower layer of potassium cyanide solution removed. Any remaining cyanide solution is extracted by washing twice with 60 c.cs. of saturated brine, and a third time with 30 c.cs. to ensure a complete extraction. The washing solution is extracted several times with ether and the total ethereal solution dried for 2 hours over anhydrous sodium sulphate (calcium chloride absorbs hydracetylacetone). The ether is removed under reduced pressure and the residue fractionated three times under a pressure of 20 mms., first from 60°–110°, second 70°–90°, and third 77°–79°.

$$CH_3CHO + CH_3COCH_3 \longrightarrow CH_3CH(OH)CH_2COCH_3.$$

Yield.—25% theoretical (25 gms.). Colourless, viscous liquid, miscible with water or alcohol ; can be salted out of aqueous solution by potassium carbonate ; B.P. ^{760} 176°–177° (slight decomposition) ; B.P. ^{20} 77°–78° ; D. $^{18}_{4}$ 0·9780. (A., 306, 324 ; B., 34, 2029 ; 37, 504 ; E.P., 435466.)

Note the use of 2 mols. of acetone to minimise aldol formation.

Reaction XXVII. Condensation of Chloroform with Phenols and Hydrolysis of the Product (Reimer-Tiemann). (B., 9, 824 ; Chem. Rev., 38, 229.)—This is a well-known method for the preparation of phenolic-aldehydes. The phenol is treated with chloroform and an alkaline hydroxide, when —$CHCl_2$ enters the *ortho-* and to a lesser extent the *para-* position to the hydroxyl group ; hydrolysis to an aldehyde then takes place.



$$C_6H_4\left\langle\begin{matrix}ONa\\H\end{matrix}\right. + ClCHCl_2 + NaOH \longrightarrow C_6H_4\left\langle\begin{matrix}ONa\\CHCl_2\end{matrix}\right.$$

$$\downarrow 2C_6H_5ONa$$

$$C_6H_4\left\langle\begin{matrix}OH\\CHO\end{matrix}\right. + 2C_6H_5OH \longleftarrow C_6H_4\left\langle\begin{matrix}ONa\\CH(OC_6H_5)_2\end{matrix}\right..$$

Di-aldehydes can be obtained from some polyhydric phenols.

Though it has such a wide application, the reaction suffers from many defects. The yields are poor, being of the order of 20% theoretical. This is due to the following causes :

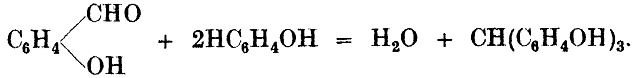
(*a*) A portion of the phenol is converted into the acetal, and regenerated as above.

(*b*) Some forms an ester of ortho-formic acid—

$$3C_6H_5ONa + CHCl_3 = 3NaCl + CH(OC_6H_5)_3.$$

An excess of chloroform helps to prevent this.

(*c*) A portion of the aldehyde first formed is lost by condensation with some unattacked phenol to form a derivative of triphenyl methane—



$$C_6H_4\left\langle\begin{matrix}CHO\\OH\end{matrix}\right. + 2HC_6H_4OH = H_2O + CH(C_6H_4OH)_3.$$

To minimise this side reaction excess of phenol should be avoided.

(*d*) The alkali tends to react with the aldehyde formed, the more readily the higher the temperature.

The Reimer reaction is ineffective with compounds like phloroglucinol, pyrogallol, naphthols, poly-hydric derivatives of naphthalene, etc.

Accordingly, where possible (for the *p*-hydroxybenzaldehydes), the aluminium chloride method (Reaction XXVIII) should be used. The yields are better, the reactions go more smoothly, little resin being formed, while pyrogallols and naphthols, etc., also react. Unfortunately, though the non-formation of other than *p*-hydroxyaldehydes is often an advantage, it limits the scope of the reaction and necessitates the use of the Reimer method in many cases. It should be noted that the nitro-phenols do not condense with chloroform (B., 9, 423, 824 ; 10, 1562 ; 15, 2685).

Preparation 45.—Salicylaldehyde (1 : 2-*Hydroxybenzaldehyde*) *and* **1 : 4-Hydroxybenzaldehyde.**

$OH.C_6H_4.CHO.$[1 : 2 and 1 : 4]. $C_7H_6O_2$. 122.

50 gms. (1 mol.) of phenol and 160 gms. (excess) of caustic soda in 160 c.cs. of water are heated to 50°–60° in a 1-litre flask on a water bath under a reflux. A thermometer dipping into the liquid is fitted to the flask. 75 gms. (excess) of chloroform are added, 10 c.cs. at a time, through the top of the condenser, the flask being well shaken after each addition. By alternate heating and cooling the temperature is kept at 65° throughout. The whole is then refluxed for half an hour, the excess of chloroform removed on a water bath, and the residue carefully acidified with dilute sulphuric acid and distilled in steam till no more oily drops pass over. The distillate is extracted with ether, and the extract shaken with twice its volume of a freshly-prepared, nearly saturated solution of sodium hydrogen sulphite for a time until no more crystals separate. (For preparation of bisulphite, see p. 517). The precipitated bisulphite compound is filtered off, washed free from traces of phenol with alcohol and decomposed by heating on a water bath with dilute sulphuric acid. The aldehyde which separates is extracted with ether, the extract washed with water and dehydrated over anhydrous sodium sulphate. The ether is removed on a water bath and the aldehyde distilled. Some *p*-hydroxybenzaldehyde remains in the flask after the steam distillation. Tarry matter is removed by filtering hot through a moistened filter paper. The cold filtrate is extracted with ether, the extract dried over calcium chloride, the ether removed on a water bath, and the residue recrystallised from a small quantity of hot water containing sulphur dioxide.

For equation, see p. 111.

Yield.—Salicylaldehyde, (13 gms.); 1 : 4-*Hydroxybenzaldehyde*, (3 gms.).

Salicylaldehyde.—Colourless fragrant oil, soluble in water; miscible in all proportions with alcohol and ether; B.P. 196·5°; solidifies to large crystals at 0°; D. $^{15}_{4}$ 1·172.

p-Hydroxybenzaldehyde.—Colourless needles; soluble in hot water, alcohol and ether; M.P. 116°; sublimes. (B., 9, 824; 15, 2585.)

Reaction XXVIII. Action of Hydrogen Chloride and Anhydrous Hydrogen Cyanide on a Phenol or a Phenol Ether in presence of Anhydrous Aluminium Chloride, and Hydrolysis of the Product so formed (Gattermann). (B., 31, 1765; 32, 271; A., 357, 363.)—As stated in Reaction XX (*d*), the Gattermann-Koch reaction does not apply to phenols or phenol ethers. If it is desired to obtain aldehydes from them, hydrogen cyanide is used in place of carbon monoxide, and the mixture of anhydrous hydrogen cyanide and hydrogen chloride is allowed to act in presence of aluminium chloride alone, cuprous chloride being unnecessary. The crystalline compound, HCl.HCN, which hydrogen chloride forms with hydrogen cyanide, can also be used directly.

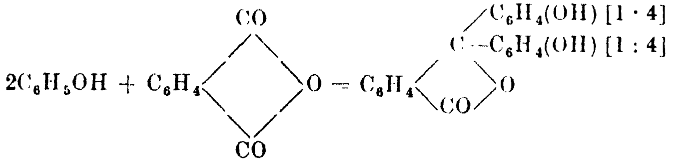
In order to avoid the preparation and handling of anhydrous hydrocyanic acid the passage of the gas direct from a generator (Am. Soc., 43, 348) and the use of zinc cyanide (Am. Soc., 45, 2373) have been tried with satisfactory results, particularly when potassium chloride is added to the latter (Am. Soc., 60, 1699).

$$\mathrm{HCN + HCl \longrightarrow ClCHNH(+HCN+AlCl_3) \longrightarrow}$$
$$\mathrm{ClCH:NCH:NHAlCl_3(+ArH) \longrightarrow}$$
$$\mathrm{ArCH:NCH:NHAlCl_3(+HOH) \longrightarrow}$$
$$\mathrm{ArCHO + 2NH_3 + HCOOH.}$$

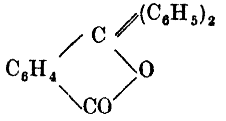
The reaction may also be extended to hydrocarbons, e.g. mesitylene, containing facilitating groups.

Combination takes place *ortho* and *para* to the hydroxyl or alkoxyl group. (B., 55, 928 ; J. C. S., 1931, 84 ; Chem. Rev., 38, 229.)

Reaction XXIX. (*a*) **Condensation of a Phenol with Phthalic Anhydride to form a Phthalein.** (A., 183, 1 ; 202, 68.)—The phthaleins result from the condensation of phthalic anhydride (1 mol.) with phenols (2 mols.) on heating with dehydrating agents—sulphuric acid, fused zinc chloride (to 120°) or anhydrous oxalic acid (to 115°). These compounds are particularly important ; some are dyes of great technical value. The simplest representative of the class is phenolphthalein.

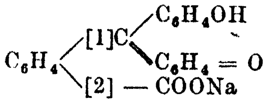


Thus the phthaleins are triphenylmethane derivatives, being all derived from phthalophenone (diphenyl phthalide).



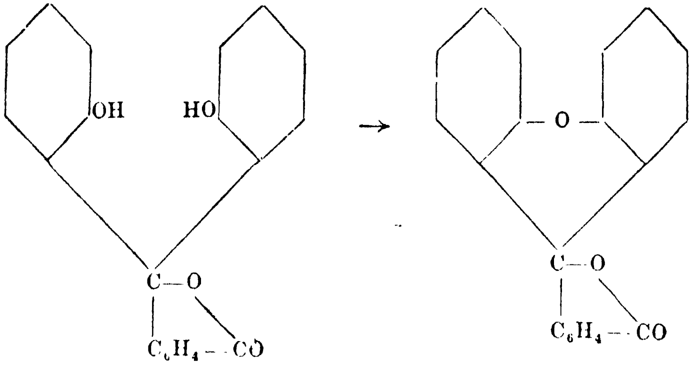
(See p. 93.)

The free phthaleins are usually colourless crystalline compounds dissolving with intense colorations in alkalis, but being reprecipitated by acids, even by CO_2. In very concentrated alkali they give colourless solutions. A quinone structure is assumed for the coloured salts, e.g. for phenolphthalein in alkali solution.



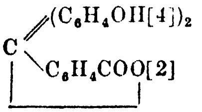
The phthaleins derived from di- or polyhydric phenols are all anhydrides formed by the elimination of water from two phenolic hydroxyls, attached to two different benzene rings. These " anhydride phthaleins " are known as pyronines, since they contain, like the pyrones, a six-membered oxygen-containing ring.

Even in the preparation of phenolphthalein a little of the simplest pyronine is obtained from an *ortho*-phthalein first formed.



From resorcinol the pyronine fluorescein is the main product (see p. 393).

PREPARATION 46.—Phenolphthalein.



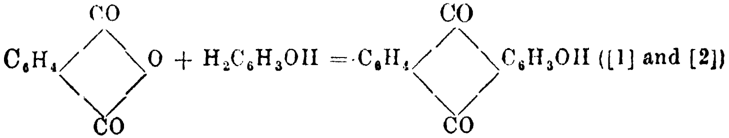
$$C\begin{cases}(C_6H_4OH[4])_2\\ C_6H_4COO[2]\end{cases} \qquad C_{20}H_{14}O_4 \qquad 318.$$

16 gms. conc. sulphuric acid are added to a mixture of 40 gms. (excess) of phenol and 20 gms. (1 mol.) of phthalic anhydride. The mixture is heated for 9 hours at 115°–120° in an oil bath, and the red oil formed poured into a litre of water. The phenol is removed by continued boiling, water being added to replace that lost by evaporation. After cooling, the liquid is filtered and the residue washed with water. It is then dissolved in dilute caustic soda solution, and again filtered. The filtrate is acidified with acetic acid and a few drops of hydrochloric acid, and after standing for some time the precipitate is filtered off and dried. It is then refluxed on a water bath with an excess of absolute alcohol, a little animal charcoal being added if necessary. After filtration, the residue is washed with boiling absolute alcohol, and the combined filtrate and washings evaporated to two-thirds its bulk. It is diluted with 8 vols. of water and filtered through a wet filter to remove resinous matter. The filtrate is then concentrated on the water bath until the phenolphthalein crystallises.

$$2C_6H_5OH + C_6H_4(CO)_2O \longrightarrow \underline{C(C_6H_4COO)}(C_6H_4OH)_2 + H_2O.$$

Yield.—25% theoretical (10 gms.). White crystalline powder; M.P. 250°–253°; slightly soluble in cold alcohol; soluble in alkalis to crimson solution. (B., 9, 1230; A., 183, 1; 202, 68.)

Reaction XXIX. (*b*) Condensation of a Phenol with Phthalic Anhydride to a derivative of Anthraquinone. (A., 212, 10.)—When equimolecular quantities of phthalic anhydride and a phenol react at 180° in the presence of conc. sulphuric acid, the product is not a phthalein, but the action takes a different course, and a derivative of anthraquinone is obtained.

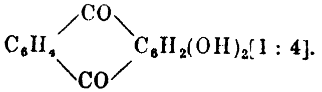


$$C_6H_4\genfrac{<}{>}{0pt}{}{CO}{CO}O + H_2C_6H_3OH = C_6H_4\genfrac{<}{>}{0pt}{}{CO}{CO}C_6H_3OH \text{ ([1] and [2])}$$

α - and β-hydroxyanthraquinone.

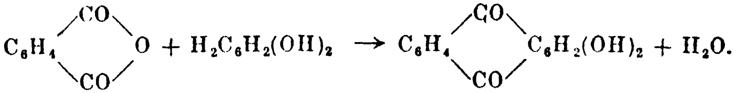
Alizarin (1 : 2-dihydroxyanthraquinone) and an isomer, hystazarin (2 : 3-dihydroxyanthraquinone), are also formed in this way from catechol and phthalic anhydride.

PREPARATION 47.—**Quinizarin** (1 : 4-*Dihydroxyanthraquinone*).



$$C_6H_4\genfrac{<}{>}{0pt}{}{CO}{CO}C_6H_2(OH)_2[1:4]. \qquad C_{14}H_8O_4. \qquad 240.$$

40 gms. (excess) phthalic anhydride and 10 gms. (1 mol.) of *pure* quinol are heated for 3 hours in a flask in an oil bath at 170°–180° with 200 gms. pure conc. sulphuric acid and 20 c.cs. of water. It is then heated for 1 hour at 190°–200°. The hot solution is gently poured into about a litre of cold water in a large basin. The whole is then heated to boiling and filtered hot with suction. The residue is again extracted with boiling water and filtered hot. It is then boiled up with 400 c.cs. glacial acetic acid and filtered hot, to remove carbonaceous matter. The filtrate is diluted with its own volume of hot water and filtered, the residue being again extracted with boiling glacial acetic acid and again precipitated with hot water. The crude quinizarin which separates on cooling is filtered, well washed with water and dried on a water bath. It is then quickly distilled from a hard glass retort with a large flame, a porcelain mortar being used as receiver. The distillate is then powdered and recrystallised from glacial acetic acid and washed with more dilute acetic acid and finally with water.



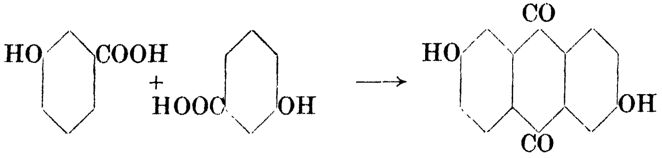
$$C_6H_4\genfrac{<}{>}{0pt}{}{CO}{CO}O + H_2C_6H_2(OH)_2 \rightarrow C_6H_4\genfrac{<}{>}{0pt}{}{CO}{CO}C_6H_2(OH)_2 + H_2O.$$

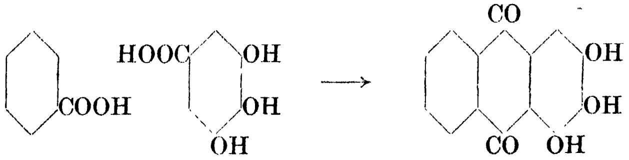
Yield.—20% theoretical (4 gms.). Dark red needles from toluene, orange-yellow leaves from glacial acetic acid ; M.P. 195° ; insoluble in water. (B., 8, 152 ; A., 212, 10 ; O. S., VI, 78.)

Note.—The quinizarin which solidifies in the neck of the retort may be recovered by distilling some glacial acetic acid from the retort, a distilling flask being used as receiver. Acetic acid vapour is inflammable, and care should be taken that it does not become ignited.

Reaction XXIX. (*c*) Condensation of Meta-hydroxy- and di-meta-dihydroxy-benzoic Acids with themselves and with Benzoic Acid under the

action of hot Sulphuric Acid. (B., 18, 2147.)—The products of this action are hydroxyanthraquinones like the above.





These reactions are of interest as confirming the structure of anthraquinone and its hydroxy derivatives.

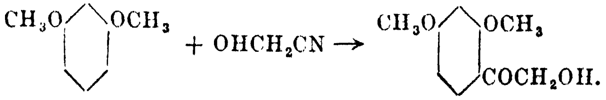
Reaction XXX. Condensation of a Nitrile with a Phenol or a Phenol Ether and Hydrolysis of the resulting Ketimine Hydrochloride to a Ketone. (J. C. S., 118, 309.)—This is a good method of synthesising phenolic ketones, and is an extension of the Gattermann method for phenolic aldehydes (Reaction XXVIII). (B., 48, 1122; H. Acta, 4, 707.)

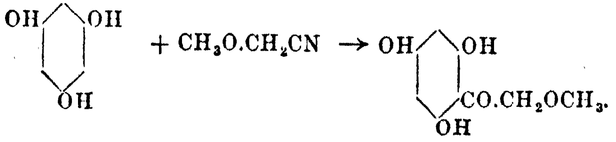
In 1915 Hoesch showed that the condensation of a nitrile with a phenolic compound led to the formation of a ketimine hydrochloride which could be easily hydrolysed to give a ketone.

The phenol and the nitrile are dissolved in *dry* ether, and anhydrous hydrogen chloride led in. On standing, the hydrochloride of the ketimine separates. Addition of fused zinc chloride is generally advantageous. The ketone is obtained on heating or boiling the hydrochloride with water. The ketimines themselves have also been isolated in some cases. They are unstable, and are hydrolysed on dissolving in water.

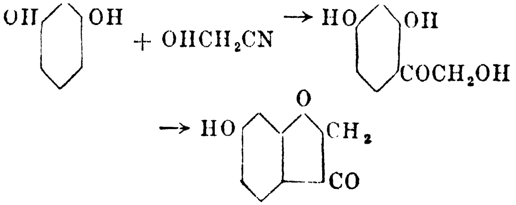
$$C_6H_5OH + C_6H_5.CH_2.CN \longrightarrow$$
$$[4]OHC_6H_4C(NH.HCl)CH_2C_6H_5 \longrightarrow$$
$$[4]OH.C_6H_4.CO.CH_2C_6H_5.$$

Condensation takes place in the *p*-position to the hydroxyl group. Di- and poly-hydric phenols and phenolic ethers can also be employed, as can hydroxy and methoxy nitriles (J. C. S., 118, 309).

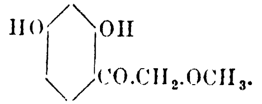




If a hydroxy nitrile is condensed with a di- or poly-hydric phenol, coumarone derivatives are obtained by elimination of water.



PREPARATION 48.—**ω-Methoxyresacetophenone** (*α-Methoxy-β-keto-β-(2 : 4-dihydroxyphenyl) ethane*).



$C_9H_{10}O_4$. 182.

6·5 gms. (1 mol.) of pure resorcinol are dissolved in 50 c.cs. of *anhydrous* ether and 5 gms. (1 mol.) of methoxyacetonitrile are added. A current of dry hydrogen chloride is passed through the solution for 2 hours, and the latter is allowed to stand in an ice chest for 5 days. The ether is then poured off from the yellow crystalline ketimine hydrochloride, which is washed twice with the same solvent and recrystallised from methyl alcohol. It forms a white crystalline mass (M.P. 205°–207°). It is dissolved in water and heated at 80° (not more, or tarry matter separates) for 30 minutes. The solution develops a deep red colour. On cooling, the ketone separates ; it is recrystallised from hot water.

$$C_6H_4(OH)_2[1:3] + CH_3OCH_2CN \rightarrow C_6H_3(OH)_2(CO.CH_2.OCH_3)[1:3:4].$$

Yield.—70% theoretical (8 gms.). Plates with nacreous lustre ; soluble in alcohol, ether, benzene ; insoluble in petroleum ether ; reduces Fehling's solution, forming copper mirror ; M.P. 136°. (J. C. S., 118, 309.)

Resacetophenone and phloroacetophenone can be prepared from resorcinol and phloroglucinol, respectively, and acetonitrile in good yield (O. S., XV, 70).

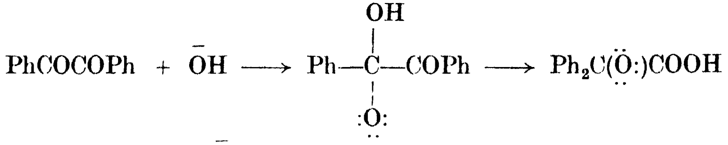
1 gm. of fused zinc chloride can be added in the above reaction either initially or after the passage of the hydrogen chloride. It improves the yield and shortens the time of standing, but, unless care is taken, it tends to cause decomposition of the product during its isolation.

Reaction XXXI. Action of Heat on Sodium Formate. (B., 15, 4507.)—When sodium formate is rapidly heated above 440°, an unusual reaction takes place. It loses hydrogen and forms sodium oxalate.

$$\begin{array}{c} HCOONa \\ + \\ HCOONa \end{array} = \begin{array}{l} COONa \\ | \\ COONa \end{array} + H_2.$$

In the presence of sodium hydroxide, carbonates or oxalates, the reaction takes place at 360° and to a greater extent. (C., 1903, II, 777; 1905, II, 367.) Oxidation of formic acid with nitric acid similarly yields oxalic acid. (B., 17, 9.)

Reaction XXXII. Action of Alkalis on certain α-di-ketones. (A., 25, 25 ; 31, 324 ; B., 14, 326 ; 19, 1868 ; 41, 1644.)—When benzil is fused with potassium hydroxide, or digested with alcoholic potash, or heated for a long time with aqueous potash, a molecular re-arrangement not unlike the pinacoline transformation (p. 86) takes place, and benzilic acid is formed. This is known as the benzilic transformation (see Ann. Rep., 1939, 195).



$$PhCOCOPh + \bar{O}H \longrightarrow Ph-\overset{\displaystyle OH}{\underset{:\underset{\cdot\cdot}{O}:}{C}}-COPh \longrightarrow Ph_2C(\overset{\cdot\cdot}{\underset{\cdot\cdot}{O}}:)COOH$$

$$\longrightarrow Ph_2C(OH)CO\bar{O} \longrightarrow Ph_2C(OH)COOK$$ (see Note, p. 104).

Anisil and cuminil in a similar way yield anisilic and cuminilic acids.

Preparation 49.—**Benzilic Acid** (*Diphenylylycollic acid*).

$(C_5H_5)_2C(OH).COOH$. $C_{14}H_{12}O_3$. 228.

50 gms. (excess) of caustic potash are melted with a small quantity of water in a silver, nickel, or copper crucible. The liquid is allowed to cool to 150° (for combined thermometer and stirrer, and precautions to be taken in alkali fusions, see p. 214), and 10 gms. of dry, finely-powdered benzil are added with constant stirring. The benzil melts and the whole soon sets to a solid mass of potassium benzilate. When all the oil has disappeared, the melt is cooled, dissolved in water, and benzilic acid precipitated by acidifying with hydrochloric acid. The precipitate is cooled with cold water and, to free it from traces of benzoic acid, is boiled in a dish with water until the smell of this acid has disappeared. On cooling, benzilic acid separates, and is purified by recrystallisation from hot water.

$$C_6H_5CO.CO.C_6H_5 + KOH = (C_6H_5)_2C(OH)COOK.$$

Yield.—80% theoretical (16 gms.). See Preparation 50. (A., 25, 25 ; 31, 329 ; B., 14, 236 ; O. S., I, 29.)

Preparation 50.—**Benzilic Acid** (*Diphenylglycollic acid*).

$(C_6H_5)_2C(OH).COOH$. $C_{14}H_{12}O_3$. 228.

20 gms. (1 mol.) of benzil, 20 gms. (excess) of solid potassium hydroxide and 40 c.cs. of water are placed in a flask, and when the potash has dissolved, 50 c.cs. of alcohol are added. The mixture is then heated for 10–12 minutes (not longer) on a boiling water bath, poured while still boiling into a beaker, and cooled and stirred to accelerate crystallisation. After half an hour's standing in ice, the crystals are filtered off at the pump through hardened filter paper, well pressed, and carefully washed with 40–50 c.cs. of ice-cold alcohol, so that the filtrate is finally almost colourless. The crystals are then dissolved in about 400 c.cs. of water, the solution filtered, brought to the boiling point, and 20 c.cs. of boiling dilute sulphuric acid are added. Part of the benzilic acid precipitates as an oil which, however, at once crystallises ; the rest separates out in

colourless needles on cooling the solution. It can be recrystallised from hot water.

$$C_6H_5.CO.CO.C_6H_5 + KOH = (C_6H_5)_2C(OH).COOK.$$

Yield.—90% theoretical (20 gms.). Colourless needles; sparingly soluble in cold water; readily in hot water, and in alcohol; M.P. 150°. For preparation from benzoin, see C. V., I, 89.

Reaction XXXIII. (*a*) **Condensation of an Aromatic Carboxylic Acid with Formaldehyde.** (Lederer-Manasse).—In the presence of mineral acids formaldehyde gives di-phenylmethane derivatives with aromatic acids in much the same way as with phenols (Reaction XIII), except that in this case the condensation takes place in the *meta* position.

Reaction XXXIII. (*b*) **Condensation of Malonic Acid with Aldehydes under the influence of ammonia or primary or secondary amines.** (Knoevenagel.) (B., 35, 1143.)—This reaction, usually conducted in alcoholic solution with piperidine as catalyst, illustrates the activating effect of two carbonyl groups on an intermediate methylene group, the initially-formed products generally undergoing dehydration and decarboxylation to give unsaturated monobasic acids. Doebner (B., 33, 2140) used pyridine as solvent with advantage. The function of the catalyst may be represented (Chem. Rev., 34, 345):

$$CH_2(COOH)_2 + \text{Base} \longrightarrow \text{Base}\overset{+}{H} + \overset{-}{C}H(COOH)_2$$

$$R\overset{+}{C}H—\overset{-}{O} + \overset{-}{C}H(COOH)_2 \longrightarrow RCH(\underset{..}{\ddot{O}}:)CH(COOH)_2$$

$$\text{Base}\overset{+}{H} + RCH(\underset{..}{\ddot{O}}:)CH(COOH)_2 \longrightarrow \text{Base} + RCH(OH)CH(COOH)_2$$

$$\longrightarrow RCH : C(COOH)_2 \longrightarrow RCH : CHCOOH + CO_2$$

Base ≐ Ammonia, Primary or Secondary Amine.

(See Note, p. 104).

In this way cinnamic aldehyde and malonic acid give cinnamylidene malonic acid.

$$C_6H_5.CH : CH.CHO + H_2C(COOH)_2$$
$$= C_6H_5CH : CH.CH : C(COOH)_2 + H_2O.$$

This latter, like all malonic acid derivatives, loses carbon dioxide on heating, and yields cinnamylidene acetic acid (see Preparation 427).

In like manner, also, crotonaldehyde yields sorbic acid (B., 33, 2140).

$$CH_3.CH : CH.CHO \longrightarrow CH_3.CH : CH.CH : C(COOH)_2$$
$$\longrightarrow CH_3CH : CH.CH : CHCOOH.$$

For another and similar condensation brought about by amines, see Reaction XLV.

PREPARATION 51.—**Cinnamic Acid** (*β-Phenylacrylic acid*).

$C_6H_5CH : CH.COOH.$ $C_9H_8O_2.$ 148.

20 gms. (1 mol.) of benzaldehyde and 80 gms. (2 mols. of NH_3) of an 8% solution of ammonia in alcohol, are added to 20 gms. (1 mol.) of malonic

acid. The mixture is heated on a water bath until a clear solution is obtained. The alcohol is then removed by evaporation and heating continued until the evolution of carbon dioxide ceases. The residue is dissolved in water, and cinnamic acid precipitated by adding hydrochloric acid. It is then purified as in Preparation 52.

$$C_6H_5CHO + H_2C.(COOH)_2 \longrightarrow C_6H_5CH : CH.COOH + CO_2 + H_2O.$$

Yield.—50% theoretical (14 gms.) (see p. 121). (A., 188, 194 ; B., 31, 2604.)

Reaction XXXIII. (*c*) **Condensation of Aromatic Aldehydes with Acid Anhydrides under the influence of Basic Catalysts.** (Perkin, J. C. S., 1868, 53, 181 ; *Organic Reactions*, Adams, Vol. I, 266 ; Ann. Rep., 1939, 210).—This is a reaction of very wide application for the synthesis of unsaturated aromatic acids, the preparation consisting in heating together the aldehyde and anhydride in presence of the basic catalyst which may be an alkali salt such as anhydrous sodium acetate (Perkin) or an alkali carbonate, sulphite, or phosphate, or pyridine, quinoline, or triethylamine (Kalnin, H. Acta, 11, 977), the function of the catalyst being expressed by *B* in the equations :

$$CH_3.CO.O.CO.CH_3 + B \longrightarrow \overset{-}{C}H_2.CO.O.COCH_3 + B\overset{+}{H}$$

$$Ar\overset{+}{C}H—\overset{-}{O} + \overset{-}{C}H_2.CO.O.CO.CH_3 \longrightarrow ArCH(\ddot{O}\colon).CH_2.CO.O.CO.CH_3 \qquad (C)$$

$$C + B\overset{+}{H} \longrightarrow ArCH(OH).CH_2.CO.O.CO.CH_3 \longrightarrow$$
$$ArCH{=}CH.COOH + CH_3COOH \quad \text{(See Note, p. 104).}$$

(i) As in all aldol-type reactions union takes place between the α-carbon atom of the acid anhydride (conveniently represented by the formula of the corresponding acid) and the aldehydic carbon (cf. aldol condensation, p. 105).

$$ArCHO + RCH_2.CH_2.COOH \longrightarrow ArCHOH.CH(CH_2R).COOH.$$

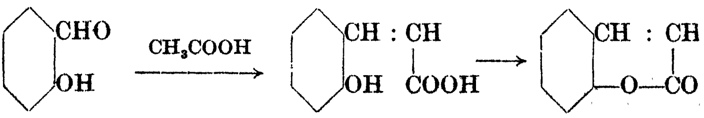
The hydroxy acid so formed is stable if (1) the α-carbon of the anhydride has only one hydrogen atom attached, or (2) if the hydroxy acid first formed is easily capable of forming a lactone :

(1) $C_6H_5CHO + (CH_3)_2CH.COOH \rightarrow C_6H_5CH(OH).C(CH_3)_2.COOH.$

(2) $C_6H_5CHO + (CH_2.COOH)_2 \rightarrow C_6H_5CHOH.CH.(COOH)CH_2COOH.$

$\rightarrow C_6H_5.\underbrace{CH.CH(COOH).CH_2COO}$ phenylparaconic acid.

(ii) If an *ortho*-phenolic aldehyde is used, a further loss of water takes place with the formation of a lactone.

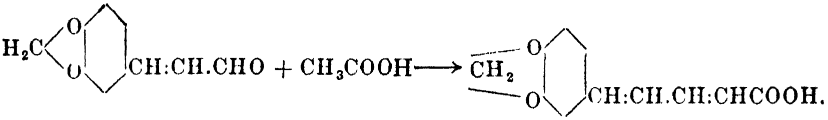


The anhydride used is generally that of the acid of which the sodium salt is employed; otherwise there is a liability to double decomposition between the sodium salt and the anhydride, giving both sodium salts and both anhydrides, thus leading to a mixture of condensation products. A low temperature helps to prevent such decomposition.

Both substituted aldehydes and acids may be used so that the reaction is capable of numerous modifications. The following equations will illustrate this:

$$C_6H_5CHO + CH_2ClCOOH \longrightarrow C_6H_5CH:CCl.COOH.$$

$$C_6H_5.CH:CH.CHO + CH_3COOH \longrightarrow C_5H_5CH:CH.CH:CHCOOH.$$



Piperic Acid.

Aliphatic aldehydes react with difficulty. See Ann. Rep., 1939, 210.

PREPARATION 52.—**Cinnamic Acid** (*β-Phenylacrylic acid*).

$C_6H_5.CH:CH.COOH.$ $C_9H_8O_2$. 148.

20 gms. (excess) of benzaldehyde, 30 gms. (excess) of acetic anhydride, both freshly-distilled, and 10 gms. (1 mol.) of freshly-prepared powdered anhydrous sodium acetate (see p. 517) are refluxed together for 8 hours in a 250-c.c. round-bottomed flask (fitted with a wide vertical air-condenser about 60 cms. long) in an oil bath, kept at 180°. A calcium chloride tube is fitted to the top of the condenser. The experiment need not be completed in one day; when finished, the hot reaction mixture is poured into a 1-litre round-bottomed flask, sodium carbonate is added till alkaline, and then water until the bulk is 5 times the original. The whole is then steam distilled until no more benzaldehyde comes over. The residue is filtered hot through a wet, folded filter paper to remove oily and resinous by-products, cooled, and acidified with dilute hydrochloric acid. The precipitated cinnamic acid is purified by reprecipitation from alkaline solution or by recrystallisation from hot water.

$$C_6H_5.CH:O + CH_3.COOH \longrightarrow C_6H_5.CH(OH).CH_2.COOH \longrightarrow$$
$$C_6H_5.CH:CH.COOH \longrightarrow C_6H_5.CH:CH.COOH.$$

Yield.—85% theoretical (15 gms.). Crystallises from hot water in fine needles; from alcohol in thick prisms; M.P. 133°.

For preparation of *m*-nitrocinnamic acid, see C. V., I, 398.

Malonic acid condenses especially readily. Even at ordinary temperatures, in presence of acetic anhydride, it yields benzalmalonic acid with benzaldehyde. Better results are obtained, however, by using a less powerful condensing agent—glacial acetic acid—at 100°. This synthesis is interesting as providing a method for the preparation of certain monobasic acids, since all malonic acids readily lose carbon dioxide on heating (see Preparation 427).

PREPARATION 53.—**Benzylidenemalonic acid** (*α-Phenylethen-ββ-di-acid*).

$$C_6H_5CH : C(COOH)_2. \qquad C_{10}H_8O_4. \qquad 192.$$

4 gms. of glacial acetic acid, 7 gms. (1 mol.) of benzaldehyde and 7 gms. (1 mol.) of malonic acid are heated together for 10 hours at 100° under a reflux. On cooling, benzalmalonic acid separates out, is filtered off and washed with chloroform.

$$C_6H_5CHO + H_2C(COOH)_2 \longrightarrow C_6H_5CH : C(COOH)_2 + H_2O.$$

Yield.—40% theoretical (5–6 gms.). Colourless crystals ; M.P. 196° with decomposition ; insoluble in chloroform ; is converted to cinnamic acid at 200°–210°. (A., 218, 129.)

Reaction XXXIII. (*d*) **Condensation of the Dichlorides of Aromatic Aldehydes with the Sodium Salts of certain Acids.** (B., 15, 969.)—This is a modification of the previous reaction used commercially to prepare cinnamic acid, by heating sodium acetate with benzal chloride. The latter is much cheaper than benzaldehyde.

$$C_6H_5.CHCl_2 + CH_3.COONa = C_6H_5.CH : CH.COONa + NaCl + HCl.$$

Reaction XXXIV. (*a*) **Condensation of Carbon Dioxide with a Phenol** (Kolbe, Schmitt). (J. pr., (2) 10, 89 ; 27, 39 ; 21, 397.)—When dry carbon dioxide is passed over dry sodium phenate at 110°, it is absorbed with the formation of sodium phenyl carbonate. If the temperature is then raised to 190° intramolecular rearrangement takes place and sodium salicylate is formed.

$$C_6H_5ONa + CO_2 \longrightarrow C_6H_5OCOONa \longrightarrow o\text{-}C_6H_4(OH)COONa.$$

$$o\text{-}C_6H_4(OH)COONa + C_6H_5ONa \longrightarrow o\text{-}C_6H_4(ONa)COONa + C_6H_5OH.$$

One half of the phenate only is converted into di-sodium salicylate.

There are indications that in the Schmitt modification of the process (see below) reaction may proceed by the direct nuclear carboxylation of the reactive phenoxide anion, all of the phenol being theoretically converted into salicylic acid :

$$C_6H_5\overset{-}{O}\overset{+}{Na} + CO_2 \longrightarrow C_6H_4(\underset{\cdot\cdot}{\ddot{O}}{:})COOH + \overset{+}{Na}$$

$$\longrightarrow C_6H_4(OH)COONa.$$

This is " Kolbe's synthesis " of phenolic acids. It is capable of very wide application. In all cases, the carboxyl group primarily seeks the *ortho*-position ; if that is occupied, some condensation in the *para*-position occurs. The following are some examples.

(i) Phenolic ethers also react, e.g. sodium guaiacolate gives 3-methoxy-2-hydroxybenzoic acid.

(ii) The polyhydric phenols react especially easily. Boiling with an aqueous solution of ammonium carbonate or under pressure with aqueous potassium carbonate is sufficient. (M., 1, 236, 468 ; 2, 448, 458.)

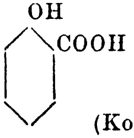
$$C_6H_4(OH)_2 + OH.COOK = C_6H_3(OH)_2COOK + H_2O,$$

(iii) α- and β-naphthols yield hydroxynaphthoic acids.

It is an interesting fact that if potassium phenolate is used in the Kolbe synthesis *para*-hydroxybenzoic acid is obtained, especially at high temperatures. Potassium phenyl carbonate is first formed, and heated up to 150° yields salicylic acid, but if the temperature be further raised, the *para*-acid is produced in increasing quantities until at 220° potassium *para*-hydroxybenzoic acid is the sole product.

Schmitt Modification.—In the formation of salicylic acid, only one half of the phenol is converted; the rest is obtained unchanged. Schmitt (*Dingler's Polytechnisches Journal*, 255, 259) succeeded in modifying the synthesis to obviate this defect, and his is the method always used industrially, although the other is more convenient in the laboratory. In Schmitt's synthesis sodium phenyl carbonate is prepared by heating up to 120°–140° dry sodium phenolate with carbon dioxide in autoclaves under pressure. Complete transformation of the intermediate sodium phenyl carbonate to mono-sodium salicylate then occurs on further heating. The carbon dioxide may be led in from a cylinder under pressure, or liquid or solid carbon dioxide may be mixed directly with the sodium phenolate in the autoclave. If preferred, the sodium phenyl carbonate can be prepared at ordinary pressures at 110° and then heated under pressure at 140°.

PREPARATION 54.—**Salicylic Acid** (1-*Hydroxy*-2-*carboxybenzene*).

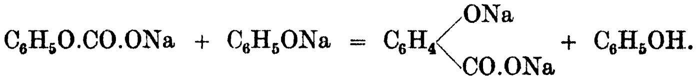


$C_7H_6O_3$. 138.

(Kolbe's Method.)

10 gms. (2 mols.) of pure sodium hydroxide are dissolved in 15 c.cs. of water in a metal basin, and, with stirring, 23 gms. (2 mols.) of crystallised phenol are gradually added. The solution is then heated over a small free flame, with continual stirring, until a crystalline film forms on the surface of the liquid. Evaporation is continued by heating with a luminous flame kept in constant motion. During the process the basin should be securely clamped. A caked mass is obtained which is crushed at intervals with a pestle. When the mass no longer cakes together, it is transferred to a dry warm mortar and pulverised as it cools. The powder, while still warm, is quickly returned to the basin, and heated as before with thorough stirring, until it is dry enough to form dust. It is then immediately placed in a 200-c.c. tubulated retort, where it is heated in a bath to 140° in a fairly rapid current of dry hydrogen (*caution*) obtained from a Kipp generator.

When in about 1 hour no more moisture condenses in the neck of the retort, and the body of the retort appears dry, the mass is allowed to cool in the current of hydrogen and then, while still warm, broken up, removed, quickly powdered in a mortar, and replaced. The object of the above operations is to obtain perfectly dry, uncharred, well-powdered sodium phenate, for it is on these factors that the success of the whole preparation depends. A moderate stream of carbon dioxide, dried through two wash bottles of conc. sulphuric acid is passed over the surface of the sodium phenate by means of a bent tube fixed through the tubulus of the retort, and terminating 1 cm. above the substance. The retort is immersed as far as possible in the oil bath, and the temperature gradually raised to 110° and kept there for 1 hour. The temperature is then raised to 190° in 4 hours, and on to 200°, where it is kept for 2 hours. During the whole operation, the mass is stirred frequently with a glass rod momentarily inserted through the tubulus, and the retort also shaken from time to time, to ensure that fresh surfaces shall be exposed to the action of the gas. During the heating phenol distils, and collects in the neck of the retort while the contents darken in colour. On cooling, the phenol is melted by application of a flame to the outside of the neck and allowed to flow away; then the crude reaction product is shaken out through the tubulus into a large beaker, and the retort washed out several times with warm water. The whole is boiled, filtered if necessary, and treated with much conc. hydrochloric acid (100 c.cs.), cooled for some hours in ice-water, and precipitation of the crude salicylic acid facilitated by rubbing the sides of the vessel with a glass rod. The precipitate is filtered off at the pump, washed with a little cold water, and dried on a porous plate. The filtrate is evaporated to low bulk and a little more acid obtained. It may be purified by recrystallising from boiling water with the addition of animal charcoal, but it is better to distil the crude acid with superheated steam (see p. 29). The crystals are *thoroughly* dried, first on a porous plate, and then by heating on a water bath. They are placed in a short-necked flask and heated in an oil bath of 170°. Then connection is made to the steam generator and a moderate current of steam at 175° pressed in. It is important that the steam generator be not connected to the flask till the oil bath and steam reach the same temperature. A wide condenser is used (width of inner tube 3 cms.; of outer jacket 6 cms.; length of latter 80 cms.), otherwise the condensing acid soon blocks it. The connecting tube between the flask and condenser should be 2·5 cms. wide, and as short as possible. The side-piece should be near the bulb. When no more acid distils, the crystals in the condenser are added to the distillate, which is boiled and filtered. The acid separates on cooling.



$$C_6H_5O.CO.ONa + C_6H_5ONa = C_6H_4\left\langle\begin{matrix}ONa\\CO.ONa\end{matrix}\right. + C_6H_5OH.$$

Yield.—60% theoretical, allowing for phenol recovered (10 gms.). Colourless needles; soluble in alcohol and hot water; volatile in steam; much used in industry as an antiseptic and a dye intermediate; yields phenol on heating; M.P. 158·5°. (B., 8, 537; Dingl. Poly. J. (1885), 255, 259; D.R.P., 38, 742; E.P. 353464.) (J. pr., [2], 10, 95; 27, 39; 31, 397.)

For purification, see E.P., 353921.

Reaction XXXIV. (*b*) **Action of Carbon Dioxide on an Organo-magnesium Halide (Grignard).** (B., 35, 2519; 39, 634; 40, 1584.)—When an alkyl or aryl magnesium bromide or iodide dissolved in *dry* ether is treated with *dry* carbon dioxide, the mono-carboxylic acid of the next higher series is formed. Like all "Grignards" (see pp. 73, 79, 101) this reaction is of very general application. It works better with iodides than with bromides, and with aryl rather than alkyl compounds. The general remarks on the other Grignard reactions apply here. Moisture must be absent, iodine can be used as a catalyst (see p. 126). Also the reaction takes place in two stages, the usual intermediate compound being obtained.

$$R.Mg.I + CO_2 = R.COOMgI.$$

$$R.COOMgI + H_2O = R.COOH + OH.MgI.$$

Either acid or alkali can be used to hydrolyse the intermediate compound. The yields in most cases are good, but the reaction can sometimes take another course. (B., 40, 1584.)

C. V., I, 361, 363, and C. V., II, 425, describe other applications of this reaction.

Preparation 55.—**Propionic Acid** (*Propan acid*).

$CH_3.CH_2.COOH.$ $C_3H_6O_2.$ 74.

All vessels used in this experiment must be absolutely *dry*. 12 gms. (1 mol.) of *dry* bright magnesium turnings (see Preparation 19) are treated with a solution of 28 gms. (1 mol.) of *dry* ethyl iodide in 20 c.cs. of *dry* ether (see p. 219) contained in a flask fitted with a reflux condenser. The action may, if necessary, be started by adding a crystal (0·05 gm.) of iodine; should it become too vigorous, it is moderated by cooling in water. When all the magnesium has dissolved, a not too rapid stream of carbon dioxide, washed once with sodium carbonate solution, twice with conc. sulphuric acid, and passed then over phosphorus pentoxide, is led in until it ceases to be absorbed, the flask being cooled if required. The ether is removed on a water bath and the residue distilled with dilute sulphuric acid (water is added as required) until the distillate is no longer acid. The propionic acid may be isolated by forming the lead salt, proceeding as in Preparation 473, or the aqueous solution may be treated with excess of sodium carbonate and evaporated to dryness. The powdered residue is then distilled with conc. sulphuric acid until the temperature reaches 155°. The distillate is again distilled, the fraction 137°–142° being retained.

$$C_2H_5I + Mg = C_2H_5.Mg.I.$$

$$C_2H_5.Mg.I + CO_2 = C_2H_5.COOMgI.$$

$$C_2H_5.CO.OMgI + H_2O = C_2H_5.COOH + (OH)MgI.$$

Yield.—50% theoretical (7 gms.). Colourless liquid; acetic acid odour; M.P. 24°; B.P. 141°; D. ${}^{0}_{4}$ 1·913.

The yield increases with aryl-compounds, as may be seen from the two following preparations.

Preparation 56.—**Benzoic Acid** (*Benzenemonocarboxylic acid*).

$C_6H_5.COOH.$ $C_7H_6O_2.$ 122.

2·6 gms. (1 mol.) of clean magnesium powder (or thin shavings or ribbon about 2 mms. in width, each piece about 1 cm. long, cleaned with fine emery paper and then with filter paper) are dried in an air oven at 110° for 20 minutes and placed in a dry flask fitted with a reflux. A mixture of 40 c.cs. of *dry* ether (see p. 219) and 20·4 gms. (1 mol.) of *dry* iodobenzene of constant boiling point, and a crystal of iodine are then added. The flask is dipped in hot water or heated on a water bath so that the ether boils gently.

In about half an hour a white flocculent precipitate begins to form, and when the heat of the reaction makes the ether boil vigorously, the water bath is removed. The flask is now wrapped in a dry cloth to conserve the heat of the reaction, and in the course of 2 hours the magnesium is practically all dissolved. (If this does not occur, traces of moisture are probably present, and the experiment must be repeated, the ether being distilled off and again dried over sodium.) When the boiling of the ether slackens, the flask is reheated for half an hour as before on a water bath.

The flask is then cooled in ice-water, the condenser removed, and a slow current of carbon dioxide, washed and dried as in the previous experiment, led into the ethereal solution, which may still contain traces of undissolved magnesium. The cooling must be continued throughout the operation. The reaction mixture forms two layers an upper layer of ether, and a heavy resinous lower layer of the reaction product. If the gas current is too rapid, only a slight layer of resinous mass will be obtained, but the preparation will still succeed if the cooling be thorough. Powdered ice is now added, and then, slowly, 30 c.cs. (excess) hydrochloric acid (15%). The precipitated benzoic acid is extracted with ordinary ether, the latter removed on a water bath, and the residue gently warmed with dilute caustic alkali. The undissolved portion (see B., 49, 1584) is filtered off, and the benzoic acid reprecipitated with hydrochloric acid. More acid is obtained by extracting the mother liquor with ether. The whole is recrystallised from hot water.

$$C_6H_5I \longrightarrow C_6H_5.Mg.I \longrightarrow C_6H_5.CO.O.MgI \longrightarrow C_6H_5.COOH.$$

Yield.—90% theoretical (11 gms.). Colourless needles ; soluble in hot water, and in alcohol and ether ; volatile in steam ; M.P. 122° ; B.P. 250°. (C. V., I, 363.)

PREPARATION 57.—**Triphenylacetic Acid** (*Triphenylethan acid*).

$(C_6H_5)_3C.COOH.$ $C_{20}H_{16}O_2.$ 288.

10 gms. (1 mol.) of triphenyl chloromethane (see p. 440) and 0·05–0·1 gm. of iodine are dissolved by gentle heating in 50 c.cs. of ether, dried as on p. 219. 2 gms. (2½ mols.) of *clean, dry* magnesium powder (see Preparation 19) are added, and the whole boiled under a reflux while a not too rapid current of *dry* carbon dioxide (see Preparation 55) is led into the liquid. After 3 hours, a lemon-yellow precipitate of the complex magnesium compound has formed. While the carbon dioxide is passing in, the whole is frequently shaken up and dry ether is added to replace that removed by the carbon dioxide. To decompose the complex magnesium compound, 60 c.cs. of water are added to the flask, and the whole well shaken, poured into a basin, gradually treated with 40 c.cs. of conc. hydrochloric acid to dissolve the excess of magnesium, and boiled for 3 minutes, during which it is well shaken. The crude acid is filtered off on cooling, washed, and boiled in a porcelain basin with 200 c.cs. (excess) of a 10% caustic soda solution and 100 c.cs. of water, when the greater por-

tion of the acid goes into solution. The mixture is diluted with 300 c.cs. of water, cooled, filtered, and 100 c.cs. of conc. hydrochloric acid added. The liquid is heated to make the somewhat gelatinous precipitate granular, cooled, the acid filtered off, washed and dried. It is recrystallised from glacial acetic acid.

$$(C_6H_5)_3CCl \rightarrow (C_6H_5)_3CMgCl \rightarrow (C_6H_5)_3CCOOMgCl \rightarrow (C_6H_5)_3C.COOH.$$

Yield.—83% theoretical (8·5 gms.). Long glittering prisms ; sparingly soluble in water, ether or benzene ; M.P. 264°–265°. (B., 39, 634.)

For a *résumé* of some other applications of Grignard reagents, see J. S. C. I., 41, 7.

Reaction XXXIV. (*c*) **Action of Carbon Dioxide on Sodium Acetylides in Dry Ether.** (B., 12, 853 ; J. pr., [2], 27, 417 ; B., 33, 3586.)—This is an example of the great activating influence of a triple bond. When carbon dioxide is passed into a solution of the sodium derivative of an acetylenic hydrocarbon in *dry* ether, direct addition takes place to give the sodium salt of the next highest acetylenic carboxylic acid. For example, sodium allylene yields sodium tetrolate :

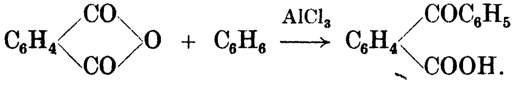
$$CH_3C \vdots CNa \longrightarrow CH_3.C \vdots C.COONa,$$

and sodium phenyl-acetylene gives sodium phenyl-propiolate :

$$C_6H_5C \vdots CNa \longrightarrow C_6H_5.C \vdots C.COONa.$$

This reaction should be compared with the preceding one. It should be noted that the presence of a triple bond attached to a carbon makes a hydrogen attached to that carbon replaceable by a metal (cf. Reaction XXIII (*a*)).

Reaction XXXV. (*a*) **Condensation of Phthalic Anhydride with Aromatic Hydrocarbons in the presence of Anhydrous Aluminium Chloride** (Friedel-Crafts). (A., 291, 9 ; C. r., 119, 139.)—When the dichloride of phthalic anhydride reacts with the hydrocarbon, benzene, in presence of anhydrous aluminium chloride, phthalophenone (diphenylphthalide) is formed (see p. 113). With phthalic anhydride itself the reaction can be made to take the same or a different course. Using an excess of hydrocarbon, condensation and hydrolysis occur, and *o*-benzoyl-benzoic acid or its homologues are obtained according to the reacting hydrocarbon. Not only can the latter be varied, but derivatives of phthalic anhydride may be used, so that a great number of compounds can be synthesised in this way.

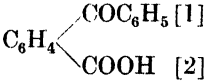


$$C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle O + C_6H_6 \xrightarrow{AlCl_3} C_6H_4\left\langle\begin{matrix}COC_6H_5\\COOH.\end{matrix}\right.$$

The *ortho*-benzoyl-benzoic acids readily yield anthraquinone and its derivatives (see p. 87). It may be noted that *o*-benzoyl-benzoic acid itself, with benzene and aluminium chloride, yields phthalophenone ; the same compound is made directly from phthalic anhydride by increasing the amount of the latter or by adding acetic anhydride. The same holds for *p*-toluoylbenzoic acid and ditoluoylphthalide.

Succinic and glutaric anhydrides condense with benzene in similar manner (O. S., XIII, 12).

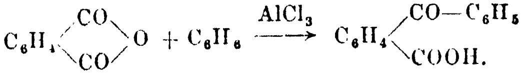
PREPARATION 58.—*o*-Benzoylbenzoic Acid (*Diphenyl ketone-2-carboxylic acid*).



$C_6H_4\left\langle\begin{matrix}COC_6H_5\ [1]\\ COOH\ [2]\end{matrix}\right.$

$C_{14}H_{10}O_3$. 226.

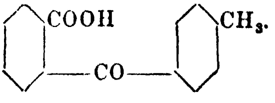
175 gms. (excess) of dry benzene are added to 50 gms. (1 mol.) of finely-powdered phthalic anhydride. To this are added 90 gms. fresh aluminium chloride and the mixture is gently heated on a water bath in a flask fitted with a good mechanical agitator and a reflux condenser (see Fig. 38). The reaction is moderated by cooling. When the mass becomes viscous, the temperature is raised to 70° and kept there till the evolution of hydrochloric acid ceases. The mechanical agitator is removed and an ordinary condenser attached. Four volumes of cold water are gradually added through a tap funnel, and the heat evolved causes most of the unchanged benzene to distil over. Steam is then passed through the mixture to remove the remainder of the benzene, and the residue is boiled for 4 hours, caustic soda solution being added to make slightly alkaline. The precipitated alumina, formed by the decomposition of the aluminium compound, is filtered off and washed with boiling water. The filtrate which contains the sodium salt of *o*-benzoylbenzoic acid is then acidified with dilute hydrochloric acid, and the free acid filtered off. It is then recrystallised from water.



$$C_6H_4\left\langle\begin{matrix}CO\\ CO\end{matrix}\right\rangle O + C_6H_6 \xrightarrow{AlCl_3} C_6H_4\left\langle\begin{matrix}CO-C_6H_5\\ COOH.\end{matrix}\right.$$

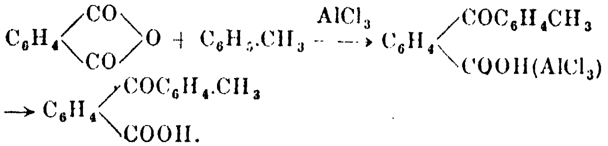
Yield.—95% theoretical (72 gms.). Colourless crystals; M.P. 127° when anhydrous; contains $1H_2O$ when crystallised from water, M.P. 94°. (A., 291, 9; B., 14, 1865; 41, 3631.)

PREPARATION 59.—2-*p*-Toluoylbenzoic Acid (4-*Methyldiphenyl ketone-2′-carboxylic acid*).



$C_{15}H_{12}O_3$. 240.

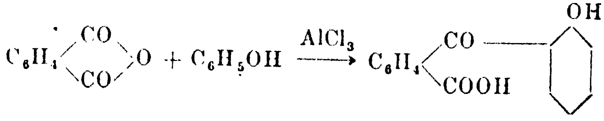
50 gms. (1 mol.) of finely-powdered phthalic anhydride and 200 gms. (excess) of dry redistilled toluene are mixed together, and 100 gms. (excess) of finely powdered, freshly-prepared, anhydrous aluminium chloride (see p. 514) are added all at once. Hydrogen chloride is evolved, and the mixture becomes warm. After 10 hours, water is added, and excess of toluene removed by steam distillation. The aqueous solution is poured off (from it a little phthalic acid may be removed by acidification), and the remaining cake is treated with sodium carbonate till alkaline. Steam is passed in for 5 hours to decompose the aluminium compound, the whole filtered, and the filtrate acidified whereby 2-*p*-toluoylbenzoic acid is precipitated.



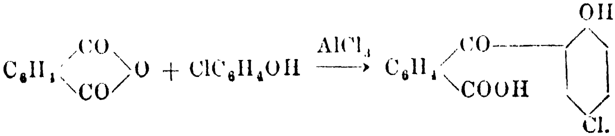
$$C_6H_4\left<\begin{matrix}CO\\CO\end{matrix}\right>O + C_6H_5.CH_3 \xrightarrow{AlCl_3} C_6H_4\left<\begin{matrix}COC_6H_4CH_3\\COOH(AlCl_3)\end{matrix}\right. \rightarrow C_6H_4\left<\begin{matrix}COC_6H_4.CH_3\\COOH.\end{matrix}\right.$$

Yield.—97% theoretical (78 gms.). Colourless crystals ; insoluble in cold water ; M.P. 146°. (B., 41, 3632 ; J. pr., [2], 33, 318 ; A., 311, 178 ; C. V., I, 517.)

Reaction XXXV. (*b*) **Condensation of Phthalic Anhydride with Phenols in presence of Anhydrous Aluminium Chloride.** (B., 52, 2098 ; 53, 826.)—This is an extension of the previous reaction to phenols ; employment of tetrachloroethane as solvent has enabled satisfactory yields to be obtained. Condensation takes place in the *ortho*-position to the hydroxyl group. Thus phenol and phthalic anhydride yield 2-(*o*-hydroxybenzoyl)-benzoic acid.

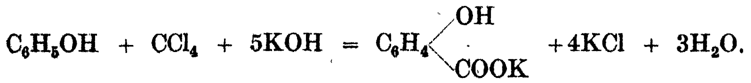


and *p*-chloro-phenol and phthalic anhydride give 2-(2-hydroxy-5-chloro-benzoyl)-benzoic acid.



This reaction is specially interesting since many of the above compounds readily yield the corresponding anthraquinone derivatives (see p. 87), e.g. 4-chloro-1-hydroxy-anthraquinone has been obtained from *p*-chloro-phenol ; substituted anthraquinones of this type are becoming increasingly important.

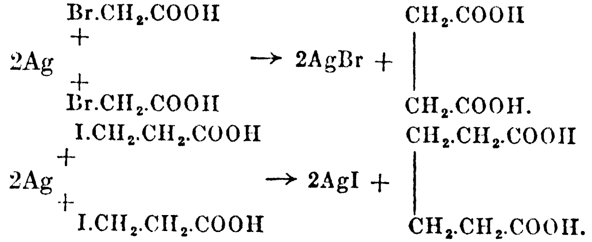
Racttion XXXVI. Condensation of Carbon Tetrachloride with Phenols and simultaneous Hydrolysis (Tiemann-Reimer). (B., 10, 2185.)—This reaction is closely analogous to that of the formation of hydroxy-aldehydes by means of chloroform and caustic alkali (see p. 111). A mixture of a phenol, carbon tetrachloride and caustic soda or caustic potash solution is boiled. Condensation occurs, chiefly in the *para*-position, but small amounts of the *ortho*-acids are also formed. The product, after the excess of carbon tetrachloride has been removed, is saturated with carbon dioxide and the unchanged phenol extracted with ether. The hydroxy acids are then precipitated by acidification with hydrochloric acid.



$$C_6H_5OH + CCl_4 + 5KOH = C_6H_4\left<\begin{matrix}OH\\COOK\end{matrix}\right. + 4KCl + 3H_2O.$$

A variation of this method consists in heating carbon tetrachloride with potassium phenolate under pressure with sufficient alcohol to give a clear solution. The product in this case is mostly the *ortho*-acid (cf. Reaction XXXIV (*a*)).

Reaction XXXVII. Action of finely-divided Metals on Halogeno Acids. (B., 2, 720 ; 28, R., 466.)—The use of metals—sodium, copper, silver—to eliminate halogen from halogen compounds, and bring about the condensation of the carbons to which the halogen atoms are attached has a very wide application. It is employed as a standard method with such halogen substituted acids as react readily, to give higher dibasic acids. Thus bromoacetic acid on heating with finely-divided metallic silver yields succinic acid ; β-iodo-propionic acid in a similar manner gives adipic acid with silver at 140° and with copper at 160°.

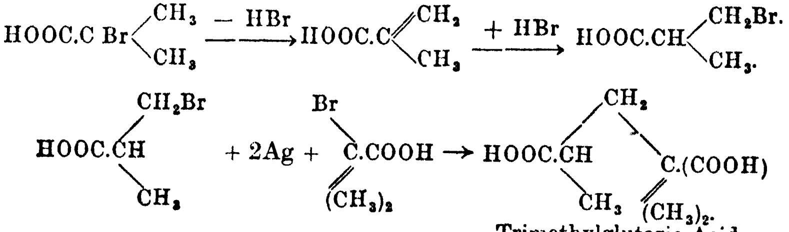


$$\begin{matrix} & Br.CH_2.COOH \\ & + \\ 2Ag & \\ & + \\ & Br.CH_2.COOH \end{matrix} \rightarrow 2AgBr + \begin{matrix} CH_2.COOH \\ | \\ CH_2.COOH. \end{matrix}$$

$$\begin{matrix} & I.CH_2.CH_2.COOH \\ & + \\ 2Ag & \\ & + \\ & I.CH_2.CH_2.COOH \end{matrix} \rightarrow 2AgI + \begin{matrix} CH_2.CH_2.COOH \\ | \\ CH_2.CH_2.COOH. \end{matrix}$$

Of the metals mentioned silver gives the best results, while iodo- and then bromo- give better yields than chloro-acids.

This synthesis has one anomalous application. When α-bromo-isobutyric acid (or its ethyl ester) is heated with silver, some tetramethylsuccinic acid is produced in the ordinary way (B., 23, 297 ; 26, 1458). But there also appears trimethylglutaric acid (A., 292, 220). To explain the unexpected formation of this acid, it has been assumed that a portion of the α-bromoisobutyric acid gives up HBr to form methylacrylic acid. This latter then forms β-bromoisobutyric acid, and the silver withdraws bromine from the α- and β acids, whereby the residues unite to tri-methylglutaric acid (B., 22, 48, 60). A similar explanation applies to some other syntheses in which tetramethylsuccinic and trimethylglutaric acids appear together.



Trimethylglutaric Acid.

(Compare this reaction with Reaction XLVII.)

Reaction XXXVIII. (*a*) **Action of Aqueous and Alcoholic Potassium or Sodium Cyanide on Aliphatic Halogen Compounds, and Hydrolysis of the Nitriles so formed.** (B., 14, 1965; 15, 2318.)—The preparation and hydrolysis of nitriles are dealt with on p. 157 and p. 242 respectively. In many cases, however, it is unnecessary to isolate the nitrile; it can be directly hydrolysed to the corresponding acid on its formation. Among others, the following syntheses have been carried out in this way :—

(i) *n*-Valeric acid [*pentan acid*] from *n*-butyl bromide (Am. Soc., 42, 310).

(ii) Methyl succinic acid [*methylbutan di-acid*] from propylene dibromide.

(iii) *n*-Pimelic acid [*heptan di-acid*] from penta-methylene di-bromide.

(iv) Tricarballylic acid [3-*carboxy-pentan di-acid*] from propenyl tribromide (Preparation 62).

(v) Citric acid [3-*hydroxy*-3-*carboxy-pentan di-acid*] from dichloroacetonic acid.

PREPARATION 60.—**Malonic Acid** [*Propan di-acid*].

$$CH_2(COOH)_2. \qquad C_3H_4O_4. \qquad 104.$$

100 gms. (1 mol.) of powdered chloroacetic acid are treated with 150 gms. of broken ice and dissolved in 125 gms. (1 mol.) of $33\frac{1}{3}\%$ caustic soda solution. If the liquid is still acid, it is exactly neutralised with caustic soda solution, and then treated with a solution of 69 gms. (1 mol.) of 98% potassium cyanide in 130 gms. of water which has been warmed to 40°. After an hour, the mixture is slowly warmed to 100° and kept at this temperature for 1 hour. It is allowed to cool to 25°, 125 gms. (1 mol.) of $33\frac{1}{3}\%$ caustic soda solution are again added, and the liquid is slowly warmed to 100° and kept at that temperature until no more ammonia is evolved (2–3 hours). When a sample of the liquid treated with more sodium hydrate solution gives no further ammonia on boiling, the conversion of the cyanoacetic acid into malonic acid is complete. The solution is cooled, acidified with dilute hydrochloric acid and carefully evaporated to complete dryness on a water bath. The residue is powdered and repeatedly extracted with ether and the ether removed on a water bath, when malonic acid remains. It may be purified by dissolving in the minimum of caustic soda solution, boiling with decolorising carbon, acidifying, evaporating to dryness, and extracting with ether as before.

$$CH_2Cl.COOH \xrightarrow{NaOH} CH_2Cl.COONa \xrightarrow{NaCN} CH_2(CN)COONa$$

$$\xrightarrow{NaOH} CH_2(COONa)_2 \xrightarrow{HCl} CH_2(COOH)_2.$$

Yield.—84% theoretical (95 gms.). Colourless crystals; easily soluble in water, alcohol, and ether; M.P. 132°; loses carbon dioxide yielding acetic acid at 140°–150°. All malonic acid homologues react similarly (see Reaction XXXIII (*b*)). (A., 204, 125; C. V., II, 376.)

Diethyl malonate may be prepared from chloroacetic acid by a similar method.

PREPARATION 61.—**Succinic Acid** [*Butan di-acid*].

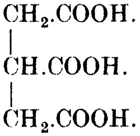
$COOH.CH_2.CH_2.COOH.$ $C_4H_6O_4.$ 118.

100 gms. (1 mol.) of ethylene dibromide and 75 gms. (excess) of potassium cyanide in alcoholic solution are refluxed on a water bath in a 750-c.c. round-bottomed flask until potassium bromide ceases to separate out from the solution. The latter is then cooled and filtered; 60 gms. (2 mols.) of solid caustic potash are added, and the mixture again refluxed on a water bath in a fume cupboard until the strong evolution of ammonia gas begins to slacken. The flask is then cooled, and the contents are acidified with dilute hydrochloric acid and carefully evaporated to dryness. The dry powdered residue is repeatedly extracted with absolute alcohol, and the extract distilled on a water bath. The succinic acid remains as small crystals; it is recrystallised from hot water, decolourising if necessary with a little decolourising carbon.

$$\begin{aligned} CH_2Br.CH_2Br + 2KCN &= CH_2(CN).CH_2.CN + 2KBr. \\ (CH_2CN)_2 + 2KOH + 2H_2O &= (CH_2COOK)_2 + 2NH_3. \\ (CH_2COOK)_2 + 2HCl &= \begin{array}{l} CH_2.COOH + 2KCl \\ \quad\vert \\ CH_2.COOH. \end{array} \end{aligned}$$

Yield.—80% theoretical (50 gms.). Colourless prisms; soluble in water, alcohol, and ether; insoluble in chloroform; sublime above 100° without decomposition; M.P. 185°; at 235° decompose forming the anhydride. (P. R. S., 10, 574; A., 120, 268.) For the isolation of ethylene dicyanide, see p. 157.

PREPARATION 62.—**Tricarballylic Acid** (*3-Carboxy-pentan-di-acid*).



$$\begin{array}{l} CH_2.COOH. \\ \vert \\ CH.COOH. \\ \vert \\ CH_2.COOH. \end{array}$$

$C_6H_8O_6.$ 176.

50 gms. (1 mol.) of glyceryl tribromide are dissolved in excess of alcohol, 36 gms. (1 mol.) of coarsely-powdered potassium cyanide are added, and the whole heated for 15 hours in a soda-water bottle with the cork well tied down, in a water bath, the bottle being well wrapped in a cloth. A small autoclave can also be used. The bottle is then cooled in a freezing mixture, *carefully* (use goggles) opened, and the alcoholic liquid filtered from the potassium bromide which has separated out.

The filtrate is now refluxed on a water bath with a sufficient quantity (40 gms.) of caustic potash, to decompose the cyanide formed, until no more ammonia is evolved. The alcohol is distilled off on a brine bath, and the cooled residue evaporated to dryness with excess nitric acid. From it, after being well dried and powdered, the tricarballylic acid may be extracted with absolute alcohol. The dark-coloured substance obtained on evaporating off the alcohol is recrystallised from hot water with the addition of decolorising carbon.

$$C_3H_5Br_3 + 3KCN = C_3H_5(CN)_3 + 3KBr.$$

$$CH_2(CN).CH(CN).CH_2CN + 3KOH + 3H_2O$$
$$= CH_2(COOH).CH(COOH).CH_2COOH + 3NH_3.$$

Yield.—70% theoretical (22 gms.). Colourless rhombic plates ; easily soluble in water and alcohol ; M.P. 161°. (P. R. S., 14, 77.). C. V., I, 523, gives preparation from diethylmalonate.

General Methods of isolating organic acids from their salts may here be noted.

(i) An insoluble acid can be precipitated from a solution of a soluble salt by addition of dilute hydrochloric, sulphuric, or nitric acid, and filtered off or extracted with a solvent (see Preparations 49, 54, 58, 189).

(ii) A volatile acid soluble in water can be obtained by treatment of a solution of its alkali salt with sulphuric acid, dilute or strong, according as the acid is more or less volatile, and subsequent distillation (see Preparations 55, 178).

(iii) A liquid or volatile acid soluble in water may be isolated by treatment of the lead salt with H_2S and filtration or evaporation of the acid (see Preparation 191).

(iv) A soluble non-volatile acid may be obtained by evaporating a soluble salt with dilute hydrochloric or nitric acids to dryness, and extracting the residue with a suitable solvent. Hydrochloric acid is usually preferable, as nitric acid may oxidise the product (see Preparations 60, 61, 62).

(v) If the metal present is not an alkali metal, and if the acid is soluble, the former may be precipitated by addition of the exact quantity of sulphuric acid, say, or by means of H_2S or hydrochloric acid ; the filtrate is then evaporated to dryness or distilled. Sulphuric acid is used when calcium, strontium, barium, lead, etc.,. are present ; hydrochloric acid when silver, lead, or mercury (-ous) are the metals to be dealt with ; while H_2S is advantageous when tin or lead have to be removed (see Preparations 64, 488, etc.). It is best to use sulphuric acid where a subsequent distillation is necessary.

Reaction XXXVIII. (*b*) **Action at 200° of Aqueous or Aqueous-alcoholic Potassium Cyanide in presence of Cuprous Cyanide on Aromatic Halogen Compounds, and Hydrolysis of the Nitriles so formed.** (B., 52, 1749.)—It is difficult directly to replace nuclear halogen atoms in aromatic compounds, unless these atoms are rendered labile by the presence of nitro- or other negative groups (see p. 204). Lately, however, it has been shown that by the action of aqueous or aqueous-alcoholic potassium cyanide at 200°, using cuprous cyanide as catalyst, combined replacement of the halogen by CN and hydrolysis of the nitrile so formed occurs. In this way bromo-benzene has been directly converted into benzoic acid, *p*-dibromobenzene into terephthalic acid, and *p*-bromoaniline into *p*-aminobenzoic acid. Similar transformations have also been effected with derivatives of naphthalene and thiophen. For the action of copper powder on aromatic halogen compounds, see Reactions VII (*b*) and LII (*a*).

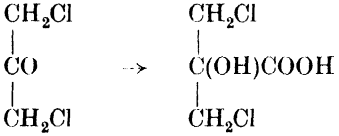
Reaction XXXVIII. (*c*) **Action of Hydrogen Cyanide on Aldehydes and Ketones and Hydrolysis of the Cyanohydrins so formed.** (B., 14, 235 ; C. Z., (1896), 90 ; C., (1900), I, 402.)—As is explained under Reaction L, aliphatic and aromatic aldehydes and ketones or their bisulphite compounds react with hydrogen cyanide to form cyanohydrins (α-hydroxy-nitriles). These are readily hydrolysed to α-hydroxy-acids, for the preparation of which the above reaction is often directly used since the isolation of the nitrile is unnecessary.

In the sugar group it is of especial interest, not only for its value in determining constitution, but also for the syntheses of sugars and other derivatives containing long carbon chains. Thus *d*-glucose yields in this way the lactone of α-*d*-glucoheptonic acid, which may be reduced to α-*d*-glucoheptose—that is to a sugar containing one more secondary-alcohol group than the original sugar (see Reaction LXV (*b*), where the subject is further treated).

In this way, too, lactic acid has been synthesised from acetaldehyde.

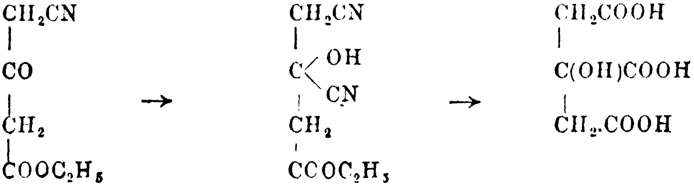
$$CH_3CHO + HCN \longrightarrow CH_3.CH(OH)CN \longrightarrow CH_3CH(OH)COOH.$$

Dichloroacetonic acid has been prepared from dichloroacetone.



$$\begin{array}{l} CH_2Cl \\ | \\ CO \\ | \\ CH_2Cl \end{array} \longrightarrow \begin{array}{l} CH_2Cl \\ | \\ C(OH)COOH \\ | \\ CH_2Cl \end{array}$$

while citric acid has been obtained from γ-cyano-aceto-acetate.



$$\begin{array}{l} CH_2CN \\ | \\ CO \\ | \\ CH_2 \\ | \\ COOC_2H_5 \end{array} \longrightarrow \begin{array}{l} CH_2CN \\ | \\ C\begin{array}{l} \diagup OH \\ \diagdown CN \end{array} \\ | \\ CH_2 \\ | \\ CCOC_2H_5 \end{array} \longrightarrow \begin{array}{l} CH_2COOH \\ | \\ C(OH)COOH \\ | \\ CH_2.COOH \end{array}$$

PREPARATION 63.—Glycollic Acid (*Ethanol Acid*).

$$CH_2(OH)COOH. \qquad C_2H_4O_3. \qquad 76.$$

20 gms. (1 mol.) of potassium cyanide (98%) are powdered and dissolved in 100 c.cs. of water, 26 c.cs. (1 mol.) of 40% formaldehyde are added, the mixture warmed—not above 30°—until homogeneous and after standing 1 hour, treated slowly in a *good* draught cupboard with cold dilute hydrochloric acid (2 mols. ; 64 c.cs. conc. acid in 100 c.cs. of water), the whole being well stirred during the addition. Any hydrogen cyanide remaining is expelled by boiling (*caution !*) and the solution evaporated to dryness on a water bath. The powdered residue is extracted in a reflux apparatus with 50 c.cs. of boiling acetone and the filtered extract evaporated to dryness on a bath kept at 65°.

$$H.CH:O + KCN + 2H_2O = HCH(OH).COOK + NH_3.$$

$$CH_2(OH).COOK + HCl = CH_2(OH).COOH + KCl.$$

Yield.—70% theoretical (16 gms.). Colourless deliquescent crystals ; soluble in water and in acetone ; M.P. 80° ; K = 152. (B., 14, 1965 ; 15, 2318 ; C., (1900), I, 402.)

PREPARATION 64.—α-*d*-**Glucoheptonic Acid** (*Heptan-2 : 3 : 4 : 5 : 6 : 7-hexol-acid*).

$$CH_2OH.(CHOH)_5.COOH. \quad C_7H_{14}O_8. \quad 226.$$

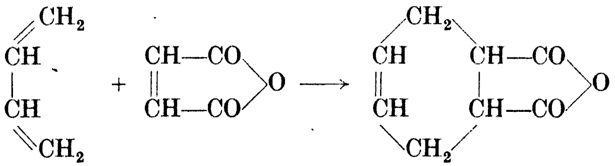
100 gms. (1 mol.) of anhydrous grape-sugar are dissolved in 500 c.cs. (1 mol. of HCN) of 3% hydrocyanic acid (*caution !*) and treated with 10 drops of dilute ammonia. The mixture is allowed to stand for 4–5 days in a fume cupboard at room temperature, and is then treated with a solution of 130 gms. (excess) of barium hydrate in 400 c.cs. of water and boiled in a dish in a fume cupboard until the smell of ammonia has disappeared.

The liquid is now acidified with dilute sulphuric acid ; the hydrocyanic acid is driven off by boiling in a fume chamber (*caution !*) and the sulphuric acid exactly neutralised with strong baryta-water. After boiling with decolorising carbon, the solution is filtered and evaporated to a syrup on a water bath. On long standing, the lactone of α-*d*-glucoheptonic acid separates in crystals. These are macerated with a little 80% alcohol, and filtered at the pump. The substance is then dissolved in 3 times its weight of water, and treated with decolorising carbon in the warm. The filtrate is concentrated and set aside to crystallise.

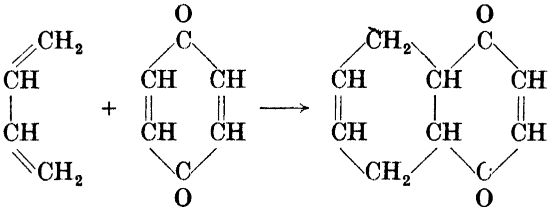
$$CH_2OH(CHOH)_5CHO \longrightarrow CH_2(OH)(CHOH)_5CH(OH)CN \longrightarrow$$
$$CH_2OH.(CHOH)_5.CHOH.COOH.$$

Yield.—70% theoretical (90 gms.). Colourless crystals ; soluble in water ; M.P. 140°. (B., 19, 1916 ; 23, 936 ; A., 270, 65, 272, 200.)

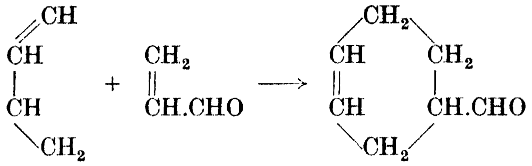
Reaction XXXIX. The addition of Maleic Anhydride to Conjugated Dienes (Diels-Alder). (A., 460, 98 ; Chem. Rev., 31, 319.)—The so-called diene synthesis consists of the 1 : 4-addition to a conjugated diene of αβ-unsaturated compounds, notably maleic anhydride, but including also quinones, acrolein, and even conjugated dienes, such as butadiene or isoprene. The following illustrate the hydroaromatic type of derivative formed :



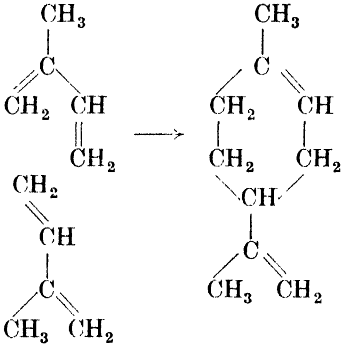
Anhydride of tetrahydrophthalic acid.



Tetrahydronaphthaquinone



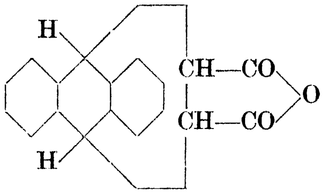
Tetrahydrobenzaldehyde



Dipentene

See also *Preparative Organic Chemistry*, Alder, p. 381.

PREPARATION 64*a*.—Anthracene-9 : 10-endo-αβ-succinic anhydride.



$C_{18}H_{12}O_3$. 326.

2 gms. anthracene, 5·6 gms. maleic anhydride and 40 c.cs. benzene are heated under reflux on a boiling water bath for 3 hours. On cooling, the addition compound separates as colourless plates.

Yield.—73% theoretical (2·7 gms.). M.P. 263° (A., 486, 196.)

Reaction XL. Condensation of a Phenol with a "Methane Carbon Atom." (A., 194, 123 ; 196, 77 ; B., 28, R., 743.)—Phenols condense with compounds which can yield a methane carbon atom, to give dyes of the rosolic acid series. The *leuco*-compound—tri-hydroxytriphenyl carbinol—first formed, is unstable and immediately yields the dyestuff, no oxidising agent being necessary. In this respect these compounds differ from the analogous rosaniline compounds (see p. 390).

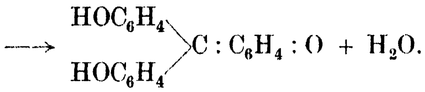
Aurin, the simplest member of the series, is prepared by heating together phenol, oxalic, and strong sulphuric acids at 130° for 6 hours.

$$(COOH)_2 + 3C_6H_5OH \longrightarrow (HOC_6H_4)_2C : C_6H_4 : O + 3H_2O + CO.$$

The methane carbon atom can also be supplied by formaldehyde; the steps in the synthesis are—

$$CH_2O + 2C_6H_5OH \longrightarrow CH_2(C_6H_4OH)_2 + H_2O$$

$$CH_2(C_6H_4OH)_2 + C_6H_5OH + 2O \longrightarrow H_2O + HOC(C_6H_4OH)_3$$



$$\longrightarrow \begin{matrix} HOC_6H_4 \\ HOC_6H_4 \end{matrix}\!\!>\!C : C_6H_4 : O + H_2O.$$

Rosolic acid (methyl aurin) another important member of this series, is prepared by oxidising a mixture of phenol and *o*- and *p*-cresols with arsenic acid and sulphuric acid. 1 mol. of each of the cresols and 1 mol. of phenol react, the methyl carbon of the *p*-cresol molecule serving to link the structures.

These compounds dissolve in alkalis and alcohols, with a bright red colour, but they are now little used as dyes. As will be seen, they are assumed to have a quinonoid formula like all the triphenylmethane dyes (see p. 389).

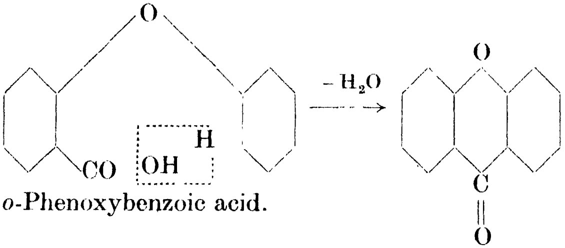
CHAPTER VII

CARBON TO CARBON

OXIDE-OXY COMPOUNDS

In this section those syntheses of which the product is necessarily an ester or some other compound containing both an oxy (carbonyl) and an oxide (ether) group are described.

Reaction XLI. Elimination of Water from *o*-Phenoxybenzoic Acids (*o*-Phenylsalicylic Acid). (B., 21, 502; 25, 1652; 26, 71.)—The xanthones (di-benzpyrones) possess a chromogenic nature, and form the basis of some dyestuffs. They are obtained by loss of water from the *o*-phenoxybenzoic acids by treating the latter with dehydrating agents or by heating (C. V., I, 552).



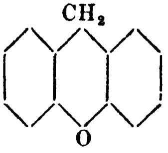
o-Phenoxybenzoic acid.

Xanthone.

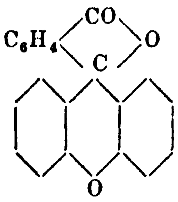
They have also been synthesised by condensing salicylic acid with phenols through the agency of sulphuric acid, acetic anhydride, etc. (B., 21, 502; 24, 3982; 25, 1652; 26, 71; 27, 1989; A., 254, 265). All four possible mono-hydroxyxanthones have been prepared in this way, as have some of the poly-hydroxy compounds. These latter are the more important.

$$(HO)C_6H_3\left\langle\begin{matrix}H\\OH\end{matrix}\right. + \left.\begin{matrix}OH.CO\\OH\end{matrix}\right\rangle C_6H_4 \rightarrow HOC_6H_3\left\langle\begin{matrix}CO\\O\end{matrix}\right\rangle C_6H_4.$$

The xanthones are allied to the thio-xanthones (J. C. S., 97, 1290), the acridones (B., 25, 1734) and the fluorones (J. C. S., 99, 545). The parent substance obtained by reduction of xanthone is xanthene (methylene-diphenylene oxide). (B., 26, 72.)



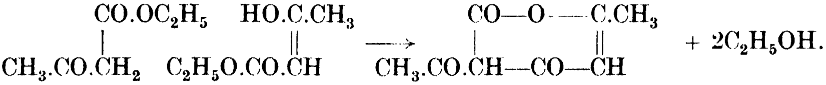
Xanthene.



Fluorane.

Although the xanthones contain a ketone oxygen atom, they, like the pyrones (see p. 113), do not react with hydroxylamine, or phenyl hydrazine.

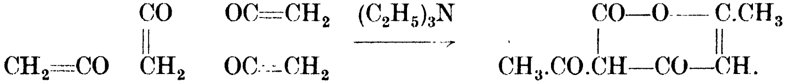
Reaction XLII. Prolonged action of Heat on Ethyl Acetoacetate. (A., 273, 186.)—By prolonged boiling of acetoacetic ester under a reflux condenser at ordinary pressures, condensation occurs, and dehydracetic acid is formed. The parent acid, a δ-hydroxy-acid, is unstable, and has not yet been isolated.



$$\begin{array}{cc} CO.OC_2H_5 & HO.C.CH_3 \\ | & \| \\ CH_3.CO.CH_2 & C_2H_5O.CO.CH \end{array} \longrightarrow \begin{array}{c} CO-O-C.CH_3 \\ | \qquad\quad \| \\ CH_3.CO.CH-CO-CH \end{array} + 2C_2H_5OH.$$

1 mol. of the keto reacts with 1 mol. of the enol form ; it will be noted that the activated methylene group enters into the reaction.

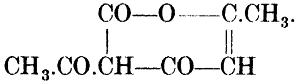
The lactone formed is important because hydriodic acid reduces it to di-methyl pyrone $\overbrace{CH_3C:CH.CO.CH:C}^{O}.CH_3$, a certain amount of rearrangement occurring. This latter compound is, like all the pyrones, of great theoretical interest (see p. 113). Dehydracetic acid is related to, and is formed by polymerisation of ketene (O. S., 21, 64) in presence of zinc bromide or tertiary amines, or even spontaneously. Ketene, now available industrially, is an important acetylating agent (Bl., 1895, 1129).



$$\begin{array}{ccc} & CO & OC{=}CH_2 \\ & \| & \\ CH_2{=}CO & CH_2 & OC{-}CH_2 \end{array} \xrightarrow{(C_2H_5)_3N} \begin{array}{c} CO-O-C.CH_3 \\ | \qquad\quad \| \\ CH_3.CO.CH-CO-CH. \end{array}$$

(A., 273, 186 ; C., 1900, II, 625 ; A., 257, 261.)

PREPARATION 65.—**Dehydracetic Acid** (*Methylacetopyronone*).



$$\begin{array}{c} CO-O-C.CH_3. \\ | \qquad\quad \| \\ CH_3.CO.CH-CO-CH \end{array}$$

$C_8H_8O_4$. 168.

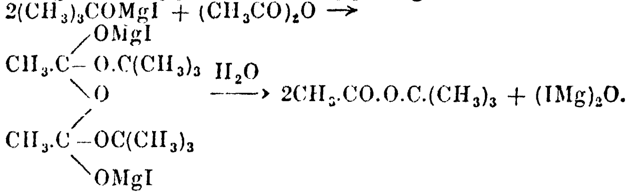
20 gms. (2 mols.) of ethyl acetoacetate are boiled under a reflux for 6 hours, pieces of porous porcelain being added to promote regular ebullition. The liquid is then distilled to 200° ; the distillate may be fractionated *in vacuo* to recover unchanged acetoacetic ester (see Preparation 75). The brown residue solidifies on cooling to a crystalline mass. It is boiled with 5N caustic soda solution with the addition of decolorising carbon and filtered hot. The sodium salt crystallises from the filtrate; acidification with dilute sulphuric acid precipitates the required lactone.

$$2CH_3.CO.CH_2COOC_2H_5 = C_8H_8O_4 + 2C_2H_5OH.$$

Yield.—80% theoretical allowing for acetoacetic ester recovered (10 gms.). Colourless needles ; insoluble in water ; M.P. 108° ; B.P. ^{760} 269° ; K = 0·00053. (A., 257, 261 ; B., 27, R., 417 ; O. S., 20, 26).

Reaction XLIII. (*a*) **Formation of Esters by the action of Acid Anhydrides or of Acid Chlorides on an Alcohol in the presence of Magnesium Alkyl Halide** (Grignard). (B., 39, 1738.)—This application of the Grignard reaction to the preparation of esters is of theoretical rather than practical interest as illustrating the wide applicability of this many-sided reaction. The steps in the synthesis will be clear from the examples given ; they are somewhat different from the usual phases of a Grignard reaction.

(i.) $RMgI + (CH_3)_3C(OH) = (CH_3)_3COMgI + R.H.$

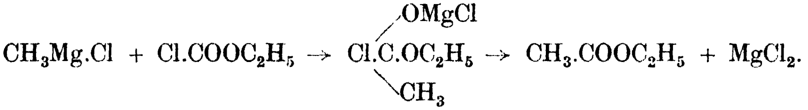


(ii.) $(CH_3)_3COMgI + CH_3COCl = CH_3CO.O.C(CH_3)_3 + MgClI.$

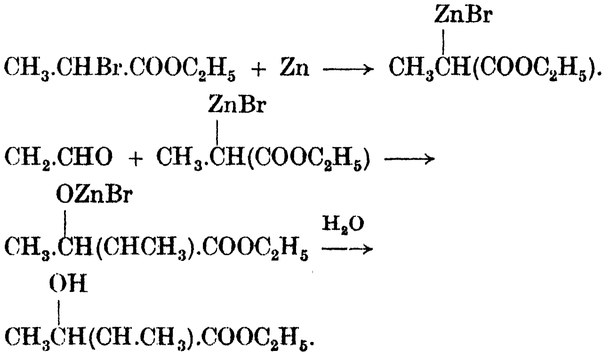
Isoamyl acetate has been obtained in this way from isoamyl alcohol and acetyl chloride. The method does not offer any advantages over the more usual esterification reactions.

For the general experimental method and precautions necessary in Grignard reactions, see Preparation 19.

Reaction XLIII. (*b*) **Formation of Ethyl Esters by the Action of Ethyl Chloroformate on Magnesium Alkyl Halide in Dry Ethereal Solution** (Grignard).—This application of the Grignard reaction to the synthesis of esters is more direct than the previous (see C. V., II, 198).



Reaction XLIII. (*c*) **Condensation of α-Halogen Fatty Acid Esters with Aldehydes and Ketones by means of Zinc** (Reformatsky). (*Organic Reactions*, Adams, Vol. I, 1.)—This is an extension of the Grignard and zinc alkyl reactions which enables α-halogen esters to be condensed with carbonyl compounds similarly to simple alkyl halogen compounds. The zinc alkyl derivative is neither prepared beforehand nor isolated in the reaction, but there is little doubt that some such compound is transitorily formed. The product is a β-hydroxy ester, and the method is the standard one for obtaining the higher β-hydroxy acids.



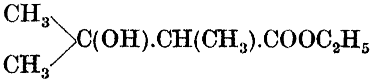
$$CH_3.CHBr.COOC_2H_5 + Zn \longrightarrow CH_3\overset{ZnBr}{\overset{|}{C}}H(COOC_2H_5).$$

$$CH_2.CHO + CH_3.\overset{ZnBr}{\overset{|}{C}}H(COOC_2H_5) \longrightarrow$$

$$CH_3.\overset{OZnBr}{\overset{|}{C}}H(CHCH_3).COOC_2H_5 \xrightarrow{H_2O}$$

$$CH_3\overset{OH}{\overset{|}{C}}H(CH.CH_3).COOC_2H_5.$$

Preparation 66.—Ethyl β-hydroxy-αβ-dimethylbutyrate [*Ethyl ester of* 2 : 3-*dimethyl*-3-*butanol acid*].

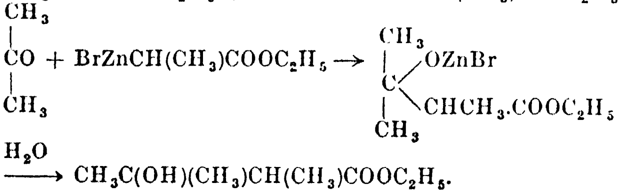


$$(CH_3)_2{>}C(OH).CH(CH_3).COOC_2H_5$$

$C_8H_{16}O_3$. 160.

60 gms. of zinc are freed from oxide and oil by washing successively with warm caustic soda solution, then dilute acid, water and alcohol. After being dried in an air oven, a small quantity is added to a mixture of 90 gms. pure dry acetone and 182 gms. of ethyl-α-bromopropionate contained in a large flask provided with a reflux condenser. The flask is gradually warmed on a water bath until a reaction commences, and if it proceeds too vigorously, cooling must be applied. More zinc is added from time to time as the action subsides, until some of the metal remains undissolved (about 45 gms. Zn are usually required), and after the final addition, heating is continued for 2–3 hours. The syrupy liquid is poured off from the unattacked metal, and water added. The basic zinc bromide which is precipitated is dissolved by the addition of a sufficient quantity of dilute sulphuric acid, and the oily layer is extracted with ether and separated. The extract is washed three times with dilute sulphuric acid, then with water, and dried over calcium chloride. After the ether is removed, the residue is distilled at 30 mms. pressure, when the pure ester passes over about 105°.

$$CH_3CHBrCOOC_2H_5 + Zn \rightarrow BrZn - CH(CH_3)COOC_2H_5.$$



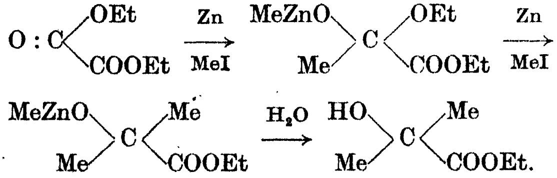
$$(CH_3)_2CO + BrZnCH(CH_3)COOC_2H_5 \rightarrow (CH_3)_2C(OZnBr)CHCH_3.COOC_2H_5$$

$$\xrightarrow{H_2O} CH_3C(OH)(CH_3)CH(CH_3)COOC_2H_5.$$

$Zn[CH(CH_3)COOC_2H_5]_2$ might also be considered an intermediate compound in the reaction.

Yield.—50% theoretical (60 gms.). Colourless oil, insoluble in water; B.P. ^{30}, 105°. (C., (1901), I, 1196 ; II, 30 ; (1902), I, 856.)

Reaction XLIII. (*d*) **Condensation of Diethyl Oxalate with Alkyl Halides in the presence of Zinc** (Frankland-Duppa). (A., 185, 184.)—This is a type of condensation very similar to those just described. The zinc alkyl is not isolated, and simple halogen compounds are used. The product is a derivative of glycollic acid.



$$O:C(OEt)COOEt \xrightarrow[MeI]{Zn} (MeZnO)(Me)C(OEt)COOEt \xrightarrow[MeI]{Zn}$$

$$(MeZnO)(Me)C(Me)COOEt \xrightarrow{H_2O} (HO)(Me)C(Me)COOEt.$$

Reaction XLIV. (*a*) **Condensation of Alkyl or Acyl Halides with Ethyl Sodio-malonate and its Homologues.** (B., 7, 1383 : Am. Soc., 43, 680.)—The malonic esters are almost as valuable as the acetoacetic esters (see Reaction XLIV (*b*)) in the syntheses of mono- and poly-carboxylic acids owing to the successive replaceability by sodium of the hydrogen atoms of the methylene group, activated by the two neighbouring carbonyl groups. These sodio-derivatives are very reactive, and undergo the following changes :

(i) By the action of alkyl halide on the sodio compound, a mono-alkyl compound is formed.

$$CH_2(COOC_2H_5)_2 \xrightarrow{Na} CHNa(COOC_2H_5)_2 \xrightarrow{RI} CHR(COOC_2H_5)_2.$$

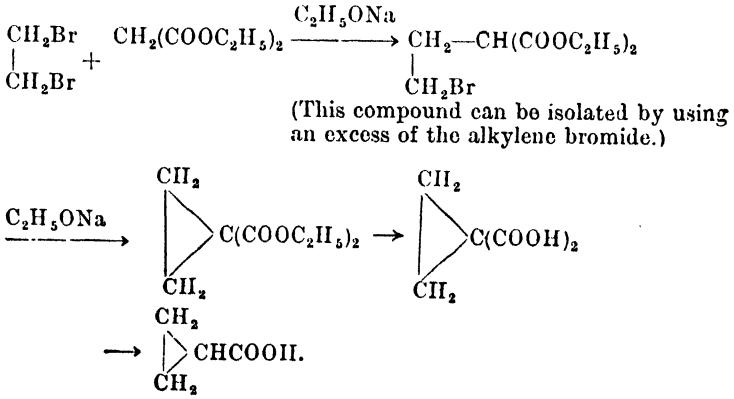
(ii) By the action of alkyl halide on the sodio-derivative of a mono-alkyl malonic ester, a di-alkyl compound is produced.

$$CHR(COOC_2H_5)_2 \xrightarrow{Na} CNaR(COOC_2H_5)_2 \xrightarrow{R_1I} CR_1R(COOC_2H_5)_2.$$

From these esters the corresponding dibasic acids can be obtained by hydrolysis, so that the homologues of malonic acid can be synthesised in this way.

Again, as all these acids have two carboxyls attached to the same carbon atom, they lose carbon dioxide on heating and pass into mono-basic fatty acids (B., 27, 1177). This affords an important and standard synthesis for these latter acids (see Preparation 427, also Preparation 60 and p. 119).

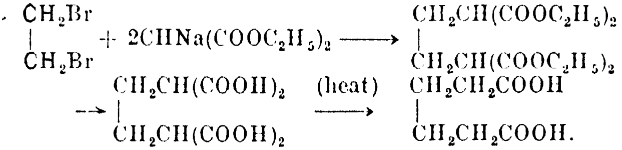
(iii) Cyclo paraffin derivatives can also be synthesised. Malonic ester and ethylene bromide in the presence of sodium alcoholate yield tri-methylene-di-carboxylic ester and thence a di- and mono-carboxylic acid. (Am. Soc., 42, 314'; 43, 680.)


(This compound can be isolated by using an excess of the alkylene bromide.)

C_2H_5ONa is frequently used to obtain the sodio-derivatives of the malonic esters, though metallic sodium can also be employed.

By using various alkylene dibromides, 4, 5, 6 or 7 membered rings can also be obtained. (A., 284, 197.)

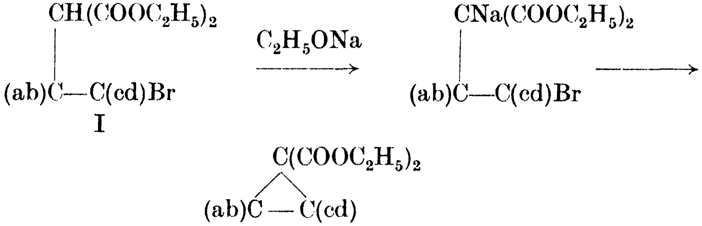
(iv) Simultaneously, there is formed in the above reaction butane-tetra-carboxylic ester, and it yields a tetra- and thence a di-basic acid (adipic acid).



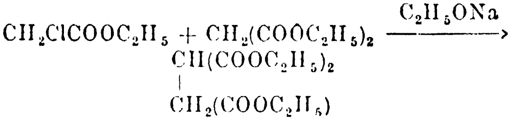
$$\begin{array}{l}CH_2Br\\|\\CH_2Br\end{array} + 2CHNa(COOC_2H_5)_2 \longrightarrow \begin{array}{l}CH_2CH(COOC_2H_5)_2\\|\\CH_2CH(COOC_2H_5)_2\end{array} \longrightarrow \begin{array}{l}CH_2CH(COOH)_2\\|\\CH_2CH(COOH)_2\end{array} \xrightarrow{\text{(heat)}} \begin{array}{l}CH_2CH_2COOH\\|\\CH_2CH_2COOH.\end{array}$$

The tetra-basic ester can also yield ring compounds (Reaction XLVII).

(v.) Also by starting with compounds such as I, ring compounds may be synthesised by intra-molecular condensation.



(vi.) Halogen esters react like simple alkyl halides.



$$CH_2ClCOOC_2H_5 + CH_2(COOC_2H_5)_2 \xrightarrow{C_2H_5ONa} \begin{array}{l}CH(COOC_2H_5)_2\\|\\CH_2(COOC_2H_5)\end{array}$$

Ethane-tricarboxylic Ester.

(vii) The acyl malonic esters are produced from the acyl chlorides, and sodio-malonic ester in a manner analogous to the alkyl malonic esters (B., 20, R., 381).

Benzoyl chloride, and sodio-ethyl malonate yield diethyl benzoyl-malonate.

$$C_6H_5COCl + CHNa(COOC_2H_5)_2 \longrightarrow (C_6H_5CO)CH(COOC_2H_5)_2.$$

The structure of the sodio-derivatives of diketomethylene compounds, like malonic ester, is dealt with in Reaction XLIV (*b*), and an explanation is given as to why only one hydrogen is replaceable at a time.

PREPARATION 67.—**Diethyl Ethylmalonate.**

$C_2H_5CH(COOC_2H_5)_2$. $C_9H_{16}O_4$. 188.

To 25 gms. of absolute alcohol contained in a flask provided with a reflux condenser, 2·3 gms. of sodium are added, and when the metal has dissolved, 16 gms. of ethyl malonate are added. The sodio-derivative of the ester is precipitated as a white solid. The flask is shaken while 20 gms. of ethyl iodide are slowly run in from a dropping funnel; the precipitate gradually reacts and sodium iodide is deposited. Heating is conducted on a water bath (1–2 hours) until the product ceases to show an alkaline reaction. The alcohol is distilled off, the residue diluted with water and extracted with ether. The extract is dried over calcium chloride, the ether distilled off, and the residue fractionated, when the product passes over at 200°–210°.

$$CH_2(COOC_2H_5)_2 \longrightarrow CHNa(COOC_2H_5)_2 \longrightarrow C_2H_5.CH(COOC_2H_5)_2.$$

Yield.—75% theoretical (15 gms.). Colourless oil of fruity odour; B.P. 207°; D. $^{18}_{4}$ 1·008. (A., 204, 134.)

Methyl, propyl, butyl (C. V., I, 250), malonic esters are also obtained similarly. It is to be observed that aryl halides do not undergo this reaction. The di-alkyl esters are obtained from the mono-alkyl esters in the same way as the latter are obtained from malonic ester. But although di-alkyl compounds are not formed directly in any quantity, yet it frequently happens that a little is obtained in the preparation of the mono-alkyl compound from 1 mol. of sodium ethoxide and 1 mol. of alkyl halide, owing to the mono-derivative reacting with more sodium and alkyl halide. This may be prevented when necessary by using only half the calculated quantity of sodium and alkyl halide. By this means the yield of benzoyl malonic ester, for example, is raised from 55% to 85% in its preparation from sodium, benzoyl chloride and malonic ester. (B., 44, 1507.)

Reaction XLIV. (*b*) **Condensation of Alkyl and Aryl Halogen Compounds with the Sodio- and other Metallo-derivatives of Ethyl Acetoacetate and its Homologues.** (A., 186, 214; 201, 143; 213, 143.)—Like malonic ester, acetoacetic ester contains two 1 : 3-carbonyl groups with a methylene group in position 2. It is only to be expected then that it yields with metallic sodium or sodium alcoholate sodio-derivatives from which mono- and di-, alkyl and aryl homologues can be obtained by treatment with a suitable halide, including halogen esters. Acetoacetic acid shows the same property, but its great instability necessitates the use of its very stable ethyl ester. Other examples of 1 : 3 di-keto-2-methylene compounds, of which all possess similar properties to the esters described in this and the previous reaction, will be found on p. 104. Reference may also be made to Reaction XLVI.

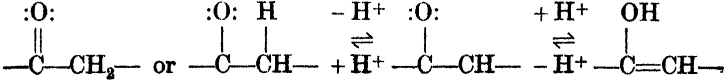
These compounds are alike in being tautomeric, the keto and enol forms being in an equilibrium which varies both with substance and with temperature:

$$—CO.CH_2.CO— \rightleftarrows —C(OH):CH.CO—$$

and

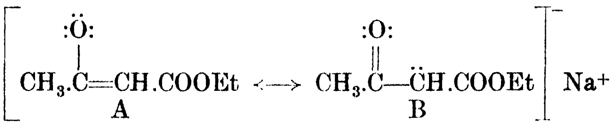
$$—CO.CHR.CO— \rightleftarrows —C(OH):CR.CO—$$

The change is prototropic, i.e. due to the shifting of a proton:



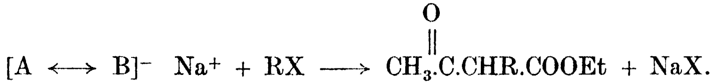
$$—\overset{\overset{:O:}{\|}}{C}—CH_2— \text{ or } —\overset{\overset{:\ddot{O}:}{|}}{C}—\overset{\overset{H}{|}}{C}H— \underset{+H^+}{\overset{-H^+}{\rightleftharpoons}} —\overset{\overset{:\ddot{O}:}{|}}{C}—CH— \underset{-H^+}{\overset{+H^+}{\rightleftharpoons}} —\overset{\overset{OH}{|}}{C}=CH—$$

When sodium, sodium ethoxide or sodamide reacts with ethyl acetoacetate or with any similar compound the reagent acts upon the *enol* isomer, more of which is formed from the *keto* isomer until all of the ester is converted into its monosodio derivative which is accepted as having the ionic structure :



$$\left[\underset{A}{\mathrm{CH_3.\overset{\overset{:\ddot{O}:}{|}}{C}{=}CH.COOEt}} \longleftrightarrow \underset{B}{\mathrm{CH_3.\overset{\overset{:O:}{\|}}{C}{-}\ddot{C}H.COOEt}}\right]^{-} \mathrm{Na^+}$$

The carbanion, which is a resonance hybrid, reacts with alkyl or with acyl halides to give in most instances C-derivatives to the almost total exclusion of O-derivatives, an experimental fact not readily explained on any other grounds, the contributing form (A) of the resonance hybrid being relatively inactive to these reagents (the nucleophilic reactivity of carbon being greater than that of oxygen) :

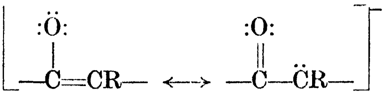


$$[A \longleftrightarrow B]^- \ \mathrm{Na^+} + \mathrm{RX} \longrightarrow \mathrm{CH_3.\overset{\overset{O}{\|}}{C}.CHR.COOEt} + \mathrm{NaX}.$$

This monoalkyl derivative of the ester, like its parent, exhibits prototropy—though to a lesser extent—and exists as the equilibrium mixture of tautomers

$$\mathrm{CH_3.CO.CHR.COOEt} \rightleftharpoons \mathrm{CH_3.C(OH):CR.COOEt}$$

which reacts with sodium to give the carbanion (resonance hybrid)



$$\left[\mathrm{{-}\overset{\overset{:\ddot{O}:}{|}}{C}{=}CR{-}} \longleftrightarrow \mathrm{{-}\overset{\overset{:O:}{\|}}{C}{-}\ddot{C}R{-}}\right]^{-}$$

capable of reacting with another molecule of alkyl halide (R_1X) to give in most instances the C-dialkyl derivative exclusively :

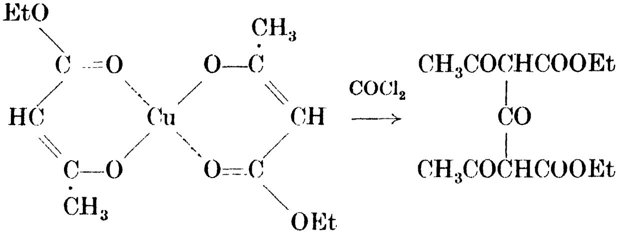
$$\mathrm{CH_3.CO.C(RR_1).COOEt.}$$

Thus only one of the hydrogens of the methylene group is replaceable by sodium—and consequently by a radical—at a time, and this holds generally for similar compounds which exhibit tautomerism.

$$\mathrm{{-}CH_2.CO{-}} \longrightarrow \mathrm{{-}CH:C(ONa){-}} \longrightarrow \mathrm{{-}CHR.CO{-}} \longrightarrow$$
$$\mathrm{{-}CR:C(ONa){-}} \longrightarrow \mathrm{{-}CRR_1.CO{-}}.$$

O-derivatives of ethyl acetoacetate are formed from the contributing form (B) of the anion, for example, from the sodio-derivatives and chloroformic ester (J. pr., (2), 37, 473 ; B., 25, 1760 ; A., 277, 64) though some C-derivative is formed at the same time. Pyridine, as solvent, favours the formation of O-derivatives in some instances.

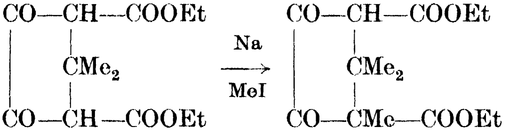
The following applications are of interest. The copper compound of the ester which is formed by adding a saturated alcoholic solution of cupric acetate to the ester, is, unlike the sodio-compound, chelated and soluble in organic solvents ; but it serves for some similar applications. With phosgene it yields carbonyl diacetoacetic ester :



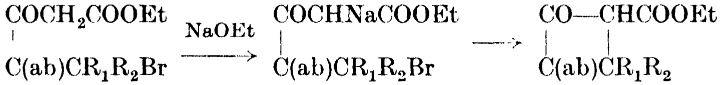
important in the synthesis of αα′-dimethyl-γ-pyrone. Benzophenone dichloride reacts with the copper compound to give diphenylacetoacrylate,

$$Ph_2C : C(COCH_3)COOEt.$$

Another important example is met with in the synthesis of ethyl diketocamphorate from ethyl diketocamphopyrate :



Cyclic compounds may be synthesised by intramolecular condensation :



$$\begin{matrix} COCH_2COOEt \\ | \\ C(ab)CR_1R_2Br \end{matrix} \xrightarrow{NaOEt} \begin{matrix} COCHNaCOOEt \\ | \\ C(ab)CR_1R_2Br \end{matrix} \longrightarrow \begin{matrix} CO\text{—}CHCOOEt \\ |\qquad | \\ C(ab)CR_1R_2 \end{matrix}$$

The alkyl homologues of ethyl acetoacetate are important because of the hydrolysis they undergo (p. 198). Some reference to the structure of the parent ester will be found in Reaction XLVI ; and further reactions are discussed in Reactions XLVII and LIII.

The following preparations show the experimental methods used. It is to be noted that in all these reactions bromides and iodides give better yields than chlorides.

Preparation 68.—**Ethyl Ethylacetoacetate** (*Ethyl ester of 2-ethyl-3-on butan acid*).

$$CH_3.CO.CH(C_2H_5)COOC_2H_5. \quad , \quad C_8H_{14}O_3. \qquad 158.$$

32·5 gms. (1 mol.) of ethyl acetoacetate are slowly added with cooling to the solution obtained by dissolving 5·7 gms. (1 atom) of clean sodium wire in 70 gms. of absolute alcohol under a reflux. 40 gms. (1 mol.) of ethyl iodide are then slowly added, and the whole refluxed on a water bath until it shows a neutral reaction. If necessary a little more ethyl iodide is added. The alcohol is removed on a water bath and the residual oil shaken with water and extracted with ether. The ethereal extract is dried over anhydrous potassium carbonate, the ether removed on a water bath, and the residue distilled, the portion boiling at 190°–198° at 760 mms. being collected separately. If preferred, the fractionation can be done under reduced pressure.

$$CH_3.CO.CH_2.COOEt \xrightarrow{C_2H_5ONa} CH_3.CO.CHNa.COOEt \xrightarrow{C_2H_5I} CH_3.CO.CH(C_2H_5)COOEt.$$

Yield.—80% theoretical (32 gms.). Colourless oil ; insoluble in water ; B.P. ^{14} 84° ; B.P. ^{760} 198° ; D. $^{16}_{4}$ 0·9834. (A., 186, 220 ; 192, 153 ; C., (1904), II, 309 ; A., 441, 153.)

Other mono-alkyl acetoacetic esters may be prepared in an exactly analogous manner. See C. V., I, 248, for preparation of ethyl butylacetoacetate.

In the preparation of some of the higher mono-alkyl acetoacetic esters the yield is sensibly lowered, owing to the formation of di-alkyl compounds due to secondary reactions of the same type as those described on p. 142. This in like manner can be remedied by using only half the calculated quantity of sodium and alkyl halide. The unattacked acetoacetic ester is recovered by distillation.

PREPARATION 69.—**Ethyl Benzylacetoacetate.**

$CH_3COCH(CH_2C_6H_5)COOC_2H_5$. $C_{13}H_{16}O_3$. 220.

To a solution of 6 gms. (1 atom) of sodium in 75 c.cs. (excess) of absolute alcohol are gradually added 65 gms. (2 mols.) of acetoacetic ester. 32 gms. benzyl chloride are dropped in, and the temperature of the mixture is maintained at 30° for an hour. It is then refluxed for an hour. The product is distilled under reduced pressure, the fraction 164°–165° at 14 mms. consisting of benzyl acetoacetic ester being retained. Up to this temperature the unattacked acetoacetic ester passes over.

$$CH_3COCHNaCOOC_2H_5 + C_6H_5CH_2Cl \rightarrow CH_3COCH(CH_2C_5H_5)COOC_2H_5.$$

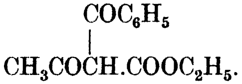
Yield.—85% theoretical (47 gms.). Colourless oil ; B.P. ^{14} 165° ; B.P. ^{760} 276° ; insoluble in water. (A., 204, 179.)

An equally good yield can be obtained by replacing the ethyl alcohol by 100 c.cs. butyl alcohol.

The di-alkyl esters are made from the mono-alkyl esters in a manner exactly similar to that by which the mono-alkyl esters are made from acetoacetic ester itself.

The method of preparation of acyl acetoacetic esters is exemplified in the following. The reaction goes through phases similar to those described for alkyl compounds, but owing to the greater reactivity of the acyl halides, special precautions have to be taken. Unlike the alkyl chlorides, the acyl chlorides give good yields ; there is no need to use the bromides or the iodides.

PREPARATION 70.—**Ethyl Benzoylacetoacetate.**



$$\overset{\displaystyle COC_6H_5}{\overset{|}{CH_3COCH.COOC_2H_5.}} \quad C_{13}H_{13}O_4. \quad 234.$$

To 600 c.cs. of absolute alcohol in a flask attached to a reflux are gradually added 35 gms. (2 atoms) of sodium cut in small pieces. When all the sodium has dissolved, the solution is cooled. To 300 c.cs. of this solution are added 100 gms. (1 mol.) of acetoacetic ester, and, with continual stirring, 45 c.cs. of benzoyl chloride are dropped in from a burette during 15 minutes, the temperature being kept below 10°. After 30 minutes, 150 c.cs. of the original solution and 22 c.cs. benzoyl chloride are added as before. This process is repeated until all the original solution is used up, and 90 c.cs. benzoyl chloride in all. After 12 hours, the sodium salt is filtered off and washed with ether. By acidifying with dilute acetic acid in presence of ice-water, the ester is liberated. It is extracted with ether, dried over anhydrous sodium sulphate, and the ether removed. The residue is then distilled under reduced pressure, the fraction 173°–177° at 12 mms. being retained.

$$CH_3CO.CHNaCOOC_2H_5 + C_6H_6COCl \longrightarrow CH_4COCH(COC_6H_5)COOC_2H_5.$$

Viscous oil; insoluble in water; B.P. ^{12} 175°, with slight decomposition; tautomeric. (B., 18, 2131; 44, 1507.)

Reaction XLIV. (*c*) **Condensation of Alkyl and Acyl Halides with the Sodio-derivatives of Ethyl Cyanoacetate.** (B., 20, R., 477; R., 353; 27, R., 262; J. pr., [2], 51, 186.)—Cyanoacetic ester (C. V., I, 254), is similar to malonic and acetoacetic esters, since the methylene hydrogen atoms are successively replaceable by sodium and this latter by alkyl and acyl radicals.

$$CH_2(CN)COOEt \xrightarrow[NaOEt]{Na\ or} [CH(CN)COOEt]^-Na^+ \xrightarrow{RI} RCH(CN)COOEt$$

The activation of the methylene hydrogens is effected by the presence of C : O groups, as well as by other groups containing double and multiple linkings. This is somewhat analogous to the activating effect of nitro groups in aromatic compounds. Reference may also be made to the hydroxymethylene compounds, Reaction XXIII (*a*).

The groups C:O and C:N resemble one another in many of their reactions and effects; both tend to render ionisable a hydrogen atom attached to an α-carbon. The synthesis may be extended to halogen esters (cf. vi, p. 143):

$$CH_2ICOOEt + CH_2(CN)COOEt \xrightarrow{NaOEt} \begin{array}{l} CH_2COOEt \\ | \\ CH(CN)COOEt \end{array}$$

Cyanosuccinic ester

Reaction XLV. Condensation of Aldehydes and Ketones with certain Esters under the influence of Acetic Anhydride, Hydrochloric Acid, Sodium Ethoxide or certain bases. (A., 218, 172; B., 29, 172; 30, 481; 31, 735, 2585.)—1 mol. of an aldehyde can be made to condense with 1 mol. of an ester containing an α-methylene group, thus

$$R_1CHO + RCH_2COOC_2H_5 = R_1CH:CRCOOC_2H_5.$$

This is another Aldol-type reaction (for full discussion, see p. 105) promoted catalytically by acids or bases, respectively, as indicated, followed by dehydration:

$$RR_1\overset{+}{C}(\underset{\cdot\cdot}{\ddot{O}}:) + \overset{+}{H} \longrightarrow RR_1\overset{+}{C}(OH)$$

$$RR_1\overset{+}{C}(OH) + RCH_2COOEt \longrightarrow RR_1C(OH)CHRCOOEt + \overset{+}{H}$$

Overall: $RR_1CO + RCH_2COOEt \longrightarrow RR_1C(OH)CHRCOOEt.$

Followed by: $RR_1C(OH)CHRCOOEt \longrightarrow RR_1C{=}CRCOOEt.$

Basic catalysts act:

$$RCH_2COOEt + B(base) \longrightarrow \overset{+}{B}H + R\overset{-}{C}HCOOEt.$$

$$RR_1\overset{+}{C}(\underset{\cdot\cdot}{\ddot{O}}:) + R\overset{-}{C}HCOOEt \longrightarrow RR_1C(\underset{\cdot\cdot}{\ddot{O}}:)CHRCOOEt.$$

$$RR_1C(\underset{\cdot\cdot}{\ddot{O}}:)CHRCOOEt + \overset{+}{B}H \longrightarrow RR_1C(OH)CHRCOOEt + B.$$

If hydrochloric acid or acetic anhydride is used, both aliphatic and aromatic aldehydes can be employed, but if sodium ethoxide or small quantities of diethylamine, piperidine, quinoline, etc., are taken, aromatic aldehydes only will react. In these reactions the methyl gives better results than the ethyl ester.

Esters, such as those of malonic, acetoacetic or cyanoacetic acids, in which the methylene group is doubly activated, will condense even with ketones. By varying the proportion of aldehyde or ketone to ester, 2 mols. of the latter can be made to condense with 1 of the former, using the basic condensing agents only (4 below). The following will illustrate these points:

(1) $PhCHO + CH_2(COOEt)_2 \xrightarrow[Ac_2O]{HCl\ or} PhCH{=}C(COOEt)_2$

Benzylidene malonic ester

(2) $CH_3CHO + CH_2(COOEt)_2 \xrightarrow{NHR_2} CH_3CH{=}C(COOEt)_2.$

Ethylidene malonic ester.

(3) $(CH_3)_2CO + CH_3COCH_2COOEt \xrightarrow{C_5H_{11}N}$ $(CH_3)_2C{=}C(COCH_3)COOEt.$

Isopropylideneacetoacetate

(4) $(CH_3)_2CO + 2CH_2(CN)COOEt \longrightarrow (CH_3)_2C[CH(CN)COOEt]_2.$

PREPARATION 71.—**Ethyl Cinnamate** (*Ethyl ester of 3-phenyl-2-propen acid*).

$C_6H_5CH : CH.COOC_2H_5.$ $C_{11}H_{12}O_2.$ 176.

To 50 gms. (excess) of pure ethyl acetate (see Preparation 199) are added 23 gms. (excess) of sodium in the form of wire. The flask is cooled in ice, and, with slight shaking, 10 gms. (1 mol.) of benzaldehyde are gradually added. When all the sodium has gone into solution, the flask is set aside for 2 hours, when it is acidified with dilute acetic acid. The ester layer which separates is removed, shaken up with dilute sodium carbonate solution, and dried over calcium chloride. It is then distilled, the fraction 265°–275° being retained.

$$C_6H_5CHO + CH_3COOC_2H_5 \xrightarrow{C_2H_5ONa} C_6H_5CH : CH.COOC_2H_5.$$

Yield.—65% theoretical (11 gms.). Colourless liquid ; insoluble in water : B.P. 271°. (B., 23, 976 ; O. S., IX, 38.)

This method of preparation can be applied generally to the esters of the phenyl-olefinic acids. Although metallic sodium is used, as in the acetoacetic ester synthesis (see Reaction XLVI) a trace of alcohol must always be present to form sodium ethoxide. This is usually the case. If necessary, sodium ethoxide itself can be employed. The use of some other condensing agents is illustrated in the following preparation.

PREPARATION 72.—**Diethyl Benzylidenemalonate** (Benzalmalonic Ester).

$C_6H_5CH : C(COOC_2H_5)_2$. $C_{14}H_{15}O_4$.   248.

100 gms. of pure, dry ethyl malonate and 70 gms. (1 mol.) of benzaldehyde (freshly purified by treatment with sodium bicarbonate solution, drying over anhydrous sodium sulphate and distilling) are mixed. 2 gms. of piperidine are added and the mixture, after keeping in a corked flask for two days at ordinary temperature, is heated for 12 hours under an upright condenser provided with a calcium chloride tube. The cold reaction mixture, diluted with 100 c.cs. ether, is washed successively with water, with dilute sulphuric acid and with water, dried over anhydrous sodium sulphate, and distilled under reduced pressure, the fraction at 185–196° and 12 mm. being retained.

$$C_6H_5CHO + CH_2(COOC_2H_5)_2 \xrightarrow{C_5H_{11}N} C_6H_5CH : C(COOC_2H_5)_2.$$

Yield.—70% theoretical (105 gms.). Colourless oil ; insoluble in water ; B.P. ^{13} 198°. (B., 14, 345 ; 31, 2591 ; A., 218, 130 ; 268, 156.)

Compare this preparation with that of benzylidenemalonic acid (Preparation 53).

PREPARATION 73.—**Tetraethyl Methylenedimalonate.**

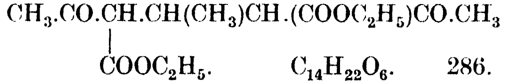
$CH_2[CH(COOC_2H_5)_2]_2$. $C_{15}H_{24}O_8$.   332.

32 gms. of ethyl malonate and 8 gms. of formalin (40%) are placed in a flask, cooled by immersion in ice, and 0·5 gm. of diethylamine added. The flask is then cooled and left to stand for 12 hours at room temperature, after which it is heated on a boiling water bath for 5–6 hours. The aqueous layer is separated and the residue distilled under reduced pressure (about 12 mms.). The distillation is conducted slowly, so that all the water passes over below 50°. Methylenedimalonic ester passes over at 190°–200°.

$$CH_2O + CH_2(COOC_2H_5)_2 \xrightarrow{NH(C_2H_5)_2} CH_2[CH(COOC_2H_5)_2]_2.$$

Yield.—80% theoretical (27 gms.). Colourless oil ; insoluble in water ; B.P. ^{18} 205° ; B.P. ^{12} 198°. (B., 22, 3294 ; 31, 738, 2585, O. S., X, 58.)

PREPARATION 74.—**Diethyl Ethylidenebisacetoacetate** (4-*Methyl*-3 : 5-*carbethoxyl-heptan*-2 : 6-*dione*).



$$\mathrm{CH_3.CO.\underset{\displaystyle|\atop\displaystyle COOC_2H_5.}{CH}.CH(CH_3)CH.(COOC_2H_5)CO.CH_3} \qquad \mathrm{C_{14}H_{22}O_6}. \qquad 286.$$

8·5 gms. (1 mol.) of *pure freshly-distilled* acetaldehyde are slowly added to 50 gms. (2 mols.) of *pure vacuum-distilled* cooled acetoacetic ester contained in a thick-walled flask closed by a cork and having a thermometer reaching almost to the bottom. The flask is cooled to $-10°$ to $-15°$ in a freezing mixture of ice and salt. A few drops of diethylamine are then added by means of a burette. Owing to neutralisation of the first portions of the amine by traces of acids nearly always present as impurities, an increase in the temperature seldom takes place at first. After the addition of about 5 drops an elevation of a few degrees will be noticed, and the liquid becomes turbid. From this point a further 5 drops are added slowly, and the temperature is allowed to rise gradually to 0°. 20 more drops are then slowly added with frequent shaking; the whole operation should take about 1 hour. In all, 30 drops ($=1·5$ gms.) of the base are required.

The whole is allowed to stand in the freezing mixture for 15 minutes, then removed and allowed to come to room temperature. Should the temperature go up to 20° on account of secondary reactions, the flask is cooled for a short time in ice-water.

The reaction product is a viscous bright yellow liquid in which numerous drops of water are suspended. It is allowed to remain until it solidifies to a crystalline mass; this generally requires from 2–3 days.

If the pure product is required, the mass is pressed on a porous plate and recrystallised from dilute alcohol. The crude product will serve for the preparation of dimethylcyclohexanone (see p. 89). The solidification of the crude product may be hastened by seeding it, after one day's standing, with crystals obtained in a previous preparation. This is best done on the upper portion of the flask, which is only moistened by the liquid.

$$\mathrm{CH_3COCH_2COOEt + NHEt_2 \longrightarrow \overset{+}{N}H_2Et_2 + CH_3COCHCOOEt}$$

$$\mathrm{CH_3CH(\ddot{\underset{\cdot\cdot}{O}}{:}) + CH_3CO\overset{-}{C}HCOOEt \longrightarrow CH_3CH(\ddot{\underset{\cdot\cdot}{O}}{:})CH(COCH_3)COOEt}$$

$$\mathrm{CH_3CH(\ddot{\underset{\cdot\cdot}{O}}{:})CH(COCH_3)COOEt + \overset{+}{N}H_2Et_2 + CH_3COCH_2COOEt}$$
$$\mathrm{\longrightarrow CH_3CH[CH(COCH_3)COOEt]_2 + NHEt_2.}$$

Yield.—70% theoretical (40 gms.). Colourless needles; M.P. 79°–80°. (A., 323, 83; 332, 1; B., 36, 2118.)

Acetaldehyde and acetoacetic ester in presence of acetic anhydride, hydrochloric acid, ammonia, diethylamine, piperidine, etc., can also be made to yield ethylidene monoacetoacetic ester. (A., 218, 192; B., 29, 172; 31, 735.)

With regard to the intermediate compounds of the types RCH : NR and RCH : $(\mathrm{NRR_1})_2$ postulated in some of the above reactions, it is to be noted that the compounds of the type RCH(OH)NHR and $RCH(OH)NRR_1$ can also be regarded as intermediates.

Reaction XLVI. Condensation of an Ester with itself or with another Ester under the influence of Sodium, Sodium ethoxide, Sodamide or Sodium triphenylmethyl (Claisen Ester Condensation) (*Organic Reactions*, Adams, Vol. I, 266 ; J. C. S., 1940, 216).—This reaction, represented by the following overall equations in the case of acetic and propionic esters, takes place between two molecules of the ester or esters employed, a hydrogen atom attached to the α-carbon of one molecule and an alkoxide group from the second molecule being eliminated as alcohol :

$$CH_3COOEt + HCH_2COOEt \longrightarrow CH_3COCH_2COOEt + EtOH$$

$$CH_3CH_2COOEt + HCH(CH_3)COOEt \longrightarrow CH_3CH_2COCH(CH_3)COOEt + EtOH.$$

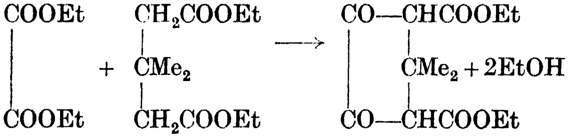
When two different esters react thus, mixtures of products may be obtained unless one of the reactants does not contain hydrogen on the α-carbon. Thus formic, benzoic and oxalic esters separately react with acetic ester to give good yields of formyl-, benzoyl- and oxal-acetic esters :

$$HCOOEt + CH_3COOEt \longrightarrow HCOCH_2COOEt + EtOH.$$

$$PhCOOEt + CH_3COOEt \longrightarrow PhCOCH_2COOEt + EtOH.$$

$$EtOOCCOOEt + CH_3COOEt \longrightarrow EtOOCCOCH_2COOEt + EtOH.$$

Similarly oxalic ester and ββ-dimethyl glutaric ester yield diketocamphoric ester, an important intermediate in the synthesis of camphor :



$$\begin{array}{l} COOEt \\ | \\ COOEt \end{array} + \begin{array}{l} CH_2COOEt \\ | \\ CMe_2 \\ | \\ CH_2COOEt \end{array} \longrightarrow \begin{array}{l} CO—CHCOOEt \\ |\qquad | \\ |\qquad CMe_2 + 2EtOH \\ |\qquad | \\ CO—CHCOOEt \end{array}$$

Keto esters are obtained in the normal course of the condensation which belongs to the same class as that described in Reaction XXIII. With esters higher than propionic the products in all cases are not analogous to those already described, being for the most part hydroxyalkyl derivatives of the corresponding higher fatty acids (A., 249, 54).

The mechanism of the reaction is accepted as ionic, being initiated by the ethoxide anion (from the sodium ethoxide if this is used, or from traces of alcohol in the ester when metallic sodium is used). The negative NH_2 or triphenylmethyl anion, in the case of sodamide or sodium triphenylmethyl, respectively, function similarly in promoting the condensation :

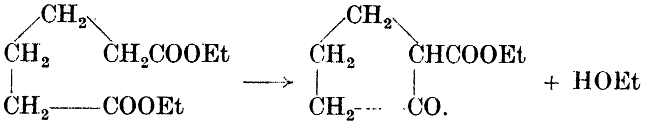
$$\bar{O}Et + HCH_2COOEt \rightleftharpoons HOEt + \bar{C}H_2COOEt \quad (A)$$

$$CH_3C(\underset{\cdot\cdot}{\ddot{O}}:)OEt + \bar{C}H_2COOEt \rightleftharpoons [CH_3C(\underset{\cdot\cdot}{\ddot{O}}:)(OEt)CH_2COOEt]^- \quad (B)$$

$$\rightleftharpoons CH_3COCH_2COOEt + \bar{O}Et.$$

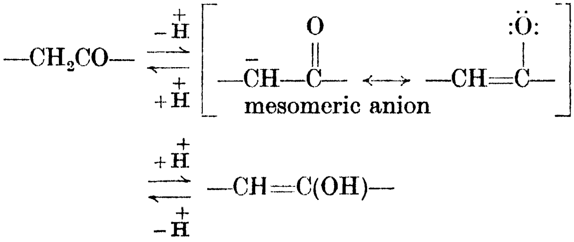
The ester anion (A) condenses with the carbon atom of the carbonyl group in a molecule of unchanged ester forming a complex intermediate anion (B) which expels the ethoxide ion forming acetoacetic ester.

Esters of some dibasic acids undergo this type of condensation intramolecularly (Dieckmann Condensation) yielding cyclic compounds. Thus adipic ester yields cyclopentanone carboxylic ester.



The condensing agent most commonly employed is the sodium alkoxide corresponding to the alcohol of the ester. If this does not promote the reaction the more powerful triphenylmethyl sodium may be effective in doing so. For influence of solvent on the reaction, see C., 1907, II, 30.

Ethylacetoacetate is by far the most important keto ester synthesised by this reaction. It yields alkyl and other derivatives (p. 142) from which ketones and acids may be obtained, and its applications in synthesis are manifold (see pp. 139, 169, 198, 200). The ester consists of an equilibrium mixture of keto and enol forms (tautomers) the tautomeric change from one to the other being considered as due to prototropic change (prototropy) which is generally exhibited by compounds containing the —CH_2CO— group.



PREPARATION 75.—Ethyl Acetoacetate (*Ethyl ester of* 3-*on-butan acid.*)

$CH_3COCH_2COOC_2H_5$ and $CH_3C(OH):CH.COOC_2H_5$. $C_6H_{10}O_3$. 130.

250 gms. of commercial ethyl acetate are shaken with sodium carbonate solution, separated and allowed to stand for 24 hours over anhydrous calcium chloride, filtered into a distilling flask, and redistilled, care being taken that all parts of the apparatus are dry.

200 gms. of the purified ethyl acetate are placed in a dry 500-c.c. round-bottomed flask and 20 gms. of clean sodium in the form of wire introduced directly from the sodium press into the ester. The flask is at once connected to a dried reflux condenser and warmed gently in an oil bath until reaction begins. If reaction becomes vigorous the flask should be cooled; when it subsides a further period (not more than 3–4 hours) of heating at ebullition point, until all the metallic sodium has dissolved, should be given and the top of the condenser should carry a calcium chloride tube

during the heating. The cooled or slightly warm, reaction mixture is then carefully acidified with about 110 c.cs. of 50% acetic acid (test with litmus). The whole is well shaken to dissolve solids, and the mixture of ethyl acetate and ethyl acetoacetate salted out by adding an equal volume of saturated brine. The upper layer or mixed esters is separated in a funnel, washed with cold, saturated sodium bicarbonate solution, dried over a little anhydrous calcium chloride and fractionally distilled in a Claisen flask under reduced pressure. The fraction boiling at 85°–95°/40 m.m. or 70°–80°/18 m.m. is collected separately. The residue in the flask contains dehydracetic acid (see Preparation 65).

For equation, see p. 152.

Yield.—30% theoretical (44 gms.). Colourless liquid ; slightly soluble in water ; B.P.^{760} 181° ; B.P.^{12} 72° ; D. $^{20°}_{4}$ 1·0256 (C. V., I, 235).

The following methods have been used for the separation of the keto and enol forms of ethyl acetoacetate.

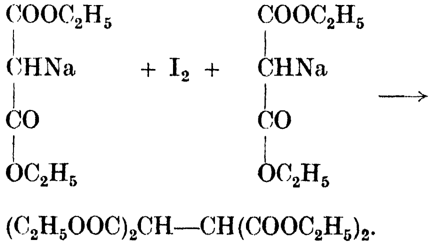
The ester is first fractionally-distilled at 10 mm. in glass apparatus, thus becoming highly enolised (80–90%), and then immediately fractionated in quartz, the first fraction being pure enol. (B., 53, 1410 ; 54, 579.)

By cooling a concentrated solution of the ester in different solvents to −78°, the pure keto (M.P. −39°) separates, which gives no coloration with ferric chloride. The enol form is obtained by treating the sodium salt with dry hydrogen chloride at −78°. (B., 44, 1147.) Both compounds form the same equilibrium mixture at ordinary temperature.

For the estimation of the amount of keto and enol forms present in the equilibrium mixture, see p. 505.

Reaction XLVII. Condensation of an Ester with itself by the action of Iodine on its Sodio-derivative. (B., 23, R., 141 ; A., 201, 144 ; 266, 88.) When iodine, usually in ethereal solution, acts on the sodio-derivatives of esters, such as malonic or acetoacetic esters, the metal is eliminated, and higher dibasic esters are obtained.

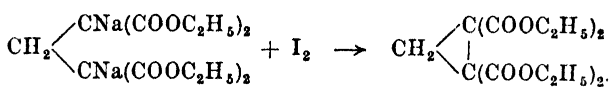
(*a*)



$$\begin{array}{l}COOC_2H_5\\ |\\ CHNa\\ |\\ CO\\ |\\ OC_2H_5\end{array} + I_2 + \begin{array}{l}COOC_2H_5\\ |\\ CHNa\\ |\\ CO\\ |\\ OC_2H_5\end{array} \longrightarrow (C_2H_5OOC)_2CH—CH(COOC_2H_5)_2.$$

The reaction is especially useful for preparing cyclo-paraffins by acting with iodine (or bromine) upon disodio-methylene- and disodio-ethylene-, etc., di-malonic esters.

(*b*)

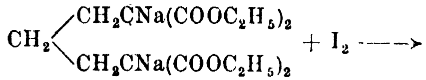


$$CH_2\left\langle\begin{array}{l}CNa(COOC_2H_5)_2\\ CNa(COOC_2H_5)_2\end{array}\right. + I_2 \rightarrow CH_2\left\langle\begin{array}{l}C(COOC_2H_5)_2\\ |\\ C(COOC_2H_5)_2.\end{array}\right.$$

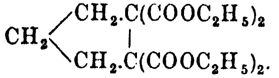
Disodio-methylenedimalonic Ester
(Propanetetracarboxylic Ester.)

*Cyclo*propanetetra-
carboxylic Ester.

(c)



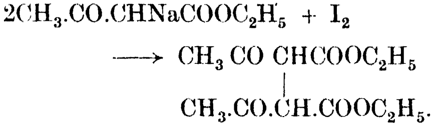
Disodio-propylenedimalonic Ester
(Pentanetetracarboxylic Ester.)



*Cyclo*pentanetetracarboxylic Ester.

Cf. Reaction XLIV. (*a*) (iii.).

(*d*)

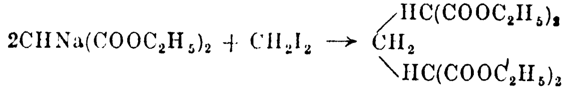


$$2CH_3.CO.CHNaCOOC_2H_5 + I_2 \longrightarrow \begin{array}{l} CH_3CO\,CHCOOC_2H_5 \\ \quad\quad\quad | \\ CH_3.CO.CH.COOC_2H_5. \end{array}$$

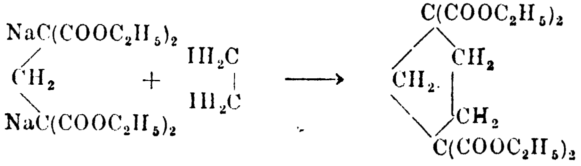
Diacetosuccinic Ester.

The action of methylene and ethylene iodides, etc., on the sodio-derivatives of the esters dealt with above might have been discussed under Reaction XLIV (*a*), but is best dealt with here. The alkylene halides react analogously to the iodine molecule:

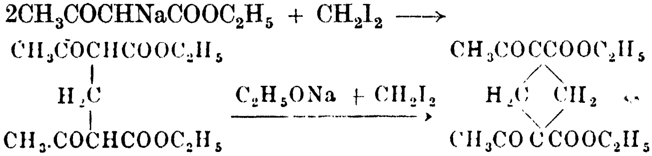
(i.)



(ii.)

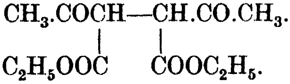


(iii)



It will be seen that whereas iodine leads to 1 : 2 tetra- and di-basic esters, methylene, ethylene, etc., iodides yield respectively 1 : 3, 1 : 4, etc., esters. The yields in these ring syntheses, as in most others, vary in agreement with Baeyer's " Strain Theory ".

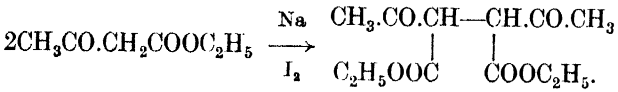
Preparation 76.—Diethyl Diacetosuccinate (*αβ-Dicarbethoxy-αβ-diacetoethane*).



$$\begin{array}{l} CH_3.COCH—CH.CO.CH_3. \\ \quad\quad\quad |\quad\quad | \\ C_2H_5OOC\quad COOC_2H_5. \end{array}$$

$C_{12}H_{18}O_6$. 258.

In a stoppered bottle of 500 c.cs. capacity provided with a reflux condenser, 25 gms. (2 mols.) of acetoacetic ester are dissolved in 150 gms. of pure ether which has been dried over sodium, and to this solution 5 gms. (2 mols.) of fine sodium wire are added. After 2 hours, the bottle is shaken at intervals, being stoppered while so doing, till no further evolution of hydrogen takes place, and all the metal has been converted into sodio-acetoacetic ester. 20 gms. (excess) of finely-powdered iodine are dissolved in pure anhydrous ether, and the solution added in small portions, and with constant shaking, to the solution of the sodio-acetoacetic ester. Sodium iodide is precipitated as soon as the colour of the iodine no longer vanishes at once, the solution is filtered, the ether evaporated off, and the diacetosuccinic ester allowed to solidify. It is then pressed on a porous tile, and recrystallised from warm 50% acetic acid.



$$2CH_3CO.CH_2COOC_2H_5 \xrightarrow[I_2]{Na} \begin{array}{cc} CH_3.CO.CH & —CH.CO.CH_3 \\ | & | \\ C_2H_5OOC & COOC_2H_5. \end{array}$$

Yield.—40% theoretical (10 gms.). Colourless crystals; plates when crystallised slowly; needles when crystallised rapidly; soluble in ether; insoluble in water; M.P. 88°. (B., 7, 892; A., 266, 88.)

(Cf. Reaction XXXVII.)

CHAPTER VIII

CARBON TO CARBON

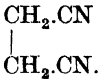
NITROGEN COMPOUNDS

NITROGEN compounds are usually very reactive; in addition to reacting with other compounds a great number readily undergo intramolecular transformations. Nitrogen also plays an important part in ring formation; nitrogen-containing rings are very stable, and the condensations which give rise to them many and varied.

Reaction XLVIII. (*a*) **Action of Alkali Cyanides on Alkyl and Acyl Halides.**—This reaction is capable of wide application, all simple alkyl and acyl halides, and halogen fatty acids coming within its scope. (C. V., I, 107, 156, 256, 536.) The nitriles so formed yield acids by hydrolysis, so it is frequently the first step in the synthesis of an acid—the preparation and hydrolysis of the nitrile are often combined. The preparations of malonic, succinic, tricarballylic and other acids (Preparations 60, 61, 62) illustrate this. The interaction of silver cyanide, and alkyl iodides, to give isonitriles is referred to in Reaction CXXXIV. Mercuric and silver cyanides, it may be be noted, give with acyl chlorides and bromides better yields of normal acyl nitriles than do the alkali cyanides.

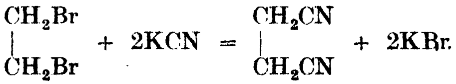
In reactions where nitriles are prepared from halogen compounds by double decompositions in alcoholic or aqueous alcoholic solution with alkali cyanide, the latter is usually added in solution or as a powder (cf. Preparations 77, 78, 79), otherwise the alkali halide which separates forms a coating round the cyanide and hinders further action. If the reaction is performed in aqueous solution, as in the preparation of malonic acid (p. 131), this precaution is not so necessary; the alkali halide, when formed, remains in solution.

PREPARATION 77.—**Succinonitrile (Ethylene Cyanide).**



$$\begin{array}{l} CH_2.CN \\ | \\ CH_2.CN. \end{array} \qquad C_4H_4N_2. \qquad 80.$$

The solution of the nitrile prepared as in Preparation 61 from 100 gms. (1 mol.) of ethylene dibromide and 75 gms. (excess) of potassium cyanide, after filtration from the separated potassium bromide, is evaporated on a water bath under reduced pressure. The residue is extracted with absolute alcohol, the extract evaporated as before, and the residue fractionated under reduced pressure, the fraction 144°–150° at 10 mms. being retained.



$$\begin{array}{l} CH_2Br \\ | \\ CH_2Br \end{array} + 2KCN = \begin{array}{l} CH_2CN \\ | \\ CH_2CN \end{array} + 2KBr.$$

Yield.—80% theoretical (34 gms.). Amorphous transparent mass; readily soluble in water, chloroform and alcohol; sparing soluble in ether; M.P. 54·5°; B.P. ^{10} 147°; B.P. ^{20} 159°. (Bl., [2], 50, 214.)

Propenyl tricyanide, the nitrile of tricarballylic acid, is obtained in a similar manner (see Preparation 62).

PREPARATION 78.—**Phenylacetonitrile** (*Benzyl Cyanide*).

$C_6H_5.CH_2.CN$. C_8H_7N. 117.

60 gms. (slightly more than 1 mol.) of commercial potassium cyanide are dissolved in 55 gms. of water in a ¾-litre round-bottomed flask fitted with a reflux condenser and placed in a fume cupboard. 100 gms. (1 mol.) of benzyl chloride dissolved in 100 gms. of alcohol are poured slowly into the hot solution of potassium cyanide through the top of the condenser, and the whole gently boiled for 4 hours on a sand bath. The flask is then cooled, and the upper dark brown liquid, consisting of an alcoholic solution of benzyl cyanide, is decanted from the crystalline deposit of potassium chloride and distilled over wire gauze in a fume cupboard, the fraction 210°–235° being retained. It is crude benzyl cyanide, and can be used for Preparation 176.

To prepare the pure substance, this fraction is redistilled and collected at 230°–235°.

$$C_6H_5CH_2Cl + KCN = C_6H_5CH_2CN + KCl.$$

Yield.—80% theoretical (75 gms.). Colourless, pungent smelling liquid; B.P., 232°; D. $^{17\cdot5}_{4}$ 1·0171. (A., 96, 247; B., 14, 1645; 19, 951; O. S., II, 9.)

Reaction XLVIII. (*b*) **Action of Alkali Cyanides on Alkyl Hydrogen Sulphates.** (A., 10, 249.)—The alkyl nitriles may also be prepared by dry distilling alkali cyanides with alkali-alkyl-sulphates.

$$M_ICN + SO_2(OM_{II})OR = RCN + SO_2(OM_{II})(OM_I).$$

PREPARATION 79.—**Propionitrile** (*Ethyl Cyanide*).

C_2H_5CN. C_3H_5N. 55.

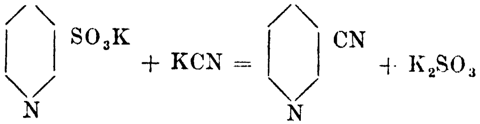
50 gms. (excess) of *finely-powdered* (*caution!*), dry, commercial potassium cyanide and 50 gms. (1 mol.) of *finely-powdered* potassium ethyl sulphate dried at 100° are intimately mixed. An iron tube, closed at one end, is one-third filled with the mixture. The tube, tapped while in a horizontal position to form a channel along the upper surface of the mixture, is placed in a combustion furnace so that the open end projects 3 cms. from the furnace, and is connected with a condenser and receiver, all being set up in a fume cupboard. The mixture is then gradually heated, from the front backwards, to a red heat. The distillate is redistilled to 110°, and the second distillate (propionitrile, isopropionitrile, alcohol and water) shaken with a small quantity of conc. hydrochloric acid to remove isopropionitrile, washed with a small quantity of water, dehydrated over calcium chloride or anhydrous potassium carbonate and fractionated

between 97° and 101°. The propionitrile dissolved in the washings is separated by adding calcium chloride, and worked up as above.

$$C_2H_5.O.SO_2.OK + KCN = KO.SO_2.OK + C_2H_5CN.$$

Yield.—60% theoretical (10 gms.). Colourless liquid, peculiar ethereal smell; slightly soluble in water; B.P. 98°; D. $^{12}_{4}$ 0·789. (A., 10, 249; 148, 252; 159, 79.)

A somewhat similar method of cyanide preparation is applicable in the aromatic series; aromatic sulphonic acid potassium salts, on fusion with potassium cyanide or potassium ferrocyanide, give aromatic nitriles in poor yield. The reaction can be extended to derivatives of pyridine.



(Nicotinonitrile.)

Reaction XLVIII. (*c*) **Action of Dimethyl Sulphate on Potassium Cyanide.** (B., 40, 3215.)—This method gives excellent yields of acetonitrile; diethyl sulphate yields propionitrile by a similar method.

PREPARATION 80.—**Acetonitrile** (*Methyl Cyanide*).

CH_3CN. C_2H_3N. 41.

68 gms. (1 mol.) of finely-powdered potassium cyanide are dissolved in 60 c.cs. of water, in a 500-c.c. round-bottomed flask, and after cooling 126 gms. (1 mol.) of dimethyl sulphate (*caution!*, see p. 266) are added in three equal portions, the whole being shaken vigorously and cooled under water after each addition. During the shaking, the flask is closed by a one-holed cork carrying a glass tube bent three or four times, so as to form a spiral, having its axis horizontal. This prevents spurting out of any liquid. The milky liquid is distilled on a water bath in a fume cupboard at 82°, a litre flask being used owing to frothing. The residue in the flask is treated on cooling with another 65 gms. (1 mol.) of potassium cyanide, added slowly, in 50% solution as before, and the whole is very cautiously distilled from a water bath. A violent reaction occurs, and when this has slackened, the distillation is continued until the residue in the flask becomes solid and nothing more comes over. The distillate is removed and shaken with half its volume of water; solid potassium carbonate is added until no more dissolves, the layer of nitrile is separated from the aqueous solution and redistilled over phosphorous pentoxide, the fraction 79°–83° being retained.

$$KCN + (CH_3)_2SO_4 = (CH_3)KSO_4 + CH_3CN.$$

$$CH_3KSO_4 + KCN = K_2SO_4 + .CH_3CN.$$

Yield.—95% theoretical (78 gms.). Colourless liquid; ethereal odour; slightly soluble in water; B.P. 82°. (B., 40, 3215.)

Reaction XLIX. (*a*) **Action of Cuprous Potassium Cyanide on Aromatic Diazonium Compounds.** (Sandmeyer). (B., 17, 1633, 2650; 18, 1492, 1496.)—If a diazonium salt is added to a hot solution of cuprous potassium cyanide, and the whole boiled on a water bath, nitrogen is evolved, and the corresponding nitrile formed. (C. r., 183, 421.)

$$2R.N_2Cl + KCN(CuCN)_2 \longrightarrow 2RCN + 2N_2 + KCN + Cu_2Cl_2.$$

As usual in Sandmeyer reactions, the product, if volatile, is separated by distillation in steam; if non-volatile, extraction or filtration is used. The cuprous salt reacts with the diazonium compound to form a double salt (cf. Reaction CLXVI). The method is widely applicable, and as the yields are usually good, it is a standard method for the preparation of aromatic nitriles.

For a new interpretation of this reaction, see J. C. S., 1947, 127.

PREPARATION 81.—**Benzonitrile** (*Phenyl Cyanide*).

$C_6H_5.CN$. C_7H_5N. 103.

The details of this preparation are practically the same as those given for *p*-toluonitrile (Preparation 82). A cuprous-potassium cyanide solution prepared as therein described, is warmed to about 70°, and added in small portions to a solution of benzene-diazonium chloride prepared from 18·6 gms. (1 mol.) of aniline as described on page 381. When the addition is complete, the liquid is warmed on a water bath for 15 minutes and distilled in steam; the distillate is extracted with ether. The ethereal solution is washed repeatedly with dilute caustic soda and with dilute sulphuric acid, dried over anhydrous potassium carbonate, filtered, and the oil which remains on driving off the ether fractionated. Owing to the evolution of cyanogen and hydrocyanic acid, this preparation *must* be carried out in a *good* fume cupboard.

$$C_6H_5NH_2 \longrightarrow C_6H_5.N_2.Cl \longrightarrow C_6H_5CN.$$

Yield.—65% theoretical (13 gms.). Colourless oil; odour resembling that of benzaldehyde or nitrobenzene; insoluble in water; soluble in ether; B.P. 191°. (B., 17, 2653. See also O. S., IV, 69.)

PREPARATION 82.—***p*-Toluonitrile** (1-*Methyl*-4-*cyanobenzene*).

$CH_3.C_6H_4.CN.[1:4]$. C_8H_7N. 117.

50 gms. (1 mol.) of copper sulphate crystals are dissolved in 200 c.cs. of water, and 56 gms. (excess) of 96% potassium cyanide added to the warm solution. As cyanogen is evolved, the operation must be carried out in a good fume cupboard, and the fumes must on no account be inhaled, 20 gms. (1 mol.) of *p*-toluidine are then diazotised as described on p. 380, and the diazo solution gradually added in a ½ hour, from a dropping funnel to the cuprous-potassium cyanide solution at 90°, the mixture being kept well shaken. The product is heated on a water bath for a ½ hour, and distilled in steam in a good fume cupboard, since hydrogen cyanide and a little isocyanide are formed; the solid distillate is filtered off, dried on a porous plate, and redistilled.

$$2CuSO_4 \xrightarrow{KCN} 2Cu(CN)_2 \xrightarrow{-(CN)_2} Cu_2(CN)_2 \xrightarrow{KCN} KCN(CuCN)_2.$$

$$CH_3C_6H_4N_2Cl + KCN(CuCN)_2 \longrightarrow CH_3C_6H_4CN.$$

Yield.—65% theoretical (14 gms.). Colourless crystals ; insoluble in water ; soluble in ether ; M.P. 24° ; B.P. 218°. (B., 17, 2653 ; C. V., I, 514.)

o-Toluonitrile is prepared in an exactly similar fashion from *o*-toluidine. It boils at 205° ; D. $^{0}_{4}$ 1·006. (O. S.. IV, 69.)

Reaction XLIX. (*b*) **Action of finely-divided Copper and Alkali Cyanides on Aromatic Diazonium Compounds** (Gattermann). (B., 23, 1218.)—This is the Gattermann modification of the preceding Sandmeyer reaction ; as usual, the cuprous salt is replaced by finely-divided copper. This method gives better yields of some aromatic nitriles.

Preparation 83.—**Benzonitrile** (*Cyanobenzene*).

C_6H_5CN. C_7H_5N. 103.

(*This reaction must be carried out in a good fume cupboard.*)

31 gms. (1 mol.) of aniline are dissolved in 80 gms. (excess) of 50% sulphuric acid, the solution cooled to 0° by addition of ice, and the base diazotised by the addition of 23 gms. (1 mol.) of sodium nitrite as described on page 381. 80 gms. (excess) of 96% potassium cyanide in 50% solution are poured in, and then, with constant stirring, 40 gms. of copper paste (see p. 515) are added in small quantities, and the whole allowed to stand until the evolution of nitrogen ceases and the copper sinks to the bottom of the vessel. The reaction is then over. The product is steam distilled, and the nitrile extracted and purified as described under Preparation 81.

$$C_6H_5N_2SO_4H + KCN \xrightarrow{Cu} C_6H_5CN + KHSO_4 + N_2.$$

Yield.—60% theoretical (20 gms.). Colourless oil ; insoluble in water ; soluble in ether ; odour resembling that of benzaldehyde or nitrobenzene ; B.P. 191°. (B., 23, 1218.)

The preparation of *o*- or *p*-toluonitrile is exactly similar.

Reaction L. (*a*) **Addition of Hydrogen Cyanide to Aldehydes or Ketones.** (B., 14, 235 ; 39, 1224, 1857 ; 28, 10 ; C. Z., (1896), 90.)—Hydrocyanic acid combines with aldehydes and ketones to yield α-hydroxynitriles (cyanohydrins).

$$RR_1CO + HCN \longrightarrow RR_1C(OH)CN.$$

Anhydrous hydrogen cyanide acts readily, particularly under the influence of a basic catalyst (e.g. ammonia). A common procedure is to mix the carbonyl compound with an aqueous solution of potassium cyanide and add a mineral acid. Good yields are obtained by the use of carbonyl bisulphite compounds (see Prep. 84). The reaction is initiated, as shown by Lapworth (J. C. S., 1903, 995), by the cyanide ion :

$$\rangle C\text{—}\underset{..}{\ddot{O}}: + \overset{-}{C}N \longrightarrow \rangle C(CN)\text{—}\underset{..}{\ddot{O}}: \xrightarrow{\overset{+}{H}} \rangle C(CN)OH.$$

See also Reaction XXXVIII (*c*) where cyanohydrins are treated as intermediates for hydroxy acids.

Preparation 64 illustrates the importance of this reaction in the sugar group. For the hydrolysis of nitriles, see p. 242.

PREPARATION 84.—**Acetone Cyanohydrin** (*β-Hydroxy-β-cyanopropane*).

$(CH_3)_2C(OH)CN$. C_4H_7ON. 85.

10 gms. (1 mol.) of acetone are shaken with a saturated sodium bisulphite solution containing 18 gms. (1 mol.) of $NaHSO_3$, and, after cooling, 30 gms. (excess) of a cold 50% solution of 96% potassium cyanide are slowly added. The crystalline bisulphite compound soon dissolves and a fluorescent oil is formed. This is extracted several times with ether, and the ethereal extracts are shaken with saturated bisulphite solution (to remove acetone) and then washed with saturated brine. The ether is removed on a water bath, and the residual oil dried under reduced pressure over conc. sulphuric acid. It is then fractionated under reduced pressure, the fraction 80°–85° at 23 mms. being retained.

$$(CH_3)_2CO + NaHSO_3 = (CH_3)_2C(OH)SO_3Na$$

$$(CH_3)_2C(OH)SO_3Na + KCN = (CH_3)_2C(OH)CN + NaKSO_3.$$

Yield.—96% theoretical (15 gms.). Colourless, odourless liquid; soluble in water; soluble in ether; B.P. ^{23} 82°. (B., 39, 1225, 1857; Rec., 28, 10; C. Z., (1896), 90; O. S., XI, 4; XV, 1.)

The action of hydrogen cyanide on the aldehyde itself, and the action of potassium cyanide on the bisulphite compound, are directly contrasted in the following preparation.

PREPARATION 85.—**Mandelonitrile** (*Phenylhydroxycyanomethane*).

$C_6H_5CH(OH)CN$. C_8H_7NO. 133.

Method I.—14 gms. (1 mol.) of finely-powdered 96% potassium cyanide, and 20 gms. (1 mol.) of freshly-distilled benzaldehyde are placed in a flask cooled with ice and salt. 7 gms. (1 mol.) hydrogen chloride (about 20 c.cs. conc. acid), are slowly dropped in with frequent shaking. This must be done in a good fume cupboard. The whole is allowed to stand for 1 hour, being shaken at frequent intervals; it is then poured into 5 volumes of water, and the oil which separates well washed with water several times; a further purification is impossible owing to its instability.

$$C_6H_5.CHO + KCN + HCl = C_6H_5CH(OH)CN + KCl.$$

Yield.—Theoretical (26 gms.). (B., 14, 235.)

Method II.—50 c.cs. (excess) of a saturated solution of sodium bisulphite are added to 15 gms. (1 mol.) of freshly-distilled benzaldehyde in a beaker, and the whole stirred until the mass is semi-solid owing to the separation of the bisulphite compound of the aldehyde. The latter is filtered off at the pump, pressed, and washed with a little water and alcohol. It is then stirred up with water to a thick paste, and a 30% solution of 12 gms. (excess) of potassium cyanide is added. After stirring for a short time, the crystals go into solution and the nitrile appears as an oil, which is separated and washed with water as above.

$$C_6H_5CHO + NaHSO_3 = C_6H_5CH(OH)O.SO_2Na.$$

$$C_6H_5CH(OH)O.SO_2Na + KCN = C_6H_5CH(OH)CN + KNaSO_3.$$

Yield.—Theoretical (20 gms.). M.P. 29°; decomposes on heating. (B., 39, 1224; D.R.P., 85230; C. Z., (1896), 90; B., 64, 427.)

Reaction L. (*b*) **Condensation of an Aldehyde with Ammonia and Hydrogen Cyanide** (Strecker). (A., 75, 27; 94, 234; 176, 341; 211, 359; B., 13, 381; 33, 2372; 39, 989, 1722, 2796, 4059, 4073, 4087.)—When an aldehyde-ammonia is treated with hydrogen cyanide, an amino-nitrile is formed.

$$R.CH(OH)NH_2 + HCN = RCH(CN)NH_2 + H_2O.$$

The two steps in this synthesis are interchangeable (B., 13, 381).

$$R.CH(CN)OH + NH_3 = RCH(CN)NH_2 + H_2O.$$

The use of the conc. hydrocyanic acid necessary in the above reactions can be avoided, and the amino-nitrile synthesised in one stage by using ammonium cyanide or an equimolecular mixture of ammonium chloride and potassium cyanide; this also brings ketones within the scope of the reaction (O. S., XI, 4). The condensation is carried out in aqueous or aqueous alcoholic solutions. An extension of this reaction permits the use of primary aromatic amines and potassium cyanide in place of ammonium chloride and potassium cyanide (D.R.P., 157710; 157709; 158090, 158346; J. C. S., 1931, 653; Am. Soc., 53, 2809; Ann. Rep., 1939, 210).

Better results are obtained by using the bisulphite compound of the aldehyde or ketone (cf. Reaction L (*a*)).

$$RR_1CO \longrightarrow RR_1C(OH)SO_3Na \xrightarrow{ArNH_2 + KCN} RR_1C(CN)(NHAr).$$

In the following preparation, the amino-nitrile formed is hydrolysed directly to the corresponding amino-acid. These latter are of great importance in the chemistry of the proteins.

PREPARATION 86.—**Racemic Leucine** [*Racemic*-4-*methyl*-2-*amino-pentan acid*].

$$(CH_3)_2.CH.CH_2.CH(NH_2).COOH. \quad C_6H_{13}O_2N. \quad 131.$$

(*This preparation must be carried out in a good fume cupboard.*)

50 gms. (1 mol.) of pure redistilled *iso*-valeric-aldehyde are dissolved in 100 c.cs. of absolute ether (see p. 219) and the solution cooled in ice and saturated with dry ammonia (see p. 514). The water formed in the reaction is separated by means of a funnel, the ethereal solution is shaken with a little potassium carbonate, filtered, and evaporated under reduced pressure at a temperature not greater than 25°. The oily residue of *iso*-valeraldehyde-ammonia which usually crystallises rapidly is at once suspended in 100 c.cs. of water; the liquid is cooled, and 36 c.cs. (1 mol. HCN) of 50% hydrocyanic acid are gradually added (*caution!*). The mixture is allowed to stand, with frequent shaking, for 12 hours, and then a mixture of 400 c.cs. (excess) of conc. hydrochloric acid (D. 1·19) and 200 c.cs. of water is added. This produces a lumpy precipitate, which is dissolved by prolonged boiling in a flask; another 200 c.cs. of water are added, and the boiling continued for 2 hours more. The mixture is finally

evaporated to dryness on a water bath to remove hydrochloric acid. The residue is warmed with about 60 c.cs. of water and made faintly alkaline with ammonia. When cold, the leucine which has separated is filtered off at the pump and washed with cold water until all the ammonium chloride has been removed. Further purification is effected by recrystallising from hot water with the addition of decolorising carbon. The mother liquor is concentrated or treated with absolute alcohol to obtain any leucine remaining dissolved therein.

$$(CH_3)_2CHCH_2CHO + NH_3 \longrightarrow (CH_3)_2CHCH_2CH(OH)NH_2 \quad (A)$$

$$A + HCN \longrightarrow (CH_3)_2CHCH_2CH(CN)NH_2 + H_2O.$$

$$(CH_3)_2CHCH_2CH(NH_2)CN + 2H_2O \longrightarrow (CH_3)_2CHCH_2CH(NH_2)COOH + NH_3.$$

Yield.—33% theoretical (25 gms.). Shining leaflets ; slightly soluble in cold water ; very slightly in hot alcohol ; decomposes on heating. O. S., 21, 74 gives preparation from bromoisocaproic acid.

PREPARATION 87.—**o-Carboxyphenaminoacetonitrile** (1-(*cyanomethylamino*)-*2-carboxy-benzene*).

$C_6H_4.(NH.CH_2CN)(COOH)[1:2]$. $C_9H_8O_2N_2$. 176.

Method I.—7 gms. (1 mol.) of finely-powdered potassium cyanide and 14 gms. (1 mol.) of finely-powdered anthranilic acid are suspended in 50 c.cs. of ether or benzene in a flask fitted with a reflux condenser. The whole is well cooled in a freezing mixture, and 7·5 c.cs. (1 mol. CH_2O) of 40% formalin are slowly added. A brisk reaction sets in, and two layers are formed, the lower of which solidifies on cooling to a mass of crystals of the potassium salt of the required acid. This is collected, dissolved in water, the free acid precipitated by acidification with acetic or hydrochloric acid, washed with cold water, and recrystallised from alcohol, benzene, or chloroform.

$$C_6H_4(NH_2)(COOH)[1:2] \xrightarrow{CH_2O} CH_2(OH).NHC_6H_4.COOH[1:2]$$

$$\xrightarrow{KCN} CH_2(CN).NH.C_6H_4COOK[1:2] \xrightarrow{HCl} CH_2(CN)NH.C_6H_4COOH[1:2].$$

Yield.—Theoretical (18 gms.).

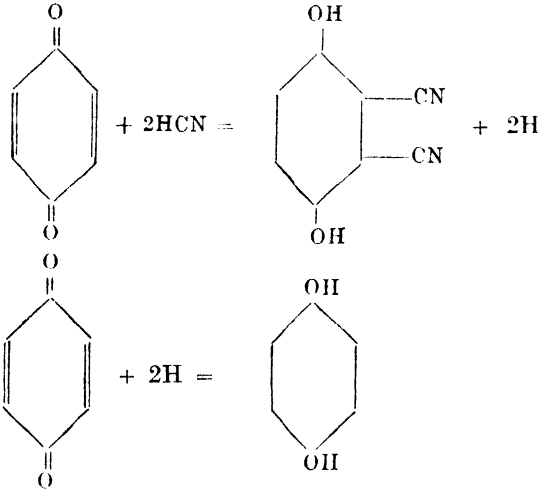
Method II.—20 c.cs. (1 mol. $NaHSO_3$) of 40% sodium bisulphite solution, and 7·5 c.cs. (1 mol. CH_2O) of 40% formalin are mixed, and the mixture kept at 60°–70° for about 20 minutes until the smell of formaldehyde has vanished. A solution of 14 gms. (1 mol.) of anthranilic acid in 10·3 c.cs. (exactly 1 mol. NaOH) of 30% caustic soda solution is then added and the whole heated on a water bath until no more anthranilic acid is present (about 45 minutes). To test the reaction mixture, a sample is withdrawn at intervals, acidified with an excess of acetic acid, a few drops of sodium nitrite added to the well-cooled mixture, and the whole poured into an alkaline solution of R-salt. Anthranilic acid is absent when no red azo-colour is obtained. When the test is negative, or nearly so, a solution of 7 gms. (1 mol.) of potassium cyanide in 25 c.cs. of water is added, and the whole heated to 70°–80° for 20 minutes. On cooling, an excess of glacial acetic acid is added, and the nitrile filtered off, and purified as before.

$$C_6H_4(NH_2)(COONa)[1:2] \xrightarrow{CH_2(OH)(SO_3Na)} CH_2(SO_3Na)NH.C_6H_4COONa[1:2]$$

$$\xrightarrow{KCN} CH_2(CN)NH.C_6H_4COONa[1:2] \xrightarrow{CH_3COOH} CH_2(CN)NH.C_6H_4COOH[1:2]$$

Yield.—Theoretical (18 gms.). Crystallises from alcohol (3 parts) in leaflets ; from benzene or chloroform in long needles ; insoluble in water ; M.P. 183°. (D.R.P., 157909 ; B., 39, 2807.)

Reaction L. (*c*) **Action of Hydrogen Cyanide on Quinones.** (B., 33, 675 ; D.R.P., 117005.)—Hydrogen cyanide reacts easily with quinones to give dicyano-dihydroxy derivatives of the parent hydrocarbons. A molecule of the quinone is simultaneously reduced.



Preparation 88.—**Dicyanoquinol** (1 : 4-*Dihydroxy*-2 : 3-*dicyanobenzene*).

$C_8H_4O_2N_2$. 160.

(*This preparation must be carried out in a fume cupboard.*)

20 gms. (2 mols.) of *p*-benzoquinone are dissolved in 60 c.cs. of alcohol, and a cold mixture of 25 c.cs. (excess) of conc. sulphuric acid and 50 c.cs. of alcohol are added. The mixture is well cooled in a freezing mixture, and a 50% solution of potassium cyanide (*caution !*) slowly run in until a

green fluorescence appears, and the liquid reacts alkaline. About 110 gms. of solution will be required. The whole is then acidified with sulphuric acid (*caution !*) and the alcohol removed by distillation under reduced pressure from a water bath. The residue is washed with water, and recrystallised from hot water with the addition of decolorising carbon.

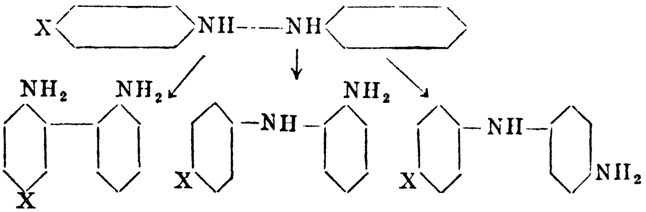
$$2C_6H_4O_2 + 2HCN = C_6H_2(OH)_2(CN)_2[1:4:2:3] + C_6H_4(OH)_2[1:4].$$

Crystallises in pale yellow leaflets, which contain 2 mols. of water; slightly soluble in water; its neutral solution fluoresces blue, its acid solution violet, and its alkaline solution green; on heating it decolorises at 230°. (B., 33, 675; D.R.P., 117005.)

Reaction LI. (*a*) **Action of Acids on the non-para substituted Hydrazo Compounds.** (J. C. S., 1933, 984; 1941, 220; 1946, 406, 777. A., 428, 76.)—When hydrazobenzene is treated with mineral acids, an intermolecular rearrangement (benzidine transformation) to benzidine takes place.

$$C_6H_5.NH.NH.C_6H_5 \longrightarrow H_2N.C_6H_4.C_6H_4NH_2[4:4'].$$

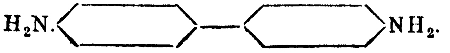
This reaction can be extended to almost all non-*para* substituted hydrazo compounds. If one or both *para*-positions are substituted, either *ortho*-benzidine or diphenylamine derivatives known as *ortho*- or *para*-semidines are formed.



o-Benzidine. *o*-Semidine. *p*-Semidine.

Benzidine and its homologues are very important intermediates in the dye industry.

Preparation 89.—Benzidine (4 : 4′-*Diaminodiphenyl*).



$C_{12}H_{12}N_2$. 184.

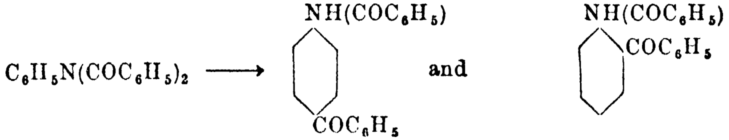
5 gms. hydrazobenzene are slowly heated to boiling in a narrow-necked flask, with 6 c.cs. conc. hydrochloric acid in 50 c.cs. water, a crystal of sodium bisulphite being added occasionally to minimise oxidation of the hydrazobenzene. The solution at the boil should be acid to Congo red (test). The hot solution is filtered from insoluble matter (azobenzene), and a saturated solution of sodium sulphate added until the benzidine sulphate is completely precipitated (test). The sulphate is then filtered and washed free from acid with hot water. The moist sulphate is removed, heated while stirring to 50° with a little water, and caustic soda solution added until an alkaline reaction to phenolphthalein is obtained. When

cold, the free base is filtered, dried at 50°, and crystallised from benzene, alcohol or hot water. From the last solvent, it crystallises under certain conditions as the monohydrate. (See p. 499.)

$$C_4H_8NH.NH.C_6H_5 \longrightarrow H_2N.C_6H_4C_6H_4NH_2[4:4'].$$

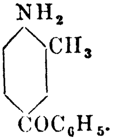
Yield.—90% theoretical (4·5 gms.). Lustrous plates when freshly crystallised; M.P. 127°; darkens in air; soluble in hot water; forms monohydrate, M.P. 105°; forms a difficultly soluble sulphate. (J. pr., [1], 36, 93.) See Prep. 369.

Reaction LI. (*b*) **Molecular rearrangement of Dibenzanilides.**—When dibenzanilide is heated at 230° for 2 days, rearrangement takes place, and 2- and 4-(benzoylamino)-benzophenones are formed.



If either the *o*- or *p*-position is occupied, only one isomer is obtained; transformation to the *meta*-isomer does not occur. This is a standard method of preparation of acyl-amino-ketones, or by a further hydrolysis of amino-ketones. The tendency, illustrated in this reaction, of groups to wander from the amino group to the nucleus, is also shown in previous reactions and in the preparation of aminoazobenzene from diazoaminobenzene (Preparation 456), of sulphanilic acid from aniline sulphate (Preparation 292), of *o*- and *p*-chloroacetanilides from acetochloranilide (Preparation 328), of *o*- and *p*-toluidine from methylaniline hydrochloride, and of 1 : 2 : 4-aminodimethylbenzene (2 : 4-xylidine) from dimethylaniline hydrochloride.

PREPARATION 90.—4-Amino-3-methylbenzophenone (1-*Methyl*-3-*benzoyl*-6-*aminobenzene*).



$C_{14}H_{13}ON$. 211.

To 26 gms. (2 mols.) of benzoyl chloride are added gradually 10 gms. of *o*-toluidine (1 mol.) and the mixture is heated for 15 hours in an oil bath at 230°. A brown viscid liquid is formed which solidifies on cooling. In order easily to separate the 4-amino-3-methylbenzophenone, the mass is hydrolysed by boiling for 14 hours with excess of alcohol containing half its bulk of conc. hydrochloric acid. The product thus obtained is steam distilled when alcohol and then ethyl benzoate pass over. The acid residue which contains the hydrochloride of the base is boiled for some time with water and filtered from tarry matter. The filtrate is then made slightly alkaline, and *o*-toluidine derived from untransformed dibenzoyl-*o*-toluidine, removed by steam distillation. A solid separates from the alkaline liquid in the flask, and after cooling this is filtered off and extracted with absolute alcohol. The alcohol is almost completely removed on the water bath, and a few drops of conc. sulphuric acid are added. On adding a little ether, the base crystallises out in the form of colourless needles.

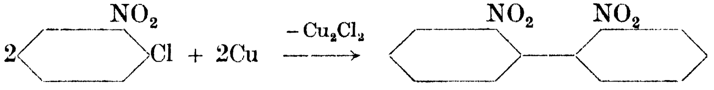
$$CH_3C_6H_4NH_2[1:2] + 2C_6H_5COCl \xrightarrow{-2HCl} CH_3C_6H_4N(COC_6H_5)_2$$

$$\longrightarrow CH_3C_6H_3(COC_6H_5)NHCOC_6H_5[1:5:2] \xrightarrow[C_2H_5OH]{HCl} C_6H_5COOC_2H_5$$

$$+ CH_3C_6H_3(COC_6H_5)NH_3Cl \xrightarrow{NaOH} CH_3C_6H_3(COC_6H_5)NH_2[1:5:2].$$

Colourless needles ; M.P. 112°, soluble in alcohol ; insoluble in ether and in water. (J. C. S., 85, 386, 591.)

Reaction LII. (*a*) **Action of Copper Powder on 2- and 4-mono-nitro- and 2 : 4-di-nitro-chloro- and -bromo-benzenes and their Homologues** (Ullmann). (B., 34, 2172)—Symmetrical diphenyl derivatives can be prepared from aromatic iodo-compounds and copper powder (see Reaction VII (*b*)). Chloro- and bromo-compounds, however, only react when activated by nitro groups in the *ortho*- or *para*-positions. Di-nitro-diphenyl derivatives can be obtained from them in good yield by heating with the metallic powder to about 250° in sealed tubes. If both the *ortho*- and *para*-positions are occupied by nitro groups, the activation of the halogen atom is such that the corresponding diphenyl derivative can be prepared by boiling with copper powder in nitrobenzene. (J. C. S., 1931, 3176 ; Chem. Rev., 1946, 139.)



Preparation 91.—2 : 2′ : 4 : 4′-Tetranitrodiphenyl.

$[2:4](NO_2)_2C_6H_3.C_6H_3(NO_2)_2[2':4']$. $C_{12}H_6O_8N_4$. 334.

10 gms. (1 mol.) of 2 : 4-dinitrochlorobenzene (see p. 278), 10 gms. (excess) of copper powder, and 20 c.cs. of nitrobenzene are refluxed for 1 hour and the cooled solution diluted with ether and filtered. Ligroin is slowly added to the filtrate and the oil which separates crystallised by scratching the sides of the vessel. It is recrystallised from benzene.

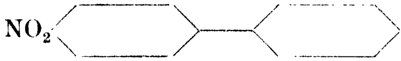
$$[1:2:4](NO_2)_2C_6H_3Cl + 2Cu + ClC_6H_3(NO_2)_2[1:2:4]$$
$$= [2:4](NO_2)_2C_5H_3.C_6H_3(NO_2)_2[2':4'] + Cu_2Cl_2.$$

Yield.—66% theoretical (5·5 gms.). Yellowish prisms ; insoluble in petroleum ether ; M.P. 163°. (B., 34, 2177.)

Reaction LII. (*b*) **Action of Cuprous Chloride on Nitro-diazonium Compounds.** (B., 34, 3802 ; 38, 725.)—Ordinarily when cuprous chloride acts on a diazonium salt in acid solution, a chloro-compound is the chief product (Sandmeyer's reaction, p. 352), and only a small quantity of the corresponding diphenyl compound is formed. But if a nitro-diazonium salt be used, the diphenyl derivative is formed in much larger quantities. The same holds good for Gattermann's modification of the reaction using copper powder (B., 23, 1226).

$$2C_6H_4(NO_2)N_2Cl + Cu_2Cl_2 = (NO_2)C_6H_4.C_6H_4(NO_2) + 2CuCl_2 + 2N_2.$$

PREPARATION 92.—*p*-*p*′-**Dinitrodiphenyl.**



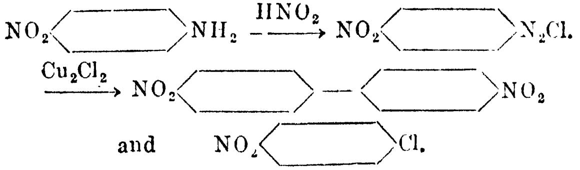
$C_{12}H_8N_2O_4$. 244.

By-product: *p*-**Chloronitrobenzene.** (1-*Chloro*-4-*nitrobenzene*).

$C_6H_4(Cl)(NO_2)[1:4]$. $C_6H_4O_2NCl$. 157·5.

A cold solution of 21·6 gms. (1 mol.) of cuprous chloride in 100 c.cs. of conc. hydrochloric acid (see p. 515) is added to the diazonium solution prepared from 30 gms. (1 mol.) of *p*-nitroaniline, 45 gms. (excess) of conc. sulphuric acid, 60 c.cs. of water and 15·3 gms. (1 mol.) of sodium nitrite (p. 380).

During the addition of the copper salt the whole is vigorously stirred. There is a brisk evolution of nitrogen, the mass turns black and a brownish-yellow substance is precipitated. When the liquid becomes green, the reaction is finished. The product is distilled in steam until no more *p*-chloronitrobenzene passes over. There remains in the distilling flask almost pure 4 : 4′-dinitrodiphenyl. It is filtered off, dried and re-crystallised from benzene. The by-product *p*-chloronitrobenzene is worked up by filtering it from the liquid portion of the distillate, drying on a porous plate, and recrystallising from benzene.

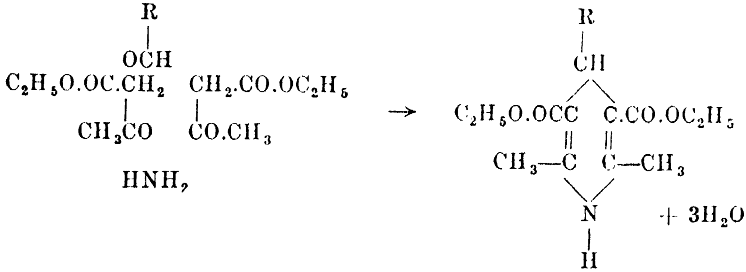


Yield.—4 : 4′-*dinitrophenyl* 55% theoretical (14 gms.); *p-chloronitrobenzene* 40% theoretical (13 gms.). 4 : 4′-*dinitrodiphenyl* is a crystalline solid; M.P. 237°; *p-chloronitrobenzene* is a crystalline solid; M.P. 83°; B.P. 238·5°. (B., 38, 726.)

In an analogous manner there is obtained from 30 gms. of *m*-nitroaniline, 23 gms. (87%) of 3 : 3′-dinitrodiphenyl (yellow needles; insoluble in cold glacial acetic acid; M.P. 200°) and 6 gms. (20%) of *m*-chloronitrobenzene (colourless crystals; insoluble in cold benzene; M.P. 45°; if rapidly cooled after fusion, melts at 24°, but in a short time reverts to the stable modification). (O. S., IX, 92.)

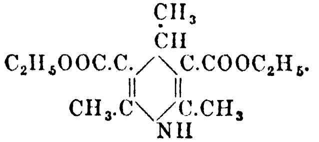
Similarly 30 gms. of *o*-nitroaniline yield 17·6 gms. (64%) of 2 : 2′-dinitrodiphenyl (crystalline solid, insoluble in cold benzene; M.P. 127°) and 9 gms. (30%) of *o*-nitrochlorobenzene (colourless crystals, insoluble in cold benzene; M.P. 32·5°). See also O. S., XX, 45.

Reaction LIII. Action of Ethyl Acetoacetate on Aldehyde-ammonias (Hantzsch). (A., 215, 1.)—When acetoacetic ester is heated with aldehyde-ammonias alkyl derivatives of dimethyldihydropyridinedicarboxylic ester are produced.



Many aldehydes can be employed—propaldehyde, nitrobenzaldehyde, phenylacetaldehyde, furfural—so that the reaction is of wide application. For the steps in the conversion of the compounds obtained to alkyl or aryl derivatives of dimethylpyridine, see pp. 245, 419, 420.

Preparation 93.—**Diethyldihydrocollidinedicarboxylate** [2 : 4 : 6-*Trimethyl*-3 : 5-*dicarbethoxy-piperidine*-(2)-(5)-*di-en*.]



$C_{14}H_{21}O_4N$. 267.

13 gms. (slightly more than 1 mol.) of acetaldehyde-ammonia (see p. 424) are covered with 80 gms. (2 mols.) of ethyl acetoacetate and warmed gently (in a fume cupboard) until ebullition has commenced (100°–110°). Should the reaction become too violent, the heating is stopped until it subsides. In 5 minutes the reaction is completed, and an equal volume of dilute hydrochloric acid is added with stirring to the hot liquid, the stirring being continued until the oil which separates sets to a white crystalline mass. This latter is powdered, filtered, washed first with diluted hydrochloric acid and then with water, well pressed, and recrystallised from the minimum quantity of hot alcohol.

For equation, see above.

Yield.—66% theoretical (30 gms.). Colourless plates with bluish fluorescence ; insoluble in water ; sparingly soluble in alcohol, ether, and carbon disulphide ; readily soluble in benzene ; M.P. 131°. (A., 215, 1.)

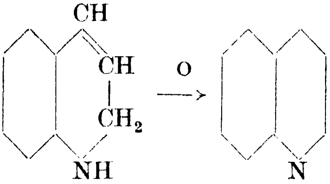
Reaction LIV. (*a*) **Condensation of Non-di-ortho-substituted-primary-aromatic Amines with Acrolein** (Skraup). (M., 1, 316 ; 2, 141 ; B., 13, 911 ; 14, 1002 ; 29, 705.)—When a primary aromatic amine which has a non-substituted carbon in the *ortho*-position is heated with glycerol and conc. sulphuric acid in the presence of an oxidising agent, the following series of reactions occurs :

(1) glycerol is dehydrated to acrolein,
(2) acrolein condenses with two molecules of amine, and
(3) ring closure followed by oxidation yields quinoline.

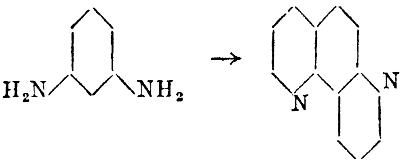
(1) $CH_2OH.CHOH.CH_2OH—2H_2O \rightarrow CH_2 : CH.CHO.$

(2) $CH_2 : CH.CHO + 2C_6H_5NH_2 \rightarrow C_6H_5NHCH_2CH_2CH : NC_6H_5$ (A)

(3) $A - C_6H_5NH_2 \rightarrow$

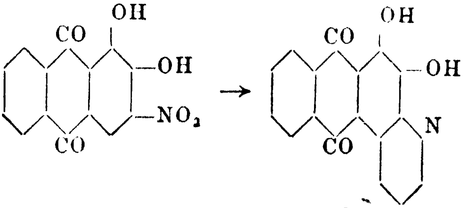


The oxidising agent usually employed is the nitro-compound corresponding to the amine, e.g. nitrobenzene when aniline is the base ; for *p*-toluidine, *p*-nitrotoluene serves, and so on. Arsenic acid, however, can be generally employed, and gives better results. The reaction is capable of very wide application ; nitro-, halogen-, hydroxy-, carboxy-quinolines can all be obtained from the corresponding amines ; the amino-naphthalenes also react. Diamines yield the so-called phenanthrolines. (B., 16, 2519 ; 23, 1016.)



m-Phenanthroline.

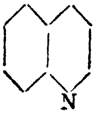
Sometimes the amine can be dispensed with, and the corresponding nitro-body used alone. It is reduced by the hydrogen arising in the reaction. Of technical interest is the fact that β-nitro-alizarin on heating with glycerol and sulphuric acid yields a blue dye—Alizarin Blue. (B., 16, 445 ; 29, 708 ; A., 201, 333.)



Alizarin Blue.

For an extensive review, see Chem. Rev., 35, 77.

PREPARATION 94.—**Quinoline** (*Benzpyridine*).



C_9H_7N. 129.

125 gms. of conc. sulphuric acid are gradually added, with shaking, to a mixture of 46 gms. (1 mol.) aniline, 30 gms. nitrobenzene, 125 gms. (excess) dehydrated glycerol (p. 341), and 12 gms. ferrous sulphate, in a 2-litre round-bottomed flask. The latter is fitted with a long wide reflux condenser, and heated on a sand bath until white vapours are evolved. Heating is discontinued until the reaction moderates, when the flask is again heated to gentle ebullition for 5 hours. Water is added, and the unchanged nitrobenzene distilled off in steam. The residue is treated with conc. caustic soda solution until it is strongly alkaline, and the quinoline and aniline present distilled off in steam. The distillate is treated with dilute sulphuric acid until the bases are both completely dissolved and the solution contains *excess* of acid. To the cooled solution sodium nitrite solution is added until a drop of the solution gives a blue coloration with potassium iodide-starch paper (see p. 380). The aniline is thus converted into the diazonium compound, and on boiling on a water bath the latter passes into phenol. The solution is again made alkaline, and the quinoline distilled off in steam. The distillate is extracted with ether, dehydrated over solid caustic potash, the ether removed on a water bath, and the residue distilled.

(For equations of the reaction, see p. 171.)

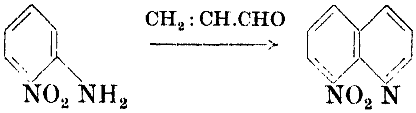
Yield.—80% theoretical (50 gms.). Colourless liquid; B.P. 237°; D. $^{0}_{4}$ 1·108. (C. V. I, 478.)

When boric acid is employed to moderate the vigour of the reaction 25 gms. of it are dissolved in the 125 gms. of glycerol taken and the solution cooled prior to incorporation in the above mixture. (Am. Soc., 52, 3685.)

PREPARATION 95.—α-**Nitroquinoline** (*o-Nitrobenzpyridine*).

$C_9H_6O_2N_2$. 174.

100 gms. of conc. sulphuric acid and 51·5 gms. of arsenic acid are well shaken in a flask with 110 gms. glycerine and 50 gms. of *o*-nitroaniline and then carefully heated on a sand bath under a reflux condenser. As soon as reaction begins, the flask is removed from the sand bath until it has moderated; boiling is continued for 3 hours. When cold, a large volume of water is added to the flask, and the whole allowed to stand overnight, and then filtered. Caustic soda is carefully added to the filtrate until a brown precipitate appears, which is filtered off and discarded. Caustic soda is then added to the filtrate until alkaline. The nitro-quinoline thus obtained is washed with water, boiled up with alcohol and decolorising carbon, and after filtration is precipitated by the addition of water.

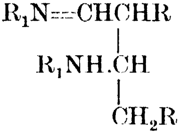


Yield.—55% theoretical (35 gms.). Colourless monoclinic needles; insoluble in water; soluble in alcohol; M.P. 88°. (B., 29, 705.)

Reaction LIV. (*b*) Condensation of Primary Aromatic Amines, other than Ortho Substituted, with two Molecules of certain Aldehydes (containing the group—CH_2CHO) under the influence of Sulphuric or Hydrochloric Acid. (B., 16, 2465 ; A., 249, 110.)—Quinolines substituted in the benzene or in both nuclei may be formed, anils being formed intermediately.

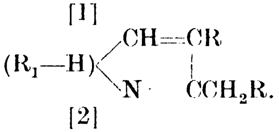
$$R_1NH_2 + OHC.CH_2.R \longrightarrow R_1N : CH.CH_2R.$$

Two molecules of the latter then combine to give



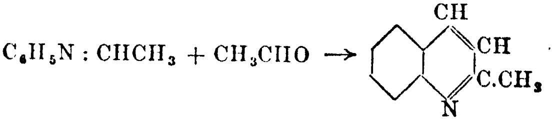
$$\begin{array}{l} R_1N{=}CHCHR \\ \phantom{R_1N{=}CHC}| \\ R_1NH.CH \\ \phantom{R_1N{=}CHC}| \\ \phantom{R_1N{=}CHH}CH_2R \end{array}$$

which splits off amine and hydrogen to give a quinoline derivative (B., 29, 59).

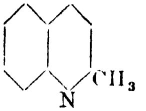


That hydrogen is set free is proved by the reduction of some of the quinoline derivative to a tetrahydroquinoline derivative. A mixture of two aldehydes, or of an aldehyde and a ketone, may be employed. (B., 20, 1098.)

An alkylidene-aniline may be substituted for the primary amine, and the condensation takes place in presence of zinc chloride.



PREPARATION 96.—**Quinaldine** (2-*Methylquinoline*).



$C_{10}H_9N$. 143.

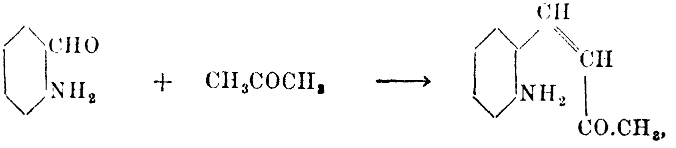
A solution of 50 gms. paraldehyde in 200 c.cs. water is added to 85 gms. amiline hydrochloride in 200 c.cs. water, and the mixture allowed to stand for 7 days. It is then evaporated, 40 gms. anhydrous zinc chloride added, and the resulting mixture melted in a round-bottomed flask heated in an oil bath at 250°. After cooling and adding excess of sodium hydroxide solution the quinaldine is steam-distilled and extracted from the distillate with ether. The ethereal solution is dried with anhydrous sodium sulphate, and the quinaldine isolated by distillation.

Yield.—40% theoretical (25 gms.).

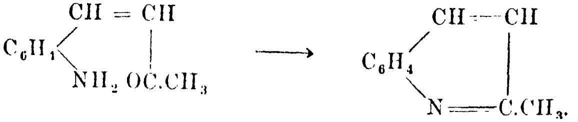
For equation, see above.

Yield.—50% theoretical (6 gms.). Colourless liquid; characteristic odour; insoluble in water; B.P. 247°. (B., 16, 2465; E.P., 395063.)

Reaction LIV. (*c*) **Condensation of** *o*-**Aminobenzaldehydes with Aldehydes, Ketones, Ethyl acetoacetate, etc., under the influence of a trace of Sodium Hydroxide, to give Quinoline Derivatives** (B., 16, 1835; 25, 1752.) —The first stage is the formation of an *o*-aminostyryl ketone.



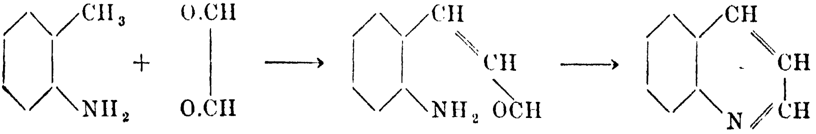
which, like all such compounds, readily condenses to a quinoline derivative.



The reaction usually takes place by gentle warming with a trace of alkali in alcoholic solution.

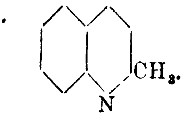
γ-Hydroxy-quinolines may be prepared by condensing anthranilic acid with aldehydes, ketones, etc. (B., 28, 2809.)

An interesting synthesis of quinoline from *o*-toluidine takes place by condensation with glyoxal (B., 27, 628).



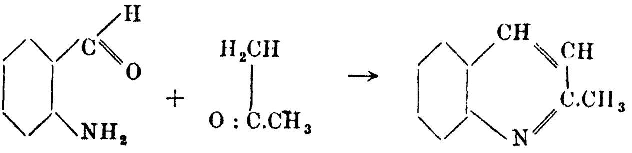
Cf. the synthesis of Carbostyril, B., 14, 1916.

Preparation 97.—**Quinaldine** (2-*Methylquinoline*).



$C_{10}H_9N$. 143.

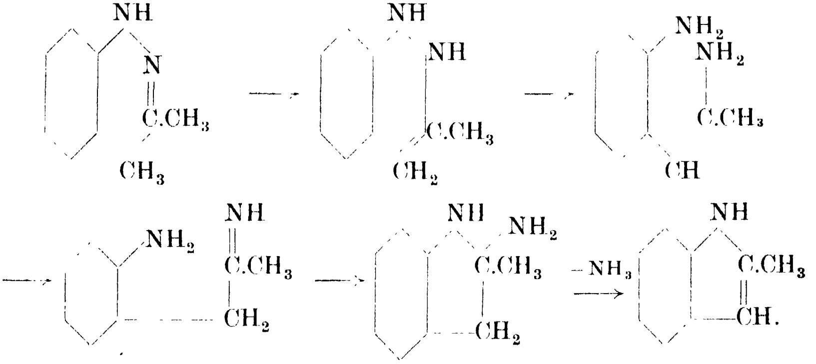
20 gms. (1 mol.) of *o*-aminobenzaldehyde and 9 gms. (1 mol.) of dried and redistilled acetone are dissolved in absolute alcohol, and a few drops of alcoholic caustic soda added. The condensation takes place at ordinary temperature. The quinaldine is distilled off in steam and washed with water until free from acetone.



Yield.—Theoretical (23 gms.). Colourless liquid ; insoluble in water ; B.P. 247°. (B., 16, 1834.)

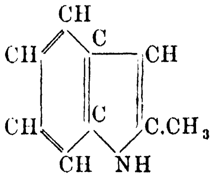
Reaction LV. Intramolecular condensation of Phenylhydrazones of Aldehydes, Ketones and Ketonic Acids by heating with Hydrochloric Acid or Zinc Chloride (Fischer). (B., 19, 1563 ; 26, R., 14 ; E.P., 385605.)—This is an important method of preparation for the alkylindols. The reactions occurring are somewhat complicated, since both rearrangement and elimination of ammonia take place.

Robinson's hypothesis (J. C. S., 113, 639 ; 125, 827), amended by Allen and Wilson (Am. Soc., 1943, 611) is that the reaction involves a rearrangement to an unsaturated hydrazine, an isomeric change of the *o*-benzidine type, and finally the elimination of ammonia from the tautomeric form of the diamine. (Chem. Rev., 30, 69.)



By the use of ^{15}N as a tracer, it has been shown that the nitrogen eliminated as ammonia is not that attached to the benzene ring. (Ann. Rep., 1943, 160.)

PREPARATION 98.—**2-Methylindole** (*Methylketole*).



C_9H_9N. 131.

30 gms. (1 mol.) of phenylhydrazine are mixed with 18 gms. (slightly more than 1 mol.) of distilled acetone (B.P., 56°–58°). The mixture becomes very warm and a good deal of water separates. The mixture is heated on a water bath for 15 minutes, a small portion being occasionally tested with Fehling's solution. As long as phenylhydrazine is present in excess, the Fehling's solution is reduced ; more acetone is then added from time to time until the reducing action of the mixture has almost ceased. The turbid oil (crude acetone-phenylhydrazone) is placed in a large copper crucible, and the excess of acetone removed by heating on a

water bath for ½ hour. 200 gms. of anhydrous zinc chloride are next added, and the mixture heated on the bath with frequent stirring. The whole is then heated on an oil bath to 180°, and, when in a few minutes the mass has acquired a dark colour, the crucible is immediately removed from the bath and stirred. The reaction is complete in a short time, and is followed by a change in colour of the fusion product and evolution of vapours. The dark fused mass is treated with 3½ times its weight of hot water, and distilled in steam after acidification with a little hydrochloric acid. The methylketole distils over, slowly but completely, as a pale yellow oil which soon solidifies. This is filtered off, melted to free it from water and distilled. It must be kept in a well-closed bottle.

Yield.—55% theoretical (20 gms.). Pale yellow crystals; obnoxious odour; M.P. 59°; B.P. ^{750} 272°. (A., 234, 126.) See also O. S., 22, 94.

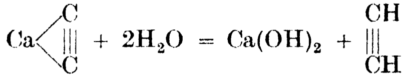
CHAPTER IX

THE LINKING OF HYDROGEN TO CARBON

HYDROGEN COMPOUNDS

ALTHOUGH neither so numerous nor important as the carbon to carbon reactions discussed in Chapter VIII, a number of reactions, more particularly those classed under the heading of reductions, are dealt with below. Some of the most important methods of preparing hydrocarbons depend on the reduction of derivatives previously obtained.

Reaction LVI. Action of Water on certain Metallic Carbides. (J. C. S., 87, 1232.)—This reaction has an important and well-known application in the production of acetylene on an industrial scale. Methane can be obtained in a similar way from aluminium carbide.



$$Ca\langle\overset{C}{\underset{C}{|||}} + 2H_2O = Ca(OH)_2 + \overset{CH}{\underset{CH}{|||}}$$

$$Al_4C_3 + 12H_2O = 3CH_4 + 4Al(OH)_3.$$

PREPARATION 99.—**Acetylene** (*Ethin*).

$$\overset{CH}{\underset{CH.}{|||}} \qquad C_2H_2. \qquad 26.$$

10 gms. of calcium carbide are placed in a shallow layer over sand in a large conical flask fitted with a two-holed rubber stopper carrying a tap funnel and a delivery tube. Water is added drop by drop from the tap funnel. The gas evolved contains sulphuretted hydrogen, hydrogen from free calcium, siluretted hydrogen from calcium silicide, phosphoretted hydrogen from calcium phosphide, and acetaldehyde vapour produced by condensation of acetylene with water. The gas is purified by passing it through (i) dilute sulphuric acid; this removes ammonia; (ii) a tower packed with a mixture of equal parts of bleaching powder and quicklime; this removes phosphorus compounds; (iii) a solution of cupric chloride acidified with dilute sulphuric acid; (iv) a solution of ferric chloride similarly acidified; (v) a solution of chromic acid; all these remove phosphorus and sulphur compounds; (vi) a 50% aqueous solution of caustic potash. The gas is collected in a gas-holder, over 50% aqueous glycerol, in which it is only very slightly soluble. Before collecting, care should be taken that all air has been removed from the apparatus; during the filling of the holder the rate of flow of liquid from it should be adjusted so that there is a slightly increased pressure in the apparatus; this can be seen from the height of liquid in the central tube of the gas-holder.

The purity of the gas is tested by explosion analysis (J. C. S., 84, 555); the ratio, contraction on explosion to absorption by baryta water after explosion, should lie between 0·73 and 0·77 (theoretical 0·75). Great care must be taken that this preparation is carried out in the absence of flame, and that neither the apparatus nor the collected gas is exposed to direct sunlight, which decomposes acetylene. Also the cupric chloride solution employed for washing should be kept acid; if it becomes alkaline the explosive copper acetylide is precipitated. Should this occur the solution is mixed with much water and poured away.

$$CaC_2 + 2H_2O = C_2H_2 + Ca(OH)_2.$$

Colourless gas; when pure has a garlic-like smell; at N.T.P. water dissolves 1 volume; acetone 31 volumes; explosive limits; in air, 3–52%, in oxygen, 2–92%. (J. C. S., 87, 1232. See also J. C. S., 1946, 39.)

Methane is prepared from aluminium carbide and dilute hydrochloric acid in a similar apparatus. It is purified as described on p. 187.

Reaction LVII. Action of Hydrogen in the presence of finely-divided Nickel on Aromatic Compounds (Sabatier-Senderens). (C. r., 132, 210.)—The addition of hydrogen to an aromatic compound by passing its vapour mixed with hydrogen over finely-divided nickel at a relatively low temperature is a reaction of wide and important application. Although nickel is the metal most usually employed, other metals can also act as hydrogen carriers. The method is chiefly used for the reduction of the nucleus in aromatic compounds—hydrocarbons, phenols, amines, etc., to the corresponding unsaturated and fully saturated paraffin derivatives. Ethylenic and acetylenic linkings, aldehydes and ketones can be reduced. The reaction has been applied on a large scale to the hydrogenation ("hardening") of fats and oils.

Raney nickel (Am. Soc., 54, 4116) is particularly reactive for hydrogenation in the liquid phase at low temperatures and pressures, whilst nickel-kieselguhr (loc. cit. 1651) is suitable for various types of hydrogenation at high pressures. (See p. 521; O. S., 21, 15; *Preparative Organic Chemistry*, Schröter, p. 61.)

Caution.—Great care must be exercised to avoid conditions which might lead to the ignition of hydrogen-air mixtures.

PREPARATION 100.—**Hexahydrobenzene** (*Cyclohexane*).

C_6H_{12}. 84.

Preparation of the Catalyst

Small pieces of pumice stone of a convenient size are soaked in a concentrated solution of nickel nitrate in distilled water, and heated in a basin over a free flame until the nitrate has been converted into the oxide. Alternatively, the pumice is impregnated with a paste of its own weight of nickel oxide and distilled water, and dried on a water bath. The nickel oxide is reduced by heating in a current of pure, thoroughly dried hydrogen in a combustion tube. The arrangement of the apparatus and the preparation and purification of hydrogen are the same as for the preparation of reduced copper (see p. 426). The pumice is loosely packed into the combustion tube and kept in position by asbestos plugs. The air bath is maintained at about 280° ; it is tilted slightly forwards so that any liquid formed may run down into the receiver. Ordinary corks should be used, and not rubber stoppers, in making the connections to the combustion tube. Unpurified hydrogen must not be admitted, as otherwise the catalyst will be poisoned. It is convenient to have a by-pass in the form of a T-piece between the copper gauze and the caustic soda tower. See Fig. 51. (For nickel-kiesulguhr, see Am. Soc., 1932, 1651.)

At first the hydrogen escapes through the by-pass. After the air has been expelled (a sample must be collected and tested) as far as the T-piece, the copper gauze tube is heated, and the current of hydrogen is then diverted through the tower into the combustion tube. Some should also be allowed to escape through the tap-funnel B to remove air from its stem. When the air has been expelled completely, the air bath carrying the combustion tube is heated. Air must not be allowed to enter the combustion tube from this until the end of the experiment. The reduction of the nickel oxide takes at least a week ; the hydrogen is passed at the rate of about 300 c.cs. per minute. The reduction is accompanied by a colour change from black to a greyish-yellow, and is complete when no more steam is evolved, i.e. when a calcium chloride tube at the exit end of the combustion tube does not gain in weight after passing the exit gas through it for $\frac{1}{4}$ hour.

Hydrogenation of Benzene

Thiophen, if present, is removed by extraction with cold conc. sulphuric acid, and the benzene redistilled and recrystallised ; sulphur and chlorine compounds completely inhibit the reaction. The benzene is passed at the rate of about 7 c.cs. per minute into the combustion tube by means of a dropping funnel, B, whose stem, drawn out to a capillary, passes through one hole of the double-holed cork at A (Fig. 51). The quantity of benzene used is obtained by weighing the amount in the funnel before and after the experiment. The temperature of the air bath should be 180°–190°, and the hydrogen should be passed at about 250 c.cs. per minute. When commencing to add the benzene at A, air must not be allowed to enter the

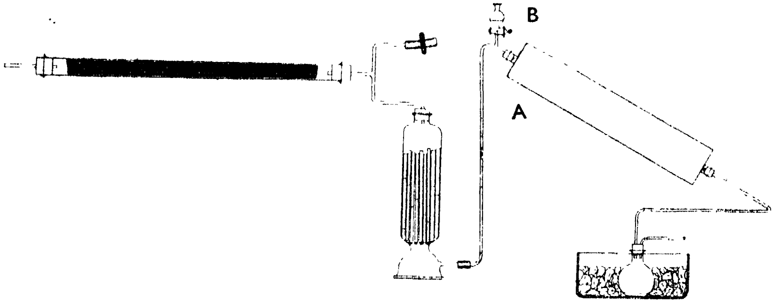


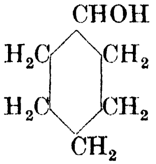
Fig. 51.

tube; the vapour issuing from the combustion tube is condensed in a flask immersed in a freezing mixture. The condensate contains some unchanged benzene. This, when 40 gms. or more have been collected, is treated with a nitrating mixture of sulphuric and nitric acids (p. 274). Cyclohexane is scarcely affected by this mixture while benzene is rapidly nitrated. It cannot otherwise easily be separated from cyclohexane; their boiling points and freezing points are almost identical. After standing for 1 hour the top layer of oil is separated, well washed with water, and dried for 24 hours over calcium chloride. It is fractionated, and the fraction 78°–85° redistilled and collected between 80°–82°.

$$C_6H_6 + 3H_2 = C_6H_{12}.$$

Yield.—80% theoretical. Calculated on the benzene volatilised (8·5 gms. cyclohexane per 10 gms. benzene). Almost theoretical allowing for unchanged benzene (11 gms. cyclohexane per 10 gms. benzene). Colourless liquid; insoluble in water; B.P. 81°. (C. r., 132, 210.)

PREPARATION 101.—**Hexahydrophenol** (*Cyclohexanol*).



$C_6H_{12}O$ 100.

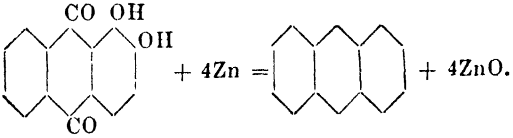
The apparatus is as in Preparation 100, except that in front of the catalyst tube is inserted a small distilling flask weighed before and after the experiment containing 100 gms. of pure redistilled phenol. Hydrogen enters by means of a one-holed cork in the neck of the flask and leaves by the side tube, which fits into a one-holed cork at A (Fig. 52). During the reduction (p. 178) of the nickel oxide the tube by which the hydrogen enters the flask is raised a little above the surface of the phenol. After reduction is complete and the temperature of the catalyst has been reduced to 180°–190°, the phenol in the flask is heated almost to its boiling point, and the hydrogen delivery tube pushed well down into the liquid. Care must be taken that phenol does not condense in the tube, and that only the vapour passes over. When sufficient liquid has condensed in the receiver, it is shaken with caustic soda solution to remove unchanged phenol, extracted with ether, and the extract dried over anhydrous potassium carbonate for 24 hours. The ether is removed on a water bath, and the residue distilled; the fraction 156°–164° is collected and refractionated between 159°–161°.

$$C_6H_5OH + 3H_2 = C_6H_{11}OH.$$

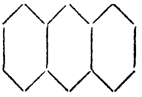
Yield.—Almost theoretical (10·5 gms. of hexahydrophenol per 10 gms. of phenol). Colourless liquid; aromatic smell, insoluble in water; B.P. 161°; yields adipic acid (nylon synthesis) on oxidation (C. V., I, 18).

Hexahydrotoluene, hexahydrocresol, etc., may be obtained by methods similar to the foregoing.

Reaction LVIII. (*a*) **Reduction of Phenols and Quinones by Distillation with Zinc Dust.** (A., 140, 205.)—When certain aromatic oxygen compounds (phenols, naphthols, quinones, etc.), are heated with zinc dust, they are reduced to the corresponding hydrocarbons. Thus, phenol yields benzene, the naphthols naphthalene ; while anthracene can be obtained from anthraquinone or its hydroxy derivatives, alizarin, or quinizarin. In this way alizarin was first proved to be an anthracene derivative. For catalytic reduction of phenols, see p. 180 and C. r., 193, 1023.

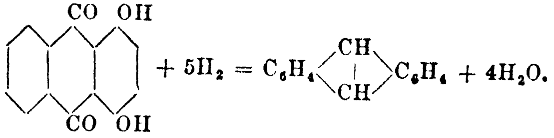


PREPARATION 102.—**Anthracene** (*s-Dibenzbenzene*).



$C_{14}H_{10}$. 178.

Pieces of porous pumic stone of a size that will conveniently pass into a combustion tube are added to a paste prepared from 100 gms. of good zinc dust and 30 c.cs. of alcohol. The mixture is stirred to incorporate the pumice and paste. The pieces are removed from the paste with tongs, and heated in a porcelain dish with stirring over a flame until the alcohol is evaporated. A hard glass combustion tube, 70 cms. long, is drawn out at one end to a narrow tube, the narrowed end is closed by a loose plug of asbestos, and a layer of zinc dust, 5 cms. long, is placed next to the plug, then a mixture of 2 gms. of quinizarin (see p. 115), alizarin, or anthraquinone with 20 gms. (excess) of zinc dust, and finally a layer of pumice zinc dust, 30 cms. long. After a canal has been formed over the zinc dust by placing the tube in a horizontal position and tapping it, the latter is transferred to a combustion furnace, tilted forwards, as in a Dumas nitrogen estimation, and a rapid current of dry hydrogen (see p. 426) is passed through the tube without heating. The open end of the tube is closed by a one-holed cork, and the issuing gas led to a draught pipe. After the gas has been passed for some time a test tube of the issuing gas is collected over water at intervals, and a light applied to the mouth of the test tube at least 12 ft. from the apparatus. When the contents of the tube burn quietly, all the air has been displaced from the apparatus. The gas current is then diminished to about 150 c.cs. per minute, and the pumice zinc dust is heated with small flames. (On no account must the apparatus be heated until all the air has been displaced.) The heating is gradually increased from the front backwards, until finally the tube is heated as strongly as possible. The rear layer of 5 cms. of zinc dust is next similarly heated, and when this glows, the mixture of anthracene derivative and zinc dust is gradually heated, all being done as in the estimation of nitrogen. The anthracene formed condenses to crystals in the forward cool part of the tube. After the reaction is complete a rapid current of hydrogen is passed while the tube is cooling ; the part containing the anthracene, when cold, is broken off and the substance removed with a small spatula ; it is purified by sublimation (see p. 35).



Yield.—Almost theoretical (1·5 gms.). Colourless crystals ; insoluble in water ; soluble in warm benzene and in glacial acetic acid ; M.P. 213° ; B.P. 351° ; M.P. of picrate, 138°. (A., 140, 205.)

It is better to use alcohol in making zinc dust paste. Much heat is evolved, and even ignition, when water is used.

The following is one of the methods employed for the separation of pure anthracene from the coal tar fraction containing it. Carbazole and phenanthrene are the chief impurities present.

Purification of Crude Anthracene

Crude anthracene (about 40%) is mixed in a vessel fitted with a mechanical stirrer, with 1½ times its weight of benzene or solvent naphtha (90% at 160°) ; this specification means that 90% by volume distils up to 160°. Sodium nitrite (one-tenth of the weight of crude anthracene taken) is dissolved in 10 times its weight of water, and sufficient 10% sulphuric acid (·75 c.c. for each c.c. of 10% nitrite) to decompose this quantity of nitrite is added to the benzene-anthracene mixture and the temperature maintained at 25°. The nitrite solution is then run in at such a speed that no red fumes escape. When all the solution has been added, the mixture is filtered at the pump. The filtrate consists of two layers, sodium sulphate solution and solvent naphtha, or benzene containing the impurities such as nitroso-carbazol. The purified anthracene on the filter is washed with benzene or solvent naphtha ; this latter on a large scale is used for the final treatment of fresh crude anthracene. The initial benzene or solvent naphtha, after separation from the aqueous solution, is recovered by distillation. The anthracene from this treatment will be about 80% pure. It may be purified to 95% by crystallising from heavy bases (pyridine, etc.), and is finally raised by sublimation and recrystallisation from benzene to 98%. (For the estimation of purity, see p. 506.) It may also be purified chromatographically in hexane solution using alumina (see p. 58).

Reaction LVIII. **(*b*) Reduction of Aromatic Ketones to the corresponding Hydrocarbons by treatment with Hydriodic Acid or with Sodium in Alcoholic Solution.** (B., 7, 1624 ; 31, 999.)—Two methods for the reduction of aromatic ketones to the corresponding hydrocarbons are exemplified below. Method I, using hydriodic acid, is a standard method for the reduction, especially the complete reduction, of an organic compound ; the sodium-alcohol method given in II is not so universally applicable—it is a milder reducing agent and more selective ; thus, it was used by

Bamberger in his researches on the formula of naphthalene, to reduce one only of the two rings in that compound and its derivatives. The nickel oxide-hydrogen method can be applied as also in the reduction of mixed aliphatic-aromatic ketones; aliphatic ketones are best reduced directly by Method I.

PREPARATION 103.—**Diphenylmethane** (*Benzylbenzene*).

$C_6H_5.CH_2C_6H_5$. $C_{13}H_{12}$. 168.

Method I.—10 gms. (1 mol.) of benzophenone, 12 gms. (nearly 2 mols.) of hydriodic acid (B.P. 127°) and 2 gms. (more than 1 atom) of red phosphorus are heated together in a sealed tube for 6 hours at 160° (see p. 47). The reaction mixture is extracted with ether and the extract washed with water several times. It is then filtered, dried over calcium chloride for 24 hours, the ether removed on a water bath and the residue distilled.

$$C_6H_5.CO.C_6H_5 + 4HI = C_6H_5.CH_2.C_6H_5 + H_2O + 2I_2.$$

Yield.—Theoretical (9 gms.). (B., 7, 1624.)

Method II.—10 gms. (1 mol.) of benzophenone are refluxed with 100 gms. (excess) of alcohol, and 10 gms. (excess) of sodium wire are gradually added through an addition tube (see p. 56) to the boiling liquid. When the solution of the sodium is complete, the liquid in the flask is cooled, saturated with carbon dioxide, poured into cold water, and the whole extracted with benzene. The extract is dried for 24 hours over calcium chloride, the benzene removed on a water bath. and the residue distilled under reduced pressure, the fraction 174°–176° at 80 mms. being retained.

Almost theoretical (8·5 gms.). Colourless oil; orange like odour, solidifies to needle-shaped crystals; M.P. 26°; B.P. ^{760} 263°; B.P. ^{80} 175°. (B., 31, 999.) For catalytic hydrogenation of ketones, see B., 66, 873.

Reaction LVIII. (*c*) Reduction of the Carbonyl to the Methylene Group by means of Zinc Amalgam and Hydrochloric Acid (Clemmensen). (B., 46, 1837; *Organic Reactions*, Adams, Vol. I, 155.)

Aliphatic aldehydes and ketones and also aliphatic-aromatic ketones can be converted into the corresponding hydrocarbons; alkyl-phenols can be obtained from phenolic-aldehydes and -ketones; *p*-hydroxybenzophenone yields *p*-benzylphenol; benzoin and benzil yield dibenzyl; anthraquinone yields anthracene dihydride.

As a general procedure, x gms. of granulated zinc are kept for an hour at ordinary temperature in contact with $2x$ c.cs. of 5% aqueous mercuric chloride. The supernatant liquid is poured off, and the ketone to be reduced together with hydrochloric acid (one vol. conc. acid + one vol. water) added without previous washing or drying of the amalgam. The mixture is heated in a flask under a reflux condenser until a brisk evolution of hydrogen is noticed; and this is maintained at a steady rate by frequent addition of acid through the condenser. Where two layers exist, it is important that they be well mixed by the escaping gas. In the more difficult reductions large quantities of metal and acid are necessary to provide this agitation.

PREPARATION 104.—**Ethylresorcinol** (1-*Ethyl*-2 : 4-*dihydroxybenzene*).

$C_2H_5C_6H_3(OH)_2$. $C_8H_{10}O_2$. 138.

50 gms. of resacetophenone (p. 98) are treated as described above with 200 gms. of zinc amalgam and 600 c.cs. of 15% hydrochloric acid. When the reaction becomes vigorous, heating is stopped until it moderates. Heating is continued for about 3 hours with frequent additions of concentrated acid. The clear yellowish liquid is drained off from the zinc, saturated with common salt, extracted with ether, and the ethereal extract evaporated. The slightly yellowish liquid which remains soon solidifies, and may be crystallised easily from chloroform, giving a pure product,

$$CH_3CO.C_6H_3(OH)_2 \longrightarrow C_2H_5C_6H_3(OH)_2.$$

Yield.—Almost theoretical (44 gms.). Colourless crystals, soluble in cold water ; M.P. 97° ; sublimes on heating.

n-Hexylresorcinol, prepared from caproylresorcinol, is an important antiseptic. (E.P., 29,970 (1923)).

Reaction LVIII. (*d*) **Reduction of Aldehydes and Ketones to Alcohols by means of Aluminium Alkoxides** (Ponndorf, Z. a., 1926, 138 ; *Organic Reactions*, Adams, Vol. II, 178.)—Aluminium isopropoxide is generally employed, reducing both aldehydes and ketones to alcohols without affecting any other reducible groups (olefine, nitro, hydroxyl, etc.) present.

$$3R.CO.R_1 + (Me_2CHO)_3Al \longrightarrow (RR_1CHO)_3Al + 3Me_2CO.$$

The reverse reaction is the basis of the Oppenauer method for converting secondary alcohols to ketones (Rec., 1937, 137 ; O. S., 21, 18).

PREPARATION 105.—**Benzhydrol.**

$(C_6H_5)_2CHOH$. $C_{13}H_{12}O$. 184.

(*a*) *Aluminium isopropoxide.*—27 gms. clean dry aluminium foil (previously washed with ether) are heated on a steam bath under a reflux (provided with a calcium chloride tube) with 300 c.cs. anhydrous isopropyl alcohol (previously distilled from calcium oxide) and 0·5 gm. mercuric chloride. When the liquid boils 2 c.cs. carbon tetrachloride are added and refluxing continued (6–12 hours) until the aluminium is completely dissolved. The resulting dark-grey solution may be used as such, or the solvent may be evaporated and the residual isopropoxide purified by distillation (B.P. ^{7} 130°–140°). (*Organic Reactions*, Adams, Vol. II, 198.)

(*b*) *Benzhydrol.*—To the dark-grey solution of isopropoxide are added 18 gms. benzophenone in 100 c.cs. dry isopropyl alcohol. The whole is carefully heated under a short column (jacket temperature, 50°–60°), so as to allow acetone and isopropyl alcohol to distil slowly in the course of 2–3 hours. When the dinitrophenylhydrazine test for acetone in the distillate is no longer positive (30–60 mins.), fresh dry isopropyl alcohol is added to restore the original volume and total refluxing continued for 5 minutes. The distillate is again collected under the same conditions as before and tested from time to time for acetone. When this is no longer present the most of the isopropyl alcohol is removed under slightly reduced pressure. The residue is cooled, hydrolysed with dilute hydrochloric acid and the resulting benzhydrol collected, washed with dilute acid, dried and crystallised from petroleum.

Yield.—95% theoretical (17-18 gms.). Properties, p. 192.

Reaction LIX. Reduction of a Primary Aryl Hydrazine to the corresponding Hydrocarbon by the action of Copper Sulphate or Ferric Chloride. (B., 18, 90, 786.)—When a primary aryl hydrazine is boiled with neutral copper sulphate or ferric chloride, or treated with alkaline copper sulphate in the cold, the hydrazine radical is replaced by hydrogen, the corresponding aryl hydrocarbon being formed.

$$C_6H_5NH.NH_2 + 2CuO = C_6H_6 + N_2 + H_2O + Cu_2O.$$

This reaction can be employed to remove a primary amino group from an aromatic compound, especially when the ordinary method of direct reduction of the diazonium compound by sodium stannite or alcohol is not applicable. Although in the application of this method the hydrazine can be prepared as the hydrochloride, and reduced in the same solution, it is better to isolate the free base and oxidise it separately, since in the oxidation of the hydrochloride there is a tendency for the hydrazine radical to be replaced by chlorine.

Reaction LX. Action of Water or Certain Hydroxy Compounds on Magnesium Alkyl or Aryl Halide (Grignard). (B., 39, 634.)—Hydrolysis occurs, and the corresponding hydrocarbon is obtained.

$$CH_3Mg.I + H_2O = CH_4 + OH.Mg.I.$$

$$CH_3MgI + C_2H_5OH = CH_4 + C_2H_5O.MgI.$$

This reaction is the basis of the Zerewitinoff determination of water and hydroxyl group, the volume of methane being measured. (See J. C. S., 1946, 404.)

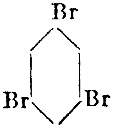
Reaction LXI. Reduction of Diazonium Compounds to the corresponding Hydrocarbons. (*Organic Reactions*, Adams, Vol. II, 262; J. C. S., 1940, 207.)—When a diazonium compound is boiled with an alcohol, oxidation of the latter to the corresponding aldehyde and simultaneous replacement of the diazonium group by hydrogen occurs.

$$RN_2Cl + C_2H_5OH = RH + N_2 + HCl + CH_3CHO.$$

This is the classical method of reducing diazonium compounds, but other reducing agents, notably sodium stannite, give better results; the alcohol tends to form with the diazonium compound the corresponding mixed ether, unless a number of negative groups be present. Hypophosphorous acid, alkaline sodium "hydrosulphite" or alkaline formaldehyde also give good yields with certain types of compounds.

The method is much used to remove the amino group from an aromatic nucleus, and has had some important theoretical applications.

PREPARATION 106.—*s*-**Tribromobenzene** (1 : 3 : 5-*Tribromobenzene*).



$C_6H_3Br_3$. 315.

50 gms. (1 mol.) of finely-powdered *s*-tribromoaniline (O. S., XIII, 96) are treated with 300 c.cs. of absolute alcohol and 75 c.cs. of benzene added to insure complete solution. 20 c.cs. (excess) of conc. sulphuric acid are run in ; should a precipitate form, it is redissolved by the addition of more benzene. 20 gms. (excess) of pure finely-powdered sodium nitrite are added to the hot liquid as rapidly as possible without the reaction becoming too violent, and the whole heated until effervescence ceases. After standing over-night, the precipitate is filtered, washed at the pump with hot water until the washings give no precipitate with barium chloride, dried on a porous plate and recrystallised from absolute alcohol.

$$C_6H_2Br_3NH_2 \xrightarrow[H_2SO_4]{NaNO_2} C_6H_2Br_3.N_2HSO_4 \xrightarrow{C_2H_5OH} C_6H_3Br_3.$$

Yield.—Almost theoretical (47 gms.). Colourless prisms ; insoluble in water ; M.P. 119°. (B., 22, 587 ; O. S., XIII, 96.)

PREPARATION 107.—**Diphenyl** (*Phenylbenzene*).

$C_6H_5.C_6H_5$. $C_{12}H_{10}$. 154.

30 gms. (1 mol.) of benzidine are added to 60 c.cs. conc. hydrochloric acid and 400 c.cs. water. The whole is heated until the benzidine is dissolved. After cooling it is diazotised with 23 gms. (2 mols.) of sodium nitrite (see p. 381). To the ice-cold tetrazonium solution are added 350 c.cs. of commercial hypophosphorous acid (D. 1·15). After standing for several days in an ice chest, until no more solid separates, the diphenyl is filtered off, treated with dilute caustic soda solution and steam distilled. It is then recrystallised from absolute alcohol.

$$NH_2C_6H_4.C_6H_4NH_2 \longrightarrow ClN_2C_6H_4.C_6H_4N_2Cl \longrightarrow C_6H_5.C_6H_5.$$

Yield.—60% theoretical (15 gms.). Colourless leaflets ; insoluble in cold alcohol ; M.P. 71° ; B.P. 254°. (B., 35, 162.)

Hypophosphorous acid may be prepared by digesting 150 gms. finely-powdered calcium hypophosphite with 45 c.cs. of conc. sulphuric acid, in 500 c.cs. water for 1 hour at 80°, and removing the calcium sulphate by filtration.

Reaction LXII. Direct Reduction of Halogen Compounds. (J. C. S., 45, 154 ; 47, 200.)—A very useful method for the preparation of hydrocarbons, more especially of aliphatic hydrocarbons, consists in replacing the halogen atom of a halogen compound by an atom of hydrogen.

$$RCl + 2H = RH + HCl.$$

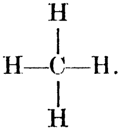
Most reducing agents which yield nascent hydrogen, e.g. zinc or iron with hydrochloric or sulphuric acid, aluminium-mercury or zinc-copper couple, can bring about the replacement of halogen by hydrogen. Catalytic methods with noble metals or nickel are almost universally suitable, even for the replacement of halogen attached to an aromatic ring, the reaction being carried out with advantage in presence of alkali to react with the hydrogen halide formed (B., 1916, 1063). As a general rule, iodine can be replaced more readily than bromine, and bromine more readily than chlorine.

For the preparation of zinc-copper and aluminium-mercury couples, see see C. V., II, 233.

Methane can be prepared from methyl iodide or chloroform etc., ethane from ethyl iodide, propane from propyl and isopropyl iodides, and so on.

The following will illustrate their use :

Preparation 108.—Methane.



$$\begin{array}{c} H \\ | \\ H—C—H \\ | \\ H \end{array}$$

CH_4. 16.

To one limb of a wide U-tube cooled in water and filled with the zinc-copper, or the aluminium-mercury couple, is attached a small tap funnel, and to the other a small reflux condenser. The zinc-copper couple is prepared by placing 30 gms. (excess) of zinc in an aqueous solution of copper sulphate until the surface of the metal is covered with a film of metallic copper. The couple is washed with water and then with absolute alcohol. The aluminium-mercury couple, which gives a better yield of gas, is prepared by immersing 20 gms. (1 atom) of small pieces of sheet aluminium in mercuric chloride solution until a film of mercury covers the surface of the aluminium, which is washed as above. 100 c.cs. (excess) of methyl alcohol (acidified with 2 drops of dilute sulphuric acid if the zinc-copper couple be used) are poured on to the couple in the U-tube and 50 gms. of methyl iodide are added gradually from the funnel so that the reaction does not become too violent nor the couple too hot. With the aluminium-mercury couple the reaction is especially vigorous, and good cooling is required. The gas is washed in worms containing (1) distilled water ; (2) sodium methoxide dissolved in methyl alcohol—2 worms ; (3) distilled water ; (4) fuming sulphuric acid—2 worms ; (5) conc. sulphuric acid—2 worms ; (6) distilled water ; (7) 50% caustic soda solution—2 worms. Conc. sulphuric acid is used to condense the acid mist from the fuming sulphuric acid washings ; distilled water is always inserted between worms containing liquids, which will react violently if mixed. The gas is then passed through a U-tube heated in boiling water and containing palladium black to absorb hydrogen, of which usually about 1% is present. Alternatively, palladium oxide may be used in the tube to oxidise the hydrogen. The gas is collected in a gas-holder over 50% aqueous glycerol, which does not dissolve methane, under a slight excess pressure, as described in Preparation 99. If the dry gas be required, it is collected over mercury or conc. sulphuric acid, being first dried by passage through two U-tubes containing phosphorus pentoxide. To free it completely from hydrogen three or four treatments with palladium or its oxide will be necessary. The gas obtained in this way is pure provided care be taken that all air has been swept out of the apparatus before collection is begun. With proper precautions, the ratio, contraction on explosion to absorption by baryta water after explosion, should be between 1·99 and 2·01 (theoretical 2·00).

$$CH_3I + Zn + CH_3OH = ZnI(OCH_3) + CH_4.$$

$$3CH_3I + 2Al + 3CH_3OH = 3CH_4 + Al_2I_3(OCH_3)_3.$$

Colourless odourless gas; very slightly soluble in water; B.P. ^{760} $-164°$; M.P. $-184°$; explosive limits: in oxygen, 5–60%, in air, 6–13%. (J. C. S., 81, 541.)

Purification by Fractional Liquefaction or Evaporation

If liquid air is available, the hydrogen in the methane prepared above is best removed by fractional distillation. The following is an outline of the method (see Fig. 52):

The gas from the holder A is passed through a series of U-tubes containing phosphorus pentoxide, then through a small bulb B. When all the air has been driven out of the apparatus, a vacuum vessel containing liquid air is brought below B and gradually raised so as slowly to increase the cooled surface of the bulb. The methane condenses rapidly in B, hydrogen passing away through C. When A is almost empty of gas, the remainder is discharged by means of the three-way tap D. Meanwhile the liquid air container is raised or lowered around B, so that the liquid in B gently boils. When about one-fifth has boiled away C is closed, and a small amount of gas allowed to pass away through D. Connection is then made to the gas-holder, which is slowly filled under a pressure slightly above atmospheric. If preferred, the methane may be distilled into another holder through C, and the gas from several holders, such as A, purified and collected in one holder. Great care must be taken in manipu-

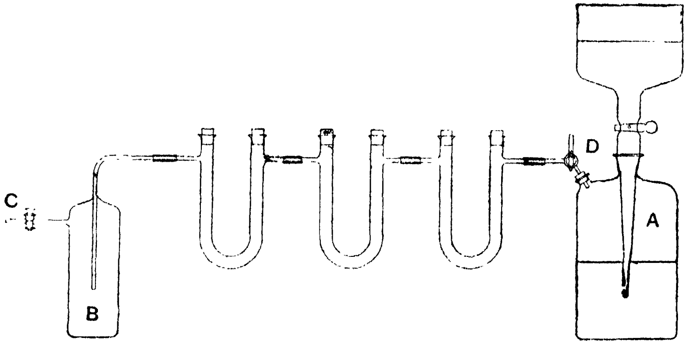


FIG. 52.

lating the liquid air container, so that the liquid in B boils gently ; if the vacuum vessel be lowered too rapidly, vigorous boiling will occur and pressure be generated in the apparatus. The last traces of gas in B are not collected.

This process can be repeated if a very pure gas is required. In each operation about one-third of the original gas is lost. The purity of the gas may be ascertained by inserting a platinum resistance thermometer in the liquefaction bulb, and determining the temperature during the operation, as in the fractional distillation of any other liquid. This is more important in preparing the higher hydrocarbons in pure condition.

The methods of fractional liquefaction and distillation have many similar and important applications in the separation and estimation of gases. See *Analyst*, 1947, 513.

A mixture of solid carbon dioxide and acetone or alcohol is a convenient cooling medium for liquefaction down to about −40° C.

A convenient apparatus for delivering a gas at constant pressure is described in J. S. C. I., 47, 187.

CHAPTER X

HYDROGEN TO CARBON

HYDROXY COMPOUNDS

Alcohols and Phenols

THE reactions discussed below are based on the reduction of the group

$$C{=}O \quad \text{to} \quad CH(OH).$$

Such reactions comprise practically all those in which hydrogen is linked to carbon to produce hydroxy compounds, many of which are of industrial importance, e.g. the manufacture of methanol and higher alcohols from carbon monoxide and hydrogen in presence of catalysts, such as zinc-chromium oxides.

Reaction LXIII. Combined Oxidation and Reduction (**dismutation, disproportionation**) **of Aromatic Aldehydes under the influence of Caustic Alkalis** (Cannizzaro). (*Organic Reactions*, Adams, Vol. II, 94 ; Am. Soc., 1935, 1510.)—The lower aliphatic aldehydes, except formaldehyde, are resinified by alkalis ; aromatic aldehydes and aliphatic aldehydes lacking hydrogen in direct union with the α-carbon atom behave differently, two molecules yielding by simultaneous oxidation and reduction one molecule each of the corresponding acid and alcohol.

$$2R.CHO + NaOH \longrightarrow RCH_2OH + RCOONa.$$

The mechanism of reaction is discussed in the above references.

PREPARATION 109.—**Benzyl Alcohol** (*Phenyl-methanol*).

$$C_6H_5CH_2OH. \quad C_7H_8O. \quad 108.$$

and **Benzoic Acid** (*Phenylmethan acid*).

$$C_6H_5COOH. \quad C_7H_6O_2. \quad 122.$$

30 gms. (2 mols.) of freshly-distilled benzaldehyde are mechanically shaken in the cold with 45 gms. (excess) of a 60% solution of caustic potash until a permanent emulsion is formed. The mixture is allowed to stand for 24 hours, during which time much potassium benzoate separates. Owing to the presence of conc. alkali, a glass stopper must not be used to close the vessel. Water is added until a clear solution is obtained, which is then extracted four times with ether. The extract which contains the benzyl alcohol formed is shaken with conc. sodium bisulphite solution (see p. 517) to remove traces of benzaldehyde, washed with dilute caustic soda and with water and filtered. The ether is removed on a water bath, and the residue fractionated, the fraction 204°–208° being redistilled to give pure benzyl alcohol.

The alkaline solution from which benzyl alcohol has been extracted is carefully neutralised, and acidified, first with concentrated, and then dilute hydrochloric acid. The precipitated benzoic acid is recrystallised from hot water.

$$2C_6H_5CHO + KOH = C_6H_5CH_2OH + C_6H_5COOK.$$

Yield.—90% theoretical of both compounds (benzyl alcohol, 13·5 gms. ; benzoic acid, 15·5 gms.).

Benzyl Alcohol.—Colourless oil somewhat soluble in water ; faintly aromatic odour ; B.P. 206·5° ; D. $^{15\cdot4}_{4}$ 1·05.

Benzoic Acid.—Colourless needles ; soluble in hot water, alcohol, ether ; melts and sublimes on heating ; can be distilled in steam ; M.P. 122° ; B.P. 250°. (B., 14, 2394.)

Reaction LXIV. (*a*) **Reduction of Aldehydes and Ketones to the corresponding Alcohols by the use of Alkaline Reducing Agents.** (B., 31, 1003 ; J. pr., [2], 33, 184 ; [2], 76, 137.)—The alkaline reducing agent most usually employed is sodium amalgam and water, especially to obtain polyhydric alcohols from the corresponding sugars ; it is easily applied owing to the solubility of the sugars in water. But even if the ketone or aldehyde be not soluble in water, the amalgam can be allowed directly to act on the moist substance, or the latter can be dissolved in ether or benzene, and the amalgam and water gradually added. Aluminium amalgam or ethylate can be employed (O. S., XV, 84). Sodium and alcohol (see also Reaction CLXXIV) are generally used in the aromatic series. In reducing ketones, especially aliphatic ketones, there is always more or less pinacone formation ; this is not so marked in the aromatic series, especially if acid reducing agents are not used (p. 61). Zinc dust and caustic soda or ammonia, and alcoholic sodium "hydrosulphite" give good results. The Sabatier-Senderens reaction can also be employed (see p. 178).

PREPARATION 110.—**Dulcitol** (*Hexahydroxyhexane* + − − +).

$$CH_2OH.(CHOH)_4CH_2OH. \qquad C_6H_{14}O_6. \qquad 182.$$

10 gms. (1 mol.) of galactose dissolved in 100 gms. of water are shaken in a stout 500-c.c. stoppered bottle with 300 gms. of 2½% sodium amalgam (see p. 515) until the first reaction has ceased. Every 10 minutes the liquid is neutralised with 10% sulphuric acid. Further amalgam is added in 20-gm. lots with shaking and neutralisation as before, until 1 c.c. of the solution reduces no more than 0·2 c.c. of Fehling's solution.

The temperature throughout must not exceed 20° ; the operation takes about 3 hours, and 400 gms. (excess) of 2½% amalgam are required. When reduction is complete, the solution is separated from the mercury, exactly neutralised with 10% sulphuric acid, heated on a water bath to 60°, and poured with stirring into 1 litre of alcohol, and the precipitated sodium sulphate filtered off at the pump. The filtrate is concentrated on a water bath to about 25 c.cs., and until crystals begin to separate, the alcohol being recovered. The residual liquid is cooled to 0° and filtered.

The precipitated sodium sulphate is extracted with 80% alcohol to recover any dulcitol it may contain.

$$CH_2OH.(CHOH)_4.CHO \xrightarrow{H_2} CH_2OH.(CHOH)_4CH_2OH.$$

Yield.—50% theoretical (5 gms.). Colourless crystals; sweet taste; very soluble in water; M.P. 188°. (B., 20, 1091; 25, 2546.)

PREPARATION 111.—**Phenylmethylcarbinol** (*1-Phenyl-1-ethanol*).

$CH(CH_3)(C_6H_5)(OH)$. $C_8H_{10}O$. 122.

15 gms. (1 mol.) of acetophenone are dissolved in 150 gms. of warm absolute alcohol. 15 gms. (excess) of sodium wire are rapidly added, and when reaction has ceased, carbon dioxide is passed in until it is no longer absorbed. 350 c.cs. water are added and the mixture distilled from a flask immersed in a boiling water bath until all the ethyl alcohol has been removed. The cooled residual solution is extracted with ether and the extract dried over anhydrous potassium carbonate. After removal of ether on a water bath, the fraction boiling at 97–103° and 15 mm. is retained. (Cf. Preparation 19.)

$$C_6H_5CO.CH_3 \xrightarrow{H_2} C_6H_5.CHOH.CH_3.$$

Yield.—45% theoretical (6·5 gms.). Colourless liquid; slightly soluble in water; B.P. ^{760} 198°; B.P. ^{40} 118°; B.P. ^{20} 111°; B.P ^{15} 100°. (B., 31, 1003.)

PREPARATION 112.—**Benzhydrol** (*Diphenyl-methanol*).

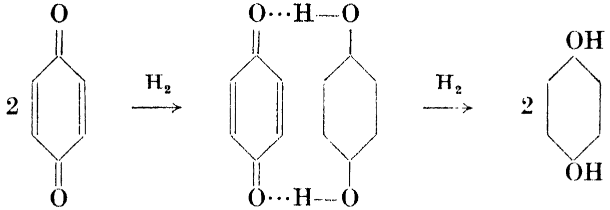
$HC(C_6H_5)_2(OH)$. $C_{13}H_{12}O$. 184.

10 gms. (1 mol.) of benzophenone are dissolved in 200 c.cs. of alcohol, and 40 gms. of 50% aqueous caustic potash added, and the mixture boiled until it turns dark brown. The mixture is treated gradually with 100 gms. of zinc dust until the brown colour disappears. The hot solution is filtered, and the filtrate poured into ice-water acidified with hydrochloric acid. Benzhydrol separates and may be crystallised from alcohol.

$$(C_6H_5)_2CO \xrightarrow{H_2} (C_6H_5)_2CHOH.$$

Yield.—90% theoretical (9 gms.). Colourless needles; slightly soluble in water; M.P. 68°. (J. pr., [2], 33, 184; O. S., VIII, 24.)

Reaction LXIV. (*b*) Reduction of Quinones. (A., 27, 268; 45, 354; 215, 127; B., 19, 1467; 20, 1854, 2283; 21, 1172; 40, 390, 924; J. pr., [2], 76, 141; Meyer and Jacobson, Lehrbuch (ii) 421.)—All benzoquinones are very readily reduced to the corresponding quinols, sulphurous acid being the reagent most usually employed. In the reduction the greenish-coloured quinhydrone (see p. 227) is intermediately formed.



Benzoquinone. Quinhydrone Quinol.

The anthraquinones may be reduced to the corresponding "anthraquinols" (hydroxyanthranols) with alkaline sodium "hydrosulphite"; this reaction has a wide application in the dye industry. These compounds are difficult to isolate pure, for they rapidly oxidise in air. The anthranols —γ-monohydroxyanthracenes—however, are stable, and may be obtained by reducing anthraquinone with acid-reducing agents—tin and hydrochloric acid, zinc and glacial acetic acid, copper or aluminium, and sulphuric acid, etc. For the reduction of anthraquinone to anthracene, see Reaction LVIII (*a*), and to anthrone, see C.V.,I, 60.

PREPARATION 113.—**Quinol** (1 : 4-*Dihydroxybenzene*).

$C_6H_4(OH)_2[1:4]$. $C_6H_6O_2$. 110.

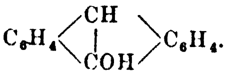
10 gms. of finely-powdered quinone are suspended in cold water, and the liquid saturated with sulphur dioxide until, after the intermediate formation of quinhydrone, complete solution and decolorisation have occurred, the operation being carried out in a fume cupboard. The liquid is repeatedly extracted with ether until extraction is complete, the ether expelled on a water bath, and the residue recrystallised from dilute sulphurous acid with the addition of decolorising carbon.

If preferred, the crude suspension of quinone obtained from 25 gms. of aniline (see p. 239) may be employed, being saturated with sulphur dioxide until it smells very strongly of the gas. After standing for 2 hours, if it still smells of the gas the liquid is extracted with ether, as above. If the odour of the gas has vanished, the liquid must be resaturated, and so on, until the smell persists for 2 hours.

$$C_6H_4O_2 \xrightarrow{H_2} C_6H_4(OH)_2.$$

Yield.—80% theoretical (8 gms.). Colourless prisms; soluble in ether, alcohol and warm water; sublimes at a gentle heat; M.P. 169°. (A., 27, 268; 45, 354; 215, 127; B., 19, 1467; 20, 2283.)

PREPARATION 114.—**Anthranol** (*γ-Hydroxyanthracene*).



$$C_6H_4\left\langle\begin{matrix}CH\\|\\COH\end{matrix}\right\rangle C_6H_4.$$

$C_{14}H_{10}O$. 194.

10 gms. (1 mol.) of anthraquinone and 30 gms. (excess) of granulated zinc are refluxed with 500 c.cs. of glacial acetic acid, the operation being

performed in a good fume cupboard. Conc. hydrochloric acid, a few c.cs. at a time, is added until no coloration occurs, and hydrogen is continuously evolved. After ½ hour and when a sample no longer deposits crystals on cooling, the whole is cooled, poured into dilute hydrochloric acid, and the precipitate recrystallised from glacial acetic acid, to which a little zinc dust and hydrochloric acid have been added to prevent reoxidation.

Yield.—80% theoretical (14·5 gms.). Colourless needles ; insoluble in water ; M.P. (decomposition) 170°. (B., 20, 1854 ; D.R.P., 201542.)

Reaction LXIV. (*c*) **Catalytic Hydrogenation of Acids and Esters to the Corresponding Alcohols.** (C. V., II, 325 ; Am. Soc., 53, 1095 ; B., 64, 2051.)—Various catalysts are used, e.g. copper chromite (C. V., II, 142), nickel, at temperatures of 250°-300°, and usually high pressures (200 atm.). Temperatures of 350° and over result in hydrocarbon formation.

$$CH_3(CH_2)_7CH : CH(CH_2)_7COOC_2H_5 \longrightarrow CH_3(CH_2)_{16}CH_2OH.$$

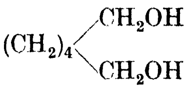
Ethyl oleate. Octadecyl alcohol.

Under certain conditions hydrogenation may be confined to the —COOH group, e.g. oleic acid → oleyl alcohol.

Salts of the hydrogen sulphate esters of these higher alcohols are used extensively in the textile industries as detergents.

The reaction is widely applied to the production of higher alcohols from oils and fats.

Preparation 114a.—**Hexamethylene Glycol** (1 : 6)



$$(CH_2)_4 \begin{cases} CH_2OH \\ CH_2OH \end{cases} \qquad C_6H_{14}O_2. \qquad 118.$$

Into a steel autoclave fitted with agitation are placed 50 gms. ethyl adipate (see Prep. 413) and 4 gms. copper chromite catalyst (see p. 521). The vessel is closed (p. 50) and hydrogen from a cylinder passed in until the pressure is 2000 lbs. per sq. in. Agitation is commenced and the temperature quickly raised to 255°. Pressure is graphed against temperature. When the pressure drops to a constant value the reaction is complete. Further hydrogen may have to be admitted during the reaction, to maintain a minimum pressure of 1500 lbs. per sq. in. Agitation is stopped, the pressure released, and the reaction mixture transferred with the aid of alcohol to a beaker. The catalyst is filtered off, and washed with alcohol. To the product are added 10 c.cs. 40% caustic soda solution and the whole boiled under reflux for 2 hours. The alcohol is then removed by distillation and the residue extracted with ether. The ether solution is distilled to remove alcohol and water, then under reduced pressure, the fraction B.P. 40°–43° at 4 mm. being collected.

$$(CH_2)_4(COOC_2H_5)_2 + 4H_2 \longrightarrow (CH_2)_4(CH_2OH)_2.$$

Yield.—85% theoretical (25 gms.). White crystals. M.P. 42° ; B.P. 144°. (C. V., II, 325.)

CHAPTER XI

HYDROGEN TO CARBON

OXY AND HYDROXY-OXY COMPOUNDS

Aldehydes, Ketones and Acids

THE reductions in this section are mostly those of acids to aldehydes; they are naturally few, since oxygenated compounds are not usually obtained by reduction of more highly oxygenated substances; the reverse process is much more often employed.

Reaction LXV. (*a*) Reduction of Phenolic Acids to the corresponding Aldehydes by the action of Sodium Amalgam and Boric Acid in the presence of Primary Aromatic Amines. (B., 41, 4147.)—This is one of the few methods of reducing an acid to the corresponding aldehyde in satisfactory yield. The presence of the primary aromatic base is essential to protect the aldehyde; it condenses with it as formed, and inhibits further reduction to the alcohol. A weak acid such as boric acid is used partly because salt formation by the base would hinder condensation and partly to avoid hydrolysis of the condensation product.

$$OH.C_6H_4.COOH \xrightarrow{H_2(R_1NH_2)} OH.C_6H_4.CH : NR_1 \xrightarrow{H_2O} OH.C_6H_4.CHO.$$

This method of preparing phenolic aldehydes has the advantage over Reimer's (pp. 111, 129) of not giving a mixture of isomers. The yields also are improved.

PREPARATION 115.—**Salicylaldehyde** (*o-Hydroxybenzaldehyde*).

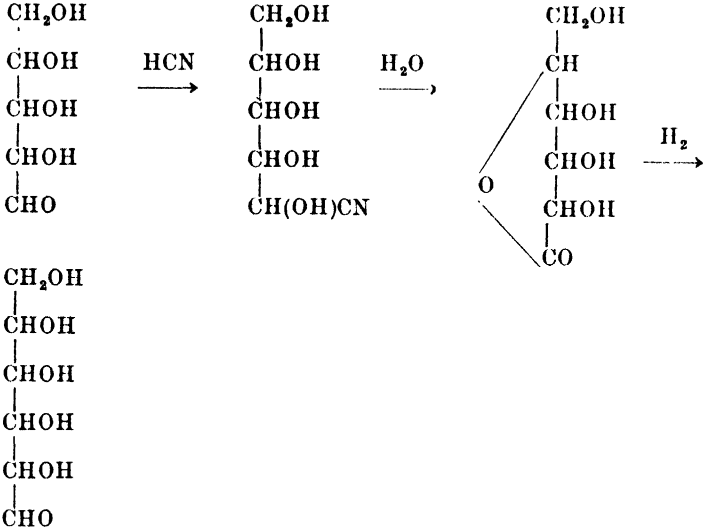
$C_6H_4(OH)(CHO)[1 : 2]$. $C_7H_6O_2$. 122.

20 gms. (1 mol.) of salicylic acid dissolved in hot water are neutralised with N/1 caustic soda, using phenolphthalein as indicator, and the solution diluted to 1 litre and boiled. 30 gms. (excess) of *p*-toluidine are added, and the whole cooled and mechanically stirred. 400 gms. of sodium chloride and 30 gms. (excess) of boric acid are added gradually, and still with stirring 400 gms. (excess) of 2½% sodium amalgam (see p. 515), the solution being maintained faintly acid by the addition of boric acid (about 200 gms.) from time to time. The reaction is complete when a sample, after filtration and acidification with hydrochloric acid, gives no precipitate of salicylic acid. The condensation product of the aldehyde and base is filtered at the pump, suspended in 10% sulphuric acid, and distilled in steam. The aldehyde distils and is extracted from the distillate with ether. The extract is dried over calcium chloride, the ether removed on a water bath, and the residue fractionated between 195° and 197°. The aldehyde may also be purified by means of its bisulphite compound (see Preparation 156).

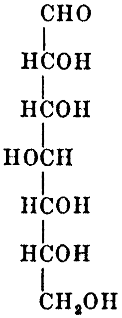
$$C_6H_4(OH)(COOH) + H_2 + (CH_3)(C_6H_4)NH_2$$
$$\longrightarrow C_6H_4(OH)CH : NC_6H_4CH_3 + 2H_2O$$
$$\longrightarrow C_6H_4(OH)CHO + H_2N.C_6H_4.CH_3.$$

Yield.—60% theoretical (8 gms.). Colourless crystals or liquid ; pungent odour ; soluble in water ; miscible in all proportions with alcohol and ether ; volatile in steam ; M.P. 20° ; B.P. 196·5° ; D. $^{13\cdot5}_{4}$ 1·173. (B., 41, 4147.)

Reaction LXV. (*b*) **Reduction of Lactones to the corresponding Hydroxy-aldehydes by the action of Sodium Amalgam in faintly Acid Solution.** (A., 270, 72, 87 ; 272, 200.)—This is a reaction very similar to the previous one. It finds an extensive application in the sugar group for reducing the lactones of the poly-hydroxy acids to the corresponding aldoses. Combined with the cyanohydrin reaction (see p. 161) it forms a means of passing from one group of sugars to the next higher group—thus :



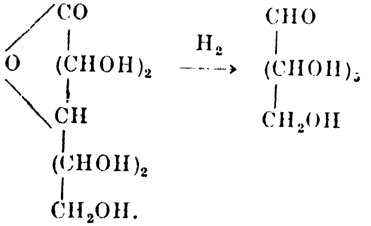
PREPARATION 116.—α-**Glucoheptose** (*Hexahydroxy-heptanal* + + — + +).



$$\begin{array}{c}CHO\\ |\\ HCOH\\ |\\ HCOH\\ |\\ HOCH\\ |\\ HCOH\\ |\\ HCOH\\ |\\ CH_2OH\end{array}$$

$C_7H_{14}O_7$. **210.**

15 gms. (1 mol.) of the lactone of α-glucoheptonic acid (see p. 135) are dissolved in 150 c.cs. of water in a thick-walled 500-c.c. vessel, and are cooled in a freezing mixture to 0°. 3 c.cs. of 10% sulphuric acid are added, and the whole mechanically agitated, being meanwhile kept immersed in the freezing mixture. 125 gms. (excess) of $2\frac{1}{2}$% sodium amalgam (see p. 515) are added, and at intervals further 2-c.c. lots of 10% sulphuric acid, so that the liquid always remains acid. The temperature must not be allowed to rise above 5°. In about 10 minutes the amalgam is used up, a further 125 gms. are added, and the procedure of treating with acid repeated. The whole operation takes about 40 minutes. The solution is separated from the mercury and any unchanged lactone, and converted to the sodium salt by adding sodium hydroxide until the liquid remains alkaline after standing for 30 minutes. The solution is then exactly neutralised, at first with 5% and ultimately with N/1 sulphuric acid, brought to the boil with decolorising carbon and filtered; 8 volumes of hot alcohol are added with constant stirring, the whole left at room temperature for 12 hours, and sodium sulphate and most of the organic sodium salts present which are precipitated are filtered off at the pump. The filtrate is slowly concentrated until crystallisation begins, is cooled and after some hours filtered at the pump. The precipitate is washed first with 55% then with 85%, and finally with absolute alcohol.



Yield.—35% theoretical (5 gms.). Colourless crystals; soluble in water; M.P. 190° (M.P. osazone 195°). (A., 270, 72, 87; 272, 200.)

Reaction LXVI. (*a*) Reduction of Olefinic Compounds by Hydrogen in presence of a Catalyst. (B., 60, 1221; Am. Soc., 54, 1138.)—The reaction is of considerable importance in determining the number of double bonds in a compound, as well as in preparative work, e.g. reduction of olefinic, acetylenic, and aromatic systems. The catalysts most commonly employed are nickel, platinum, palladium, copper chromite. Other methods of reduction applicable to similar systems involve sodium amalgam in alkaline media (A., 137, 237), or electrolysis (C. V., I, 311; Chem. Rev., 31, 77).

Preparation 117.—**Hydrocinnamic Acid** (*β-phenylpropionic acid*).

$C_6H_5CH_2CH_2COOH$. $C_9H_{10}O_2$. 150.

5 gms. (1 mol.) cinnamic acid dissolved in a hot solution of 2·5 gms. sodium carbonate (A.R.) in 50 c.cs. distilled water are placed after cooling to room temperature in the flask of a hydrogenation apparatus (see p. 54). 200 gms. platinum oxide catalyst (see C. V., I, 463) are added, the apparatus evacuated, filled with hydrogen, re-evacuated, and re-filled with hydrogen. Agitation is commenced and the uptake of hydrogen noted

from time to time. When absorption is complete the flask is disconnected, the catalyst removed by filtration, and the filtrate and washings concentrated to 25 c.cs. The hydrocinnamic acid is precipitated by the addition of conc. hydrochloric acid, filtered, dried in air, and crystallised from light petroleum.

$$C_6H_5CH : CHCOOH + H_2 \longrightarrow C_6H_5CH_2CH_2COOH.$$

Yield.—80% theoretical (4 gms.). Colourless prisms ; insoluble in cold, somewhat soluble in warm water ; soluble in alcohol ; volatile in steam. M.P. 47° ; B.P. 280°. (A., 121, 375 ; 137, 237.)

Reaction LXVI. (*b*) **Reduction of Hydroxy-Acids by the action of Hydriodic Acid.** (A., 114, 106.)—Hydriodic acid is especially useful in reducing groups or ethylene linkages in acids as, although a powerful reducing agent, it does not readily attack the carboxyl group. It may be used either in a solvent, e.g. glacial acetic acid, or more usually at a high temperature in a sealed tube. Red phosphorus is usually added to convert the liberated iodine into hydriodic acid ; thus a small amount of hydriodic acid can reduce a large quantity of substance.

PREPARATION 118.—**Succinic Acid** (*Butan di-acid*).

$COOH.CH_2.CH_2.COOH$. $C_4H_6O_4$. 118.

10 gms. (1 mol.) of malic acid are dissolved in 40 gms. (excess) of 57% (constant boiling mixture) hydriodic acid (see p. 514) and the solution, together with 3 gms. of red phosphorus, heated in a sealed tube (see p. 47) in a tube furnace at 130° for 6 hours. When cool, the tube is opened (*caution !* see p. 49), the contents evaporated to dryness on a water bath, and the cold residue extracted with small quantities of chloroform until no more free iodine is removed. The succinic acid is then heated at 70° to remove all traces of chloroform, and recrystallised from hot water.

$$COOH.CHOHCH_2.COOH + 2HI = COOH.CH_2.CH_2.COOH + H_2O + I_2.$$

Yield.—60% theoretical (5 gms.). Colourless prisms ; soluble in water, alcohol and ether ; insoluble in chloroform ; M.P. 182°. (A., 114, 106.)

PREPARATION 119.—**Diphenylacetic Acid** (*Diphenylethan acid*).

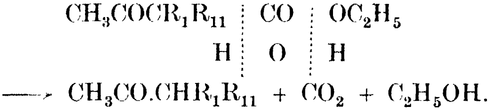
$(C_6H_5)_2CH.COOH$. $C_{14}H_{12}O_2$. 212.

20 gms. (1 mol.) of benzilic acid (see p. 118), 10 gms. of 57% hydriodic acid (constant boiling acid), 10 gms. of red phosphorus (excess of P + HI) and 120 gms. of glacial acetic acid are refluxed in a round-bottomed flask, in a fume chamber for 2 hours. The solution is filtered at the pump, poured while still hot into an excess of water, the precipitate filtered off at the pump, washed with water and recrystallised from alcohol.

$$(C_6H_5)_2C(OH)COOH + 2HI = (C_6H_5)_2CHCOOH + H_2O + I_2.$$

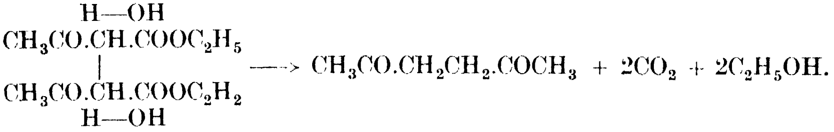
Yield.—80% theoretical (14 gms.). Colourless crystals ; insoluble in cold alcohol ; M.P. 146°. (A., 275, 84 ; O. S., III, 45.)

Reaction LXVII. (*a*) **Ketonic Hydrolysis of Alkyl Derivatives of Ethyl Acetoacetate.** (A., 138, 211.)—This reaction illustrates one of many synthetical uses of ethyl acetoacetate. When this ester or its mono- or di-alkyl derivatives is boiled with *dilute* aqueous or alcoholic alkalis or baryta water, or sulphuric acid, " ketonic hydrolysis " occurs, and acetone or its mono- or di-substituted derivatives is formed :



$$\begin{array}{r:c:l} CH_3COCR_1R_{11} & CO & OC_2H_5 \\ H & O & H \end{array}$$
$$\longrightarrow CH_3CO.CHR_1R_{11} + CO_2 + C_2H_5OH.$$

Compounds such as ethyl acetosuccinate and its derivatives which contain the acetoacetate grouping also undergo this hydrolysis.



$$\begin{array}{l} \quad H\text{—}OH \\ CH_3CO.CH.COOC_2H_5 \\ \qquad | \\ CH_3CO.CH.COOC_2H_2 \\ \quad H\text{—}OH \end{array} \longrightarrow CH_3CO.CH_2CH_2.COCH_3 + 2CO_2 + 2C_2H_5OH.$$

PREPARATION 120.—**Methyl Ethyl Ketone** (*Butanon*).

$CH_3.CO.C_2H_5$. C_4H_8O. 72.

20 gms. (1 mol.) of methylacetoacetic ester are refluxed with 250 c.cs. of saturated baryta water until the oily layer disappears. The solution is then distilled on a water bath to 90°. The distillate is mechanically shaken for 3 hours with a freshly-prepared saturated solution of sodium bisulphite, and the crystals collected and distilled with an excess of dilute sulphuric acid or sodium carbonate solution at 90°. The distillate is dried over calcium chloride and redistilled, the fraction 79°–82° being retained.

$$CH_3COCH(CH_3)COOC_2H_5 + H_2O = CH_3.COCH_2CH_3 + CO_2 + C_2H_5OH.$$

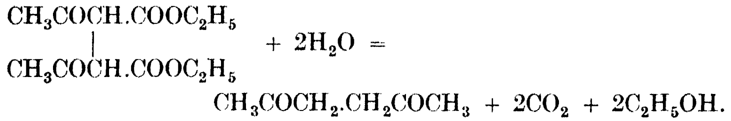
Yield.—70% theoretical (7 gms.). Colourless mobile liquid ; pleasant odour ; miscible with water ; B.P. 81°. (A., 138, 211.)

In an exactly similar way acetone (B.P. 56°) can be prepared from acetoacetic ester (see p. 153) ; methyl propyl ketone (B.P. 102°) from monoethyl acetoacetic ester (see p. 146). The higher ketones may be purified by washing with saturated brine until alcohol is removed ; they are then, after drying over calcium chloride, fractionated. In all these hydrolyses dilute aqueous or alcoholic potash, or dilute sulphuric acid, may be used in place of baryta water. See also C. V., I, 351.

PREPARATION 121.—**Acetonylacetone** (2 : 5-*Hexandion*).

$CH_3COCH_2.CH_2.COCH_3$. $C_6H_{10}O_2$. 114.

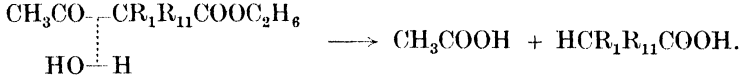
20 gms. (1 mol.) of di-aceto-succinic ester (see p. 155) are mechanically shaken for several days with 250 c.cs. (excess) of 5% aqueous caustic soda, and until no di-aceto-succinic ester separates on acidification of a sample with dilute hydrochloric acid. The solution is then saturated with potassium carbonate and extracted with ether, the extract is washed with brine to remove alcohol, dried over calcium chloride, and distilled, the fraction 192°–198° being retained.



$$\begin{array}{l} CH_3COCH.COOC_2H_5 \\ \quad\quad | \\ CH_3COCH.COOC_2H_5 \end{array} + 2H_2O = CH_3COCH_2.CH_2COCH_3 + 2CO_2 + 2C_2H_5OH.$$

Yield.—70% theoretical (6 gms.). Colourless liquid ; agreeable odour ; miscible with water, alcohol and ether ; M.P. $-9°$; B.P. 194° ; D. $^{20}_{4}$ 0·973. (B., 18, 58 ; 33, 1217.)

Reaction LXVII. (*b*) **Acid Hydrolysis of Alkyl Derivatives of Ethyl Acetoacetate.** (B., 19, 227.)—When acetoacetic ester or its mono- or di-alkyl derivatives are refluxed with *concentrated* aqueous or alcoholic potash, acid hydrolysis occurs and 2 mols. of acetic acid, or 1 mol. of that acid, and 1 mol. of a mono- or di-substituted derivative are obtained.



$$\begin{array}{l} CH_3CO\text{-}\!\vdots\!\text{-}CR_1R_{11}COOC_2H_6 \\ \quad\quad HO\text{-}\!\vdots\!\text{-}H \end{array} \longrightarrow CH_3COOH + HCR_1R_{11}COOH.$$

It is not possible to perform the acid hydrolysis without some ketonic hydrolysis occurring. This reaction and the preceding one are important in many syntheses of aliphatic ketones and acids. They might have been included equally well in the decomposition section (p. 419) ; in fact, they are often referred to as the " ketonic " and " acid " decomposition of acetoacetic ester. The malonic ester synthesis of fatty acids may be compared with the present reaction (p. 142).

Preparation 122.—**Methylethylacetic Acid** (2-*Methylbutan acid*).

$HC(CH_3)(C_2H_5)COOH$. $C_5H_{10}O_2$: 102.

20 gms. (1 mol.) of methyl ethyl acetoacetic ester are refluxed for 4 hours with 40 gms. (excess) of caustic potash dissolved in 15 gms. of 50% alcohol. The mixture is poured into 250 c.cs. of water and acidified after extraction with ether to remove unchanged ester and methyl-*iso*-butyl ketone, a by-product forms as in the previous reaction. The acid which separates as an oil is extracted with ether, the extract dried over calcium chloride, and distilled, the fraction 172°–178° being retained.

$$CH_3.CO.C(CH_3)(C_2H_5)COOC_2H_5 + 2H_2O$$
$$= CH_3.COOH + CH(CH_3)(C_2H_5)COOH + C_2H_5OH.$$

Yield.—60% theoretical (11 gms.). Colourless liquid ; B.P. 175°. (For preparation by Grignard reaction, see C. V., I, 36.)

In a similar manner the esters shown in the following table yield the corresponding acids.

Ester.	Corresponding Acid.	B.P.
Acetoacetic ester	Acetic acid	119°
Methyl acetoacetic ester	Propionic acid	141°
Ethyl acetoacetic ester	Butyric acid	162°
Dimethyl acetoacetic ester	*Iso*butyric acid	154°
Diethyl acetoacetic ester	*Iso*caproic acid	190°

The higher acids need not be extracted from the acidified reaction product with ether, but may be separated directly as they are only very slightly soluble in water.

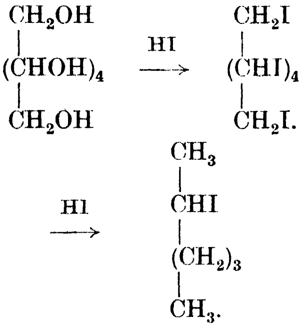
CHAPTER XII

HYDROGEN TO CARBON

HALOGEN COMPOUNDS

ONLY two reactions are of sufficient importance to be considered here.

Reaction LXVIII. Simultaneous Reduction and Halogenation of Polyhydric Alcohols. (A., 138, 364.)—When polyhydric alcohols are heated with hydriodic acid, reduction of all the hydroxyl groups save one occurs; this latter is replaced by iodine to form a secondary iodide. In this way, e.g. dulcitol, or any of the hexose alcohols, yields normal secondary hexyl iodide; this is of importance in determining the chain structure of the sugars. This reaction probably occurs:



$$\begin{matrix}CH_2OH\\|\\(CHOH)_4\\|\\CH_2OH\end{matrix}\xrightarrow{HI}\begin{matrix}CH_2I\\|\\(CHI)_4\\|\\CH_2I.\end{matrix}\xrightarrow{HI}\begin{matrix}CH_3\\|\\CHI\\|\\(CH_2)_3\\|\\CH_3.\end{matrix}$$

The primary iodide is never formed in such reactions.

PREPARATION 123.—*iso*-Propyl Iodide (*2-Iodopropan*).

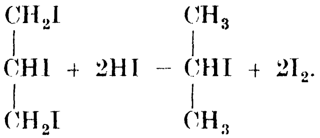
$CH_3.CHICH_3$. C_3H_7I. 170.

70 gms. (excess) of iodine, 45 gms. (excess) of glycerol, and 30 gms. (excess) of water are placed in a 250-c.c. retort connected with a condenser and receiver and placed in a fume chamber. 10 gms. (5 atoms) of yellow phosphorus (*caution !*) are added gradually in small pieces, the phosphorus being cut under water, and transferred to the retort with crucible tongs. The violent reaction which usually occurs on adding the phosphorus must be allowed to subside before any more is added. Should no reaction take place on adding the first three pieces of phosphorus, the retort is immersed in warm water until interaction commences. When the addition of the phosphorus is complete the retort is heated on a wire gauze until no further oily liquid distils. The distillate is replaced in the retort and redistilled, washed in turn with 10% caustic soda, with sodium thiosulphate, again with 10% caustic soda and with water; it is dried over calcium chloride for 24 hours and fractionated between 88°–90°.

$$2P + 3I_2 = 2PI_3.$$

$$PI_3 + 3H_2O = 3HI + P(OH)_3$$

$$C_3H_5(OH)_3 + 3HI = C_3H_5I_3 + 3H_2O.$$



$$\begin{array}{l}CH_2I\\ |\\ CHI\\ |\\ CH_2I\end{array} + 2HI = \begin{array}{l}CH_3\\ |\\ CHI\\ |\\ CH_3\end{array} + 2I_2.$$

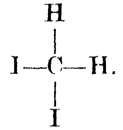
1:2:3-Triiodopropane is probably formed as an intermediate compound.

Yield.—80% theoretical (70 gms.). Colourless liquid ; insoluble in water ; B.P. 89° ; D. $^{0}_{4}$ 1·744. (A., 138, 364.)

Reaction LXIX. Partial Reduction of Trihalogen to Dihalogen Compounds. (C. r., 145, 810 ; 146, 1282 ; B., 52, 212.)—By a suitable choice of the reaction conditions halogen compounds, containing three halogen atoms linked to one carbon atom, may be reduced to dihalogen compounds. This is an important method of preparing the latter pure ; it is not easy to obtain them by direct halogenation owing to the difficulty of controlling the reaction. The success of the reduction depends on the reagent used ; sodium arsenite, for instance, reduces iodoform to methylene iodide in 95% yield. A somewhat similar reaction is seen in the simultaneous reduction and oxidation of chloral hydrate to dichloroacetic acid by the action of potassium cyanide or ferrocyanide. (C. V., II, 181.)

$$CCl_3.CH(OH)_2 + KCN = CHCl_2.COOH + HCN + KCl.$$

PREPARATION 124.—**Methylene Iodide** (*Diiodomethane*).



$$\begin{array}{c}H\\ |\\ I—C—H.\\ |\\ I\end{array} \qquad CH_2I_2. \qquad 268.$$

100 gms. (1 mol.) of iodoform are placed in a round-bottomed flask fitted with a mechanical agitator, a reflux condenser, a dropping funnel, and a thermometer. 50 c.cs. of sodium arsenite solution prepared from 27·5 gms. of arsenious oxide (excess), 53 gms. caustic soda (excess) and 260 c.cs. of water are then added. Agitation is started and the temperature is raised to 60°–65°. The remainder of the arsenite solution is now gradually added during about 30 minutes, and the whole allowed to stand for a further hour, the temperature being maintained at 60°–65° throughout. The mixture is cooled to 40°, and filtered to remove mechanical impurities ; the filtrate consists of an aqueous solution with a pale yellow oil underneath. The oil is separated, dried over calcium chloride for 24 hours, and distilled under reduced pressure, the fraction 106°–107° at 70 mms. being retained.

$$CHI_3 + Na_3AsO_3 + NaOH = CH_2I_2 + NaI + Na_3AsO_4.$$

Yield.—95% theoretical (65 gms.). Colourless oil ; insoluble in water ; B.P. 181° (with decomposition) ; D. $^{15}_{15}$, 3·3326 ; (C. r., 145, 810 ; 146, 1282 ; B., 52, 212 ; C. V., I, 358, describes preparation of methylene bromide.)

CHAPTER XIII

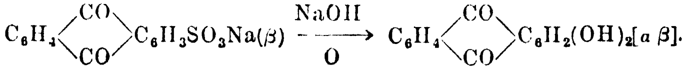
THE LINKING OF OXYGEN TO CARBON

HYDROXY COMPOUNDS

Alcohols and Phenols

The section comprises a great number of reactions since, besides those which may be classed under the heading of oxidations—and such reactions alone form a large branch of practical organic chemistry—it also includes "hydroxylation reactions", which also are numerous. The reactions given below include a few of the more important methods of replacing various elements and groups by hydroxyl.

Reaction LXX. Oxidation of Tertiary Hydrocarbons and similar Groupings.—This reaction is confined in the aliphatic series almost exclusively to the replacement by hydroxyl of the hydrogen attached to tertiary carbon atoms. A powerful oxidising agent, e.g. chromic acid in glacial acetic acid, is necessary. In the aromatic series the reaction is somewhat more easily accomplished; when the sodium salt of anthraquinone-β-monosulphonic acid, for example, is fused under pressure with caustic soda and a little potassium chlorate, replacement of both a hydrogen atom and the sulphonic acid group by hydroxyl occurs, and alizarin ($\alpha\beta$-dihydroxyanthraquinone) is obtained.



$$C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle C_6H_3SO_3Na(\beta) \xrightarrow[O]{NaOH} C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle C_6H_2(OH)_2[\alpha\,\beta].$$

Alizarin.

For a general discussion on oxidation, see Far., 1946, 99.

Preparation 125.—**Triphenylcarbinol** (*Triphenyl-methanol*).

$(C_6H_5)_3C(OH)$. $C_{19}H_{16}O$. 260.

12 gms. (1 mol.) of triphenylmethane dissolved in 60 gms. of glacial acetic acid are treated gradually in the warm with 12 gms. (excess) of chromic acid. Gentle heating is continued until a sample poured into water gives a precipitate which does not melt below 100° (1–2 hours). The whole is then poured into water and the precipitate filtered, washed with water, dried on a water bath, and recrystallised from benzene.

$$(C_6H_5)_3CH + O = (C_6H_5)_3C(OH).$$

Yield.—85% theoretical (11 gms.). Colourless crystals; soluble in hot benzene and glacial acetic acid; M.P. 158°. (B., 14, 1944.)

Reaction LXXI. Replacement of Halogen by Hydroxyl. (B., 14, 2394; 16, 2954; 25, 3290; J. pr., 11, 229; A. Ch., [3], 55, 400.)—When alkyl halides are refluxed with dilute caustic alkali or alkali carbonate, hydroxylation occurs smoothly. If the halide be tertiary the replacement takes place with great ease, warming with water being sufficient ; a secondary halide reacts less readily, but more so than a primary. Halogen in aromatic compounds is replaced with great difficulty unless there be present negative substituents in the *o*- or *p*-position (J. Soc. Dyers, 1934, 74).

$$C_6H_3Cl(NO_2)_2 \longrightarrow C_6H_3(OH)(NO_2)_2.$$

The replacement, however, can be effected under pressure (U.S.P., 1996745).

Glycerol has been synthesised industrially from propylene via trichloropropane (J. Eng., 1939, 515).

PREPARATION 126.—**Benzyl Alcohol** (*Phenyl-methanol*).

$C_6H_5.CH_2OH$. C_7H_8O. 108.

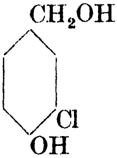
10 gms. (1 mol.) of benzyl chloride are refluxed with 10 gms. (excess) of potassium carbonate in 100 c.cs. of water until the smell of benzyl chloride disappears (about 6 hours). The liquid is extracted with ether, the extract dehydrated by standing 8 hours over anhydrous potassium carbonate, filtered into a small distilling flask, and the ether removed on a water bath. Distillation is continued with an air condenser over wire gauze, the fraction 200°–210° being collected separately.

$$2C_6H_5CH_2Cl + K_2CO_3 + H_2O = 2C_6H_5CH_2OH + 2KCl + CO_2.$$

Yield.—70% theoretical (7 gms.). Colourless liquid; aromatic odour; somewhat soluble in water ; miscible in all proportions with alcohol and ether ; B.P. 206·5° ; D. $^{0}_{4}$ 1·0628 ; D. $^{15\cdot4}_{4}$ 1·05. (B., 25, 3290.)

The use of water in the hydroxylation of compounds containing a mobile halogen atom is illustrated in the following two preparations.

PREPARATION 127.—**3-Chloro-4-hydroxybenzyl Alcohol.**



$C_7H_7O_2Cl$. 158·5.

10 gms. (1 mol.) of 3-chloro-4-hydroxybenzyl chloride are refluxed for 1 hour with 100 c.cs. of water. The cooled mixture is extracted with ether, the ether removed on a water bath and the oil which remains scratched with a glass rod until it crystallises. The crystals are pressed on a porous plate and recrystallised from benzene.

$$C_6H_3(CH_2Cl)(Cl)(OH)[1:3:4] + H_2O$$
$$= C_6H_3(CH_2OH)(Cl)(OH)[1:3:4] + HCl.$$

Colourless needles ; insoluble in water, soluble in hot benzene and in ether ; M.P. 123°. (B., 34, 2459.)

It will be observed that the nuclear halogen atom in the above compound is not replaced in the reaction.

PREPARATION 128.—**Glycollic Acid** (*Ethanol Acid*).

$CH_2(OH)COOH. \quad C_2H_4O_3. \quad 76.$

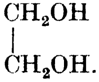
20 gms. (1 mol.) of potassium chloroacetate or 25 gms. of bromoacetate are dissolved in 80 c.cs. (excess) of water, and the solution *exactly* neutralised with sodium carbonate solution, and refluxed for 16 hours—porcelain chips being added to prevent bumping. It is cooled and concentrated to half its bulk under reduced pressure. The potassium halide which has separated is filtered off, and the filtrate evaporated to dryness under reduced pressure. The residue is extracted in a reflux apparatus with 50 c.cs. of boiling acetone and the extract evaporated to dryness on a bath kept at 65°.

$$CH_2Cl.COOK + H_2O = CH_2(OH)COOH + KCl.$$

Yield.—80% theoretical (13 gms.). Colourless deliquescent crystals; soluble in water and in acetone; M.P. 80°; $K = 0{\cdot}0152$. The presence of the carboxyl group renders halogen atoms attached to the α-carbon labile and easily replaceable.

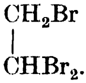
The above compound can also be prepared by boiling chloroacetic acid with an aqueous suspension of chalk (B., 16, 2954).

PREPARATION 129.—**Ethylene Glycol** (1 : 2-*Ethandiol*).



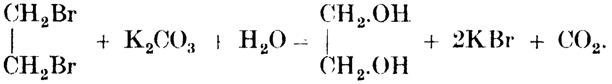
$$\begin{array}{l} CH_2OH \\ | \\ CH_2OH. \end{array} \quad C_2H_6O_2. \quad 62.$$

By-product: [1 : 2 : 2-*Tribromethan*].



$$\begin{array}{l} CH_2Br \\ | \\ CHBr_2. \end{array} \quad C_2H_3Br_3. \quad 267.$$

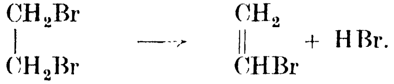
Method I.—9·4 gms. (1 mol.) of ethylene dibromide (see p. 345) are refluxed with 6·9 gms. (1 mol.) of pure potassium carbonate dissolved in 50 c.cs. of water. From the top of the reflux condenser a glass tube is led to a couple of wash bottles containing bromine. Some porcelain chips are added to the mixture to facilitate ebullition. When all the oily drops have disappeared (8–10 hours) the same quantities of ethylene dibromide and potassium carbonate are added to the solution, and the boiling continued as before. The operation is prolonged until 56·4 gms. of ethylene dibromide have been decomposed. After the third addition of ethylene dibromide, crystals of potassium bromide separate out on standing overnight. These, and those which separate out after each succeeding operation, are removed by filtration at the pump before the action is restarted. The crystals are then washed with absolute alcohol, the washings being subsequently used for the isolation of glycol (see over). After decomposition of the ethylene dibromide is complete, the solution of glycol is heated on a water bath at 50° under reduced pressure in the apparatus shown on p. 30, so as to distil off the water slowly. When the distillation has continued for some time, the liquid begins to bump violently, owing to the separation of the potassium bromide. The solution is cooled, the crystals of potassium bromide removed as before, and the distillation continued. When the solution becomes very viscid, and the temperature of the vapour passing over begins to rise, the distillation is stopped, and the residue is mixed with the alcohol used for washing the potassium bromide crystals, as explained above. After standing for some time, the crystals of potassium bromide which separate in quantity are removed by filtration at the pump, washed with absolute alcohol, and the combined alcoholic extracts concentrated by slow distillation as before from a flask fitted with a column. The residue is treated with absolute alcohol which precipitates more potassium bromide ; this treatment is repeated using a mixture of alcohol and ether, until all the potassium bromide has been removed. The solvent is removed by evaporation as above, and the residual glycol twice fractionated, at first under reduced pressure, and finally at the ordinary pressure.



$$\begin{array}{l}CH_2Br\\ |\\ CH_2Br\end{array} + K_2CO_3 + H_2O = \begin{array}{l}CH_2.OH\\ |\\ CH_2.OH\end{array} + 2KBr + CO_2.$$

Yield.—50% theoretical (10 gms.). Colourless viscid liquid ; sweet taste ; blue in thick layers in transmitted light ; miscible with water in all proportions ; D. $^{20}_{4}$ 1·134.

Isolation of By-product.—During the reaction, vinyl bromide ($CH_2 : CHBr$) is formed. It volatilises and is absorbed by the bromine in the wash bottles. The product is washed with dilute caustic soda until excess bromine is removed ; on fractionating, tribromoethane is obtained (B.P. 187°).



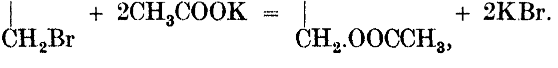
$$\begin{array}{l}CH_2Br\\ |\\ CH_2Br\end{array} \longrightarrow \begin{array}{l}CH_2\\ \|\\ CHBr\end{array} + HBr.$$

$$\begin{array}{l}CH_2\\ \|\\ CHBr\end{array} + Br_2 = \begin{array}{l}CH_2Br\\ |\\ CHBr_2.\end{array}$$

(J. C. S., 69, 176 ; J. pr., 11, 229 ; A., 192, 257 ; C., (1907), 1, 1314.)

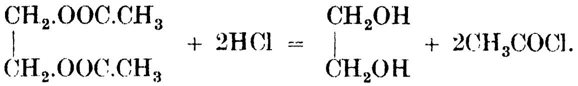
The above method is necessary where a good yield of glycol is required. If yield is not a pressing consideration, the process may be shortened by refluxing all the materials together from the beginning, evaporating at 80° under reduced pressure until little more distils, extracting the residue twice with absolute alcohol, removing the alcohol under reduced pressure and fractionating the product.

Both these methods suffer from the difficulty of separating glycol from a large excess of water without loss. There is, however, a second method available for replacing halogen by hydroxyl. It consists in preparing an ester of the desired alcohol by heating the halide with certain salts—silver, potassium, or sodium acetate—and saponifying the ester so formed.



$$\begin{array}{l}CH_2Br\\ |\\ CH_2Br\end{array} + 2CH_3COOK = \begin{array}{l}CH_2.OOCCH_3\\ |\\ CH_2.OOCCH_3,\end{array} + 2KBr.$$

For saponification, the ester is usually treated with hydrogen chloride dissolved in anhydrous methyl alcohol.



$$\begin{array}{l} CH_2.OOC.CH_3 \\ | \\ CH_2.OOC.CH_3 \end{array} + 2HCl = \begin{array}{l} CH_2OH \\ | \\ CH_2OH \end{array} + 2CH_3COCl.$$

The acetyl chloride reacts with the methyl alcohol forming methyl acetate and a fresh quantity of hydrochloric acid.

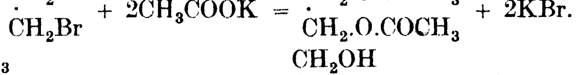
$$CH_3COCl + CH_3OH = CH_3COOCH_3 + HCl.$$

This method has a wide application, but it is especially useful for the preparation of glycol.

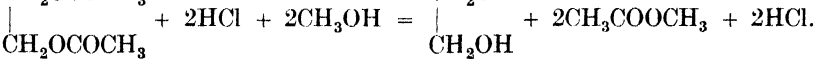
Method II.—200 gms. of pure potassium acetate are fused in a shallow dish, as described on p. 517, except that, unlike sodium acetate, the crystals contain no water of crystallisation, and only melt once. The solidified salt is finely powdered, and while still warm placed in a desiccator.

60 gms. (1 mol.) of ethylene dibromide (see p. 345), 20 gms. (excess) of glacial acetic acid, and 60 gms. (excess) of freshly-fused, finely-powdered potassium acetate are refluxed in a 500-c.c. flask for 2 hours, and the reaction product distilled, using a condenser. The distillate is again treated with 60 gms. (1 mol.) of ethylene dibromide, and 80 gms. (excess) of freshly-fused, finely-powdered potassium acetate, refluxed for 3 hours as before, and again distilled, using a good fractionating column (see p. 24), fractions (1) below 140°, (2) 140°–175°, (3) above 175°, being collected separately. The last two fractions are redistilled, the fraction 180°–190° being retained. The portion under 180° is again treated with 80 gms. of potassium acetate, refluxed and distilled as before. The total yield of glycol diacetate is about 90% theoretical (88 gms.). It boils at 180°.

40 gms. (excess) of pure anhydrous methyl alcohol (see p. 216) are cooled in water, and gaseous hydrogen chloride (see p. 513) led in until an increase in weight of 1 gm. has been obtained. Should a greater increase be found, the required 2½% solution is obtained by adding the requisite quantity of pure anhydrous methyl alcohol. The 41 gms. of 2·5% alcoholic hydrogen chloride are refluxed with 50 gms. (1 mol.) of glycol diacetate on a water bath for 30 minutes, and the reaction mixture immediately distilled from the same bath. Methyl alcohol and methyl acetate are thus removed, the residue consisting of glycol and a small quantity of acetate, two substances the boiling points of which lie close together. They are separated by extraction with an equal volume of dry ether, glycol remaining undissolved. It is removed and fractionated, the temperature being slowly raised to 100°. The fraction 192°–198° is redistilled.



$$\begin{array}{l} CH_2Br \\ \cdot \\ CH_2Br \end{array} + 2CH_3COOK = \begin{array}{l} CH_2.O.COCH_3 \\ \cdot \\ CH_2.O.COCH_3 \end{array} + 2KBr.$$



$$\begin{array}{l} CH_2OCOCH_3 \\ | \\ CH_2OCOCH_3 \end{array} + 2HCl + 2CH_3OH = \begin{array}{l} CH_2OH \\ | \\ CH_2OH \end{array} + 2CH_3COOCH_3 + 2HCl.$$

Yield.—85% theoretical (18 gms.) on glycol diacetate ; 75% theoretical (25 gms.) on ethylene dibromide. (Cf. yield p. 206).

Dioxan is obtained from ethylene glycol by action of sulphuric acid (B., 1926, 2844). With terephthalic acid glycol yields linear polymers constituting the synthetic fibre " Terylene ".

PREPARATION 130.—**2 : 4-Dinitrophenol** (2 : 4-*Dinitro*-1-*hydroxy-benzene*).

$OH.C_6H_3(NO_2)_2[1:2:4]$. $C_6H_4O_5N_2$. 184.

10 gms. (1 mol.) of chlorodinitrobenzene [1 : 2 : 4] are refluxed with 15 gms. (excess) of anhydrous sodium carbonate and 150 c.cs. of water until solution has occurred, cooled and acidified with dilute hydrochloric acid ; the precipitate is filtered, washed and dried on a porous plate.

$$2Cl.C_6H_3(NO_2)_2[1:2:4] + Na_2CO_3 + H_2O$$
$$= 2OH.C_6H_3(NO_2)_2[1:2:4] + 2NaCl + CO_2.$$

Yield.—90% theoretical (8 gms.). Colourless crystals ; insoluble in water ; M.P. 114°. (Z. Ch., (1870), 232.)

Reaction LXXII. Replacement of the Diazonium Group by Hydroxyl. (B., 22, 335 ; 23, 3705 ; 24, 1960 ; J. pr., 14, 451 ; A., 137, 39 ; D.R.P., 167211.)—This is a reaction of great importance in the aromatic series, both in the laboratory and on a manufacturing scale. When diazonium salts, especially the sulphate, are boiled with water or acids, nitrogen is evolved, and the phenol corresponding to the diazonium compound is formed. It is not necessary to isolate the diazonium salt ; the solution prepared in the usual way from the amine is boiled or slowly added to boiling dilute sulphuric acid, or an aqueous solution of sodium nitrite may be added to a boiling solution of the amine in dilute sulphuric acid. The use of the diazonium nitrate is to be avoided, as simultaneous nitration usually occurs. The reaction can be applied to substituted amines, amino-acids, amino-halogen compounds, etc., but the yields are often poor, especially with the amino-phenols ; they may be improved to some extent by the use of copper sulphate solution. Although the method is of practical importance only in the aromatic series, since aliphatic diazo-compounds are not formed except at low temperatures, yet aliphatic hydroxy compounds are readily obtained by the action of aqueous sodium nitrite solution on acid solutions of the primary amines. This reaction should be compared with the formation of ethers as by-products in the reduction of diazonium compounds with alcohol (Reaction, p. 384).

$$C_6H_5.N_2.SO_4H + H_2O = C_6H_5OH + N_2 + H_2SO_4.$$

PREPARATION 131.—**Phenol** (*Hydroxybenzene*).

$C_6H_5.OH$. C_6H_6O. 94.

20 gms. (1 mol.) aniline are dissolved by gentle warming in a mixture of 40 gms. conc. sulphuric acid in 100 c.cs. water, and the cooled liquid treated at 0°–5° with a 20% solution of sodium nitrite until the end-point is reached (p. 380) ; 16 gms. sodium nitrite will be required. The whole is kept at 50° for an hour, steam-distilled until no more phenol distils (this is shown by a sample of the distillate giving no precipitate with bromine water), the distillate is saturated with salt, extracted several times with ether until extraction is complete, and the extract dried for 24 hours over fused sodium sulphate. The ether is removed on a water bath and the residue distilled, the fraction 175°–185° being retained.

$$C_6H_5NH_2 \xrightarrow{H_2SO_4 + NaNO_2} C_6H_5.N_2.SO_4H \xrightarrow{H_2O} C_6H_5OH.$$

Yield.—35% theoretical (7 gms.). Colourless needles; characteristic odour; somewhat soluble in water; soluble in alcohol and ether; M.P. 40·8°; B.P. 182°. (B., 23, 3705; A., 137, 39; J. pr., 14, 451.)

If the residue in the flask after the steam distillation is filtered hot, and cooled, crystals of *p*-hydroxydiphenyl separate. It is formed by the reaction of a portion of the phenol first formed with undecomposed diazonium compound.

$$C_6H_5.N_2.SO_4H + H.C_6H_4OH = C_6H_5.C_6H_4OH + H_2SO_4 + N_2.$$

(Cf. p. 384.)

The yield is low owing to the heating with the mineral acid tending to cause resinification of the phenol.

In a similar manner from *o*-, *m*- or *p*-toluidine, *o*-, *m*- or *p*-cresol respectively is prepared; for these it is better to use only 10% sulphuric acid, a quantity being taken equivalent to the 30% acid employed above. The yields are about 50%.

The melting and boiling points of the cresols are:

	M.P.	B.P.
o-Cresol	31°	191°
m-Cresol	—	202°
p-Cresol	36°	202°

For the separation of *m*- and *p*-cresols, see C. r., 192, 1657.

The method is often important in the preparation of hydroxy derivatives of compounds the groups in which render them difficult to prepare by more direct means. *m*-Hydroxybenzoic acid is such a compound. It is obtained by nitration of benzoic acid followed by reduction to *m*-aminobenzoic acid and application of the present reaction (see below).

PREPARATION 132.—*m*-**Hydroxybenzoic Acid** (*1-Hydroxy-3-carboxybenzene*).

$C_6H_4(OH)(COOH)[1:3]$. $C_7H_6O_3$. 138.

10 gms. (1 mol.) of *m*-aminobenzoic acid hydrochloride are dissolved in 100 c.cs. of water (or 8 gms. of the free acid are dissolved in 200 c.cs. of 2% hydrochloric acid) and a 30% aqueous solution of 5 gms. (excess) of sodium nitrite slowly added. The whole is warmed until nitrogen ceases to be evolved, filtered at the pump and evaporated until, on cooling, crude *m*-hydroxybenzoic acid separates as a brown mass. It is purified by recrystallisation from water with addition of decolorising carbon.

$$C_6H_4(NH_2)(COOH)[1:3] \xrightarrow{HNO_2} C_6H_4(OH)(COOH)[1:3].$$

Yield.—60% theoretical (7 gms.). Colourless crystals; soluble in hot water; M.P. 200°. (A., 91, 189.)

Certain di-amino compounds can also be made to yield di-hydroxy compounds in this way.

PREPARATION 133.—**4 : 4′-Dihydroxydiphenyl.**

$[4]OH.C_6H_4.C_6H_4.OH[4']$. $C_{12}H_{10}O_2$. 186.

50 gms. (1 mol.) of benzidine (see p. 166) are dissolved in 900 c.cs. (2 mols.) of 2% hydrochloric acid, and 5 litres (excess) of 5% sulphuric acid added. The mixture is diazotised, as described on p. 381, with 20% aqueous sodium nitrite. About 40 gms. of sodium nitrite will be required. Steam is passed into the solution for 30 minutes, and until a sample gives no precipitate with an alkaline solution of phenol. The diphenyl derivative is precipitated, filtered hot, and crystallised from boiling water, in which it is not very soluble.

$$[4]HN_2.C_6H_4.C_6H_4.NH_2[4'] \xrightarrow{HNO_2 + H_2SO_4} [4]OH.C_6H_4.C_6H_4OH[4'].$$

Yield.—55% theoretical (27 gms.). Colourless needles; M.P. 275°. (B., 22, 335.)

The next preparation illustrates the use of copper sulphate solution.

PREPARATION 134.—**Quinol** (1 : 4-*Dihydroxybenzene*).

$C_6H_4(OH)_2[1:4]$. $C_6H_6O_2$. 110.

30 gms. (1 mol.) of *p*-aminophenol are diazotised, as described on p. 380, and the diazonium solution slowly added to 400 gms. boiling 25% copper sulphate solution. When the evolution of nitrogen ceases the solution is cooled and extracted with ether until extraction is complete. The ether is evaporated on a water bath, and the residue recrystallised from dilute sulphuric acid with the addition of a little decolourising carbon.

$$C_6H_4(OH)(NH_2)[1:4] \xrightarrow{HNO_2} C_6H_4(OH)_2[1:4].$$

Yield.—30% theoretical (9 gms.). Colourless prisms; soluble in hot water, in ether, and in alcohol; M.P. 169°; sublimes at a moderate heat. (D.R.P., 167211.)

o, *m*- and *p*-cresols (see p. 209) are obtained from the corresponding toluidines in a similar way.

Catechol (*o*-dihydroxybenzene, M.P. 104°; B.P. 245°) is prepared in the same manner from *o*-aminophenol, a 10% solution of copper sulphate being employed. For preparation from salicylaldehyde and hydrogen peroxide, see C. V., 1, 148.

PREPARATION 135.—**3-Nitro-4-hydroxytoluene.**

$C_6H_3(CH_3)(OH)(NO_2)[1:4:3]$. $C_7H_7O_3N$. 153.

50 gms. (1 mol.) of finely-powdered *p*-toluidine are dissolved in 500 gms. (excess) of warm 10% nitric acid (D = 1·06), and the solution diazotised at 0°, as described on p. 380, a 30% aqueous solution of 30 gms. of sodium nitrite being added until the solution colours starch-iodide paper; on no account must the temperature rise above 8°. After standing for 3 hours at 0°, 50 c.cs. of the solution are slowly heated in a litre round flask in an oil bath under a long reflux condenser until ebullition occurs and inter-

action commences. When the reaction is complete the remainder of the diazonium solution is *slowly* added, the boiling continued for 10 minutes, and the solution steam distilled until no further oil comes over. The solid nitro-cresol is filtered from the distillate, well washed with water, and purified by precipitation from an alkaline solution of its sodium salt, using dilute hydrochloric acid.

$$C_6H_4(CH_3)(NH_2)[1:4] \xrightarrow[HNO_3]{HNO_2} C_6H_3(CH_3)(OH)(NO_2)[1:4:3].$$

Yield.—60% theoretical (40 gms.). Yellowish crystals; insoluble in water; M.P. 36·5°. (B., 24, 1960.)

Reaction LXXIII. Direct Replacement of the Aromatic Amino-group by Hydroxyl (Bucherer). (D.R.P., 109102.)—The simple primary amino-groups in the benzene series are not easily replaced directly by hydroxyl unless an activating group (e.g. NO_2) be present in the *o*- or *p*-position. α-Naphthols, however, are readily obtained by heating α-naphthylamine derivatives with fairly concentrated acid under pressure.

$$C_{10}H_7NH_2 + H_2O = C_{10}H_7OH + NH_3.$$

(This reaction can be reversed, see p. 308).

It can be accomplished more readily by heating with sodium bisulphite solution, an unstable naphthol-sulphite being possibly an intermediate product. β-Compounds also react.

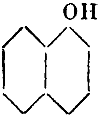
$$C_{10}H_7NH_2 + H_2SO_3 = C_{10}H_7O.SO_2H + NH_3.$$

$$C_{10}H_7O.SO_2H + H_2O = C_{10}H_7OH + H_2O + SO_2.$$

This reaction is of technical importance, being applied to the preparation of some hydroxy-sulphonic acids. See J. C. S., 1946, 1036.

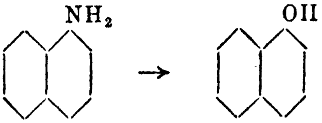
With *p*-nitroso-secondary and -tertiary bases the alkyl amino group can readily be replaced by boiling with dilute alkali. This method, too, is illustrated below.

PREPARATION 136.—α-Naphthol (1-*Hydroxynaphthalene*).



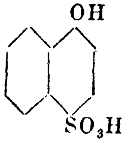
$C_{10}H_8O$. 144.

150 gms. (1 mol.) of α-naphthylamine (see p. 366) are heated with 120 gms. (excess) of conc. sulphuric acid and 1 litre of water, to 200° for 8 hours at 14 atmospheres in an enamelled autoclave (see p. 50) fitted with a stirrer. On cooling, the autoclave is opened and α-naphthol filtered off, washed, and recrystallised from water, or distilled preferably under reduced pressure.



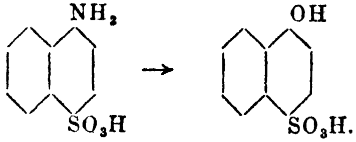
Yield.—95% theoretical (140 gms.). Colourless crystals; characteristic odour; sparingly soluble in water; M.P. 94°; B.P. 280°; is an important intermediate for dyestuffs. (D.R.P., 76545.)

PREPARATION 137.—**Nevile and Winther's Acid** (1-*Hydroxy*-4-*naphthalenesulphonic Acid*).



$C_{10}H_8O_4S$. 224.

100 gms. (1 mol.) of naphthionic acid (100%) (or the equivalent of sodium naphthionate), dissolved in 200 c.cs. of water, are refluxed for 24 hours with 600 gms. (excess) of sodium bisulphite solution (25% SO_2). 30% caustic soda solution is added until the solution is alkaline to phenolphthalein, and the whole boiled until no more ammonia is evolved. Hydrochloric acid is then added until the product is permanently acid. The Nevile and Winther's acid crystallises on cooling. It is separated from unchanged naphthionic acid by recrystallisation from warm water. It may be obtained as its sodium salt by neutralising the warm solution with caustic soda, and saturating with common salt.



Yield.—80% theoretical (80 gms.). Colourless crystals; soluble in hot water; decomposes on heating; important intermediate for azo dyestuffs. (B., 24, 3157; 27, 3458; A., 273, 102; D.R.P., 109102.)

PREPARATION 138.—*p*-**Nitrosophenol** (1-*Hydroxy*-4-*nitrosobenzene*).

$C_6H_4(OH)(NO)[1:4]$. $C_6H_5O_2N$. 123.

5 gms. (1 mol.) of *p*-nitrosodimethylaniline hydrochloride (see p. 291) are added gradually to 250 gms. (excess) of boiling 2½% caustic soda solution in a flask fitted with a reflux condenser, the free base which separates as an oil being allowed each time to dissolve before the next addition. The boiling is continued after complete addition until the solution has become reddish-yellow. When cold, the liquid is acidified and extracted with ether, and the latter removed on a water bath. The residual nitrosophenol is redissolved in a little boiling water, and after filtration and cooling it is again extracted with ether and recovered by evaporation of the ether.

$$NO.C_6H_4.N(CH_3)_2[1:4] + H_2O = NO.C_6H_4OH + NH(CH_3)_2.$$

$$NOC_6H_4OH \rightleftarrows HON:C_6H_4:O.$$

Yield.—90% theoretical (3·5 gms.). Colourless rhombic crsytals; soluble in water, and in ether; M.P. 125°. (B., 7, 809.)

This reaction is frequently applied to the preparation of dialkylamines. The dimethylamine evolved in the above reaction may be absorbed by leading through hydrochloric acid; from the latter solution the hydrochloride is obtained by evaporation. *p*-Nitrosophenol, it is to be noted, is tautomeric, in some reactions behaving as quinone monoxime.

Reaction LXXIV. (*a*) **Action of Mineral Acids on Phenylhydroxylamine.** (B., 26, 1844, 2810; 27, 1927; 20, 2040.)—In the presence of mineral acids phenylhydroxylamine undergoes rearrangement to form *p*-aminophenol.

$$C_6H_5NH.OH \longrightarrow OH.C_6H_4NH_2.$$

This isomerisation is believed to occur in the electrolytic reduction of aromatic nitro compounds (see p. 407).

PREPARATION 139.—*p*-**Aminophenol** (1-*Hydroxy*-4-*aminobenzene*).

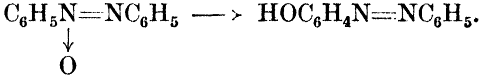
$$C_6H_4(OH)(NH_2)[1:4]. \qquad C_6H_7ON. \qquad 109.$$

5 gms. of phenylhydroxylamine (see p. 377) are slowly added to 100 c.cs. of 50% sulphuric acid, cooled in a freezing mixture, 500 c.cs. of water poured in, and the whole boiled until a sample, tested with chromic acid solution, gives a smell of quinone and no smell of nitrobenzene. The liquid is neutralised with sodium bicarbonate, saturated with common salt, and extracted with ether. The ether is removed by evaporation, and the residue washed with cold water and dissolved in hot water. The solution is filtered hot, and cooled, and the *p*-aminophenol again extracted with ether.

$$C_6H_5NHOH \longrightarrow OH.C_6H_4.NH_2.$$

Yield.—Almost theoretical (5 gms.). Colourless crystals; somewhat soluble in water; M.P. 185°. (B., 26, 1844, 2810; 27, 1927; 29, 3040.)

Reaction LXXIV. (*b*) **Transformation of Azoxy Compounds to Azophenols.** Azoxy compounds (see Reaction CLXX) are converted by conc. sulphuric acid into *p*-hydrozyazo compounds (B., 13, 525).



$$C_6H_5\underset{\downarrow \atop O}{N}{=}NC_6H_5 \longrightarrow HOC_6H_4N{=}NC_6H_5.$$

Most azoxy compounds under the influence of ultra-violet light are converted into *o*-hydroxyazo compounds. (J. C. S., 123, 2466; 127, 2374.)

Reaction LXXV. Fusion of Aromatic Sulphonic Acids with Caustic Alkalis. (Z. Ch., (1876), 3, 299; J. pr., [2], 17, 394; 20, 300.)—This method is of technical importance as it is employed to prepare phenols and naphthols which are much used in the dye industry. The method cannot easily be applied to determine structure, owing to rearrangement liable to occur at the elevated temperatures. Caustic potash is more convenient than soda, since it yields a more fusible mixture; the reaction is sometimes carried out under pressure (Prep. 291).

PREPARATION 140.—**Phenol** (*Hydroxybenzene*).

C_6H_5OH. C_6H_6O. 94.

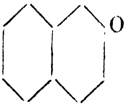
100 gms. of caustic soda and 10 c.cs. of water are heated in an iron or nickel basin (or in a glue-pot, Fig. 54) to 290°. 130 gms. of sodium benzene sulphonate are gradually added, care being taken that the temperature is maintained between 290° and 300°, the mass being stirred with a thermometer pocket (see below). After the addition, the temperature is raised to 330° (but not beyond 340°) and maintained for 15 minutes. The melt is cooled, then dissolved in the minimum of water and transferred to a beaker where it is carefully acidified under good cooling with conc. hydrochloric acid. After three extractions with ether the combined extracts are dried with anhydrous sodium sulphate for 24 hours. The ether is then distilled off and the residue fractionated at 175°-185°.

$$C_6H_5SO_3K \longrightarrow C_6H_5OK \longrightarrow C_6H_5OH.$$

Yield.—70% theoretical (65 gms.). Colourless needles ; characteristic odour ; somewhat soluble in water ; soluble in alcohol and ether ; M.P. 40·8° ; B.P. 182°. (Z. Ch., (1867), 3, 299 ; J. pr., 20, 300 ; Abs. B., 1935, 91.) See U.S.P., 1789071. For *p*-cresol, see C. V., I, 175.

For dealkylation of cresols to phenol under pressure, see E.P., 427145.

PREPARATION 141.—**β-Naphthol** (*2-Hydroxynaphthalene*).



$C_{10}H_8O$. 144.

200 gms. (excess) of solid caustic soda free from chloride, and 60 c.cs. water are placed in a fusion-pot (Fig. 54), which consists of a glue-pot, the outer pot containing the Pb-Sn eutectic mixture (p. 44). The thermometer is placed inside the iron tube containing a little mercury at the bottom, and this tube is used as stirrer. The pot is heated until the temperature is 270°. 300 gms. of dry powdered sodium β-naphthalene sulphonate are then gradually added, the temperature being allowed to rise to 290° when half of the salt has been added, to 300° when three-quarters has been added, and to 305° when all has been added, and finally to 318°—but no higher—for 15 minutes. The melt, after cooling somewhat, is poured into 2 litres of water with continual stirring (*caution !*). The solution is acidified with 50% sulphuric acid, and boiled to expel sulphur dioxide, an indicator being used to show final acidity in the solution. The β-naphthol is then filtered off, washed with water and dried. It may be recrystallised from hot water.

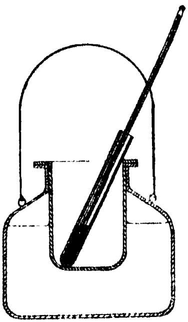


FIG. 53.

$$C_{10}H_7SO_3Na \longrightarrow C_{10}H_7ONa \longrightarrow C_{10}H_7OH.$$

Yield.—70% theoretical (130 gms.). Colourless crystals with characteristic odour; M.P. 122°; B.P. 286°. Important intermediate for dyestuffs.

α-Naphthol (M.P. 94°; B.P. 280°) is prepared from sodium α-naphthalene-sulphonate in a similar manner. For the preparation of alizarin by the application of the same reaction, see p. 399.

Reaction LXXVI. Addition of Hydroxyl to Ethylenic Bonds. (B., 21, 919; A., 268, 27.)—When compounds containing ethylenic linkages are treated with mild oxidising agents, e.g. bromine and caustic potash, dilute nitric acid and especially very dilute (2%) potassium permanganate solution, addition of hydroxyl at the double bond to form a 1 : 2-dihydroxy compound occurs. Recently, hydrogen peroxide in presence of osmium tetroxide (A., 522, 75), vanadium pentoxide, and chromium trioxide have been used. See Ann. Rep., 1945, 145.

$$R_1CH : CHR_2 \xrightarrow{O + H_2O} R_1CHOHCHOHR_2.$$

If stronger oxidising agents are employed the carbon chain can be broken at that point, and the reactions used to determine the position of the double bond.

$$R_1CHOHCHOHR_2 \xrightarrow{O_2} R_1COOH + R_2COOH.$$

This reaction is used to determine the presence and position of double bonds in organic compounds; it has been much applied to the elucidation of the structure of members of the terpene series.

Ethylene is catalytically hydrated to ethyl alcohol by steam at 100°–300°, the catalysts being salts of phosphoric acid (E.P., 423877) and to ethylene glycol in presence of selenium dioxide (E.P., 376306).

Preparation 142.—**Phenyldihydroxypropionic Acid** (*3-Phenyl-2 : 3-propandiol Acid*).

$$C_6H_5.CHOH.CHOH.COOH. \qquad C_9H_{10}O_4. \qquad 182.$$

20 gms. (1 mol.) of cinnamic acid (see p. 121) are dissolved in 3 litres of 5% aqueous caustic soda and 2 litres (excess) of 2% aqueous potassium permanganate solution are added with good cooling and mechanical stirring. The temperature must be kept at −5° throughout. The liquid is filtered, nearly neutralised with 20% hydrochloric acid, and concentrated until the dissolved salts begin to separate. Neutralisation is then completed with conc. hydrochloric acid, and the product repeatedly extracted with large quantities of ether until nothing further is removed. Owing to the solubility of phenyldihydroxypropionic acid in water this will necessitate at least ten extractions. The ethereal solution is distilled to recover ether; the residue recrystallised from ether or benzene. The pure acid separates on cooling.

$$C_6H_5CH : CHCOOH \xrightarrow{O_2} C_6H_5CH(OH)CH(OH)COOH.$$

Yield.—70% theoretical (17 gms.). Colourless needles; soluble in water; somewhat soluble in ether; M.P. 141°. (B., 21, 919; A., 268, 27.)

As this section contains the most important methods of preparing alcohols, processes for the purification of commercial methyl and ethyl alcohols are given here.

Purification of Methyl Alcohol. (*Methanol*)

CH_3OH. CH_4O. 32.

Methyl alcohol, manufactured by the dry distillation of wood, is usually contaminated with acetone, its homologues and condensation products, and also with acetaldehyde, methyl acetate, dimethyl acetal, etc. It is purified by refluxing with 5% of solid caustic potash on a water bath and distilling. It is then allowed to stand for 24 hours over 40% freshly-burnt quicklime, and redistilled from a water bath, the distillate being collected at 66°–67°. This removes all but the last traces of water. If anhydrous methyl alcohol is required the product obtained above is boiled with about 1% of freshly-prepared calcium turnings on a water bath, under a reflux condenser (see Fig. 54) fitted with a calcium chloride tube until the

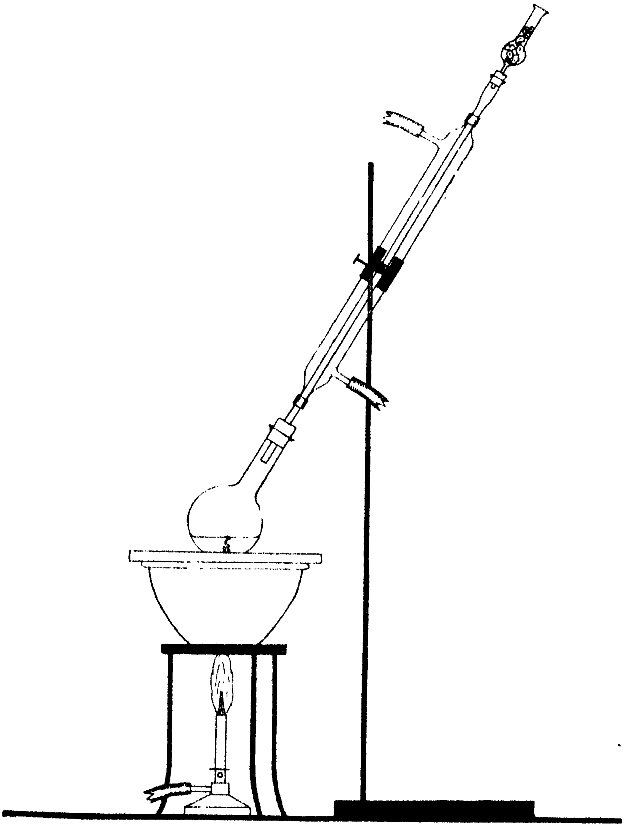


FIG. 54.

solid deposit, at first black, becomes almost white. It is then distilled into a receiver fitted with a calcium chloride tube, and the portion passing over at a constant temperature twice redistilled over 5% of calcium turnings, using a column. The solid formed should be white, and the alcohol distil at a constant temperature. As the anhydrous alcohol is very hygroscopic it must not be exposed to air.

Colourless liquid; spirituous odour; miscible in all proportions with water; B.P. 66·5°; D. $^{20}_{4}$ 0·79133. (B., 41, 4322.)

Methyl alcohol of very high purity can be obtained by fractional distillation using a column of 1·3 metres effective length and then refluxing with aluminium amalgam. It is then refluxed under a column packed with dehydrated copper sulphate, to remove ammonia. A sensitive test for acetone and formaldehyde is the addition of conc. mercuric cyanide solution, in 6N-sodium hydroxide. A white precipitate indicates ketone; if it darkens on standing aldehyde is also present. (J. C. S., 127, 2552.)

Purification of Ethyl Alcohol. (*Ethanol*)

C_2H_5OH. C_2H_6O. 46.

To prepare absolute alcohol, 100 gms. of freshly-burnt quicklime in the form of small lumps are placed in a 500-c.c. distilling flask, and 300 gms. of rectified spirits added. After 8 hours the alcohol is distilled off on a water bath until a thermometer in the neck of the flask indicates 80°. The alcohol so obtained still contains about 3% of water.

To purify the alcohol further the above product is shaken with finely-divided silver oxide. This oxidises any aldehyde present to acetic acid. Solid caustic soda is added, and the alcohol distilled, using a good column (see p. 24). The portion passing over at constant temperature is then treated with calcium turnings in the same way as methyl alcohol (see above). The anhydrous alcohol is very hygroscopic, and must not be exposed to air.

For the removal of the last traces of water the alcohol may be refluxed several hours with small quantities of sodium and ethyl succinate or phthalate. (J. C. S., 1927, 1288; Am. Soc., 1931, 1106.)

If the presence of methyl alcohol is permissible, an effective method of drying consists in refluxing for several hours with magnesium methylate. (O. S., VII, 37.)

Colourless liquid; spirituous odour; miscible with water in all proportions; binary mixture with water contains 75·57% alcohol, and boils at 78·1° at 760 mms.; B.P. ^{760} pure alcohol, 78·3°; B.P. ^{21} 13°; D. $^{15}_{4}$ 0·790. It forms a ternary mixture with benzene and water, and this property is utilised in the manufacture of industrial absolute alcohol. (J. C. S., 81, 707; see Preparation 198; B., 38, 3612.)

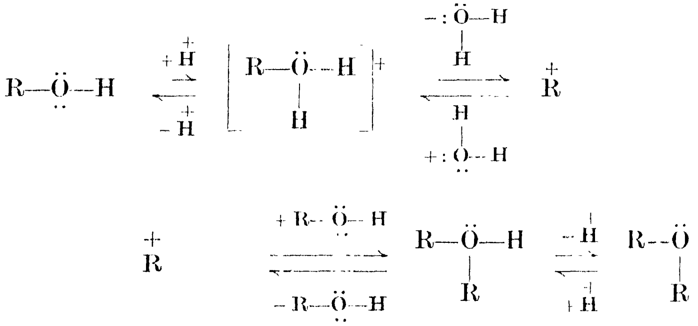
CHAPTER XIV

OXYGEN TO CARBON

OXIDE COMPOUNDS

Ethers

Reaction LXXVII. Removal of Water, under acidic conditions, from an Alcohol or a Mixture of Alcohols. (Phil. Mag., [3], 37, 350; Rec., 49, 754.) —The removal of water is effected by heating with concentrated acids, such as sulphuric (the commercial method of manufacturing ether), phosphoric, benzenesulphonic acids, or by dilute acids under pressure. It may even be effected by heating the alcohols in presence of certain salts, such as ferric sulphate, boron trifluoride, etc.



In summary, $2ROH - H_2O \longrightarrow R_2O$.

Thus, in theory, a limited quantity of sulphuric acid can convert an unlimited quantity of alcohol to ether, but in practice, owing to side reactions, this does not hold. Mixed ethers are better prepared by the methods given on pp. 219, 221.

Preparation 143.—**Diethyl Ether.**

$(C_2H_5)_2O$. $C_4H_{10}O$. 74.

100 gms. ethyl alcohol are placed in a $\frac{1}{2}$-litre distilling flask, and under good cooling 180 gms. of conc. sulphuric acid are slowly added. The flask is fitted with a thermometer dipping into the liquid and an arrangement for admitting alcohol below the surface of the acid. The best arrangement consisting of a separating funnel attached through a cork to a thistle funnel which forms part of the special apparatus (Fig. 8) and which is drawn out to a capillary and upturned. The flask is maintained at 140°–145° on a sand bath. Alcohol is run in from the tap funnel at the same rate as the

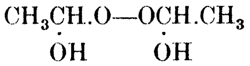
liquid distils (two drops a second) until when about 150 gms. of alcohol have been added, heating is discontinued. The distillate is freed from sulphurous acid by shaking twice with 50 c.cs. of 10% caustic soda solution and from alcohol by shaking twice with the same quantity of saturated sodium chloride solution. The ether is dried for 24 hours over anhydrous calcium chloride, distilled on a water bath, and collected at 35°. The yield is improved by adding 10% of its weight of anhydrous ferric chloride, aluminium sulphate or sand, to the mixture of acid and alcohol. The ether obtained is pure enough for most purposes; when pure, anhydrous ether is required, the last traces of alcohol and water are removed by keeping the ether over metallic sodium in the form of thin slices or wire. The flask is fitted with a calcium chloride tube to prevent the ingress of moisture. After 24 hours the ether is distilled over fresh metallic sodium. Owing to its volatility and inflammability ether should always be distilled from a water bath in the apparatus (p. 21) (*Caution*, see below).

Yield.—100 gms. (part of the alcohol is combined as alkyl hydrogen sulphate). Colourless liquid; characteristic odour; miscible with alcohol in all proportions; soluble in water (1 in 10); B.P.^{760} 34·49°; D.$^{15}_{4}$ 0·720. (J. Pharm., 1, 97; Phil. Mag., [3], 37, 350.)

The chief impurities in commercial ether (Methylated Ether) are ethyl alcohol, water, and traces of aldehyde, methyl alcohol, acetone; peroxides which are explosive may be present if the ether has been kept for any length of time. Alcohol may be detected by shaking with a spirit soluble dye, e.g. aniline violet; water by the cloudiness formed on shaking with carbon disulphide; peroxides by the brown colour on shaking with potassium iodide solution.

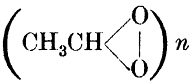
Caution.—Great care should be exercised in distilling ether which has been kept for any time. The peroxides are explosive and remain in the residue after distillation. Before distillation, therefore, ether which has been stored should be shaken with potassium dichromate, alkaline potassium permanganate, sodium bisulphite, or ferrous sulphate solution, or with lead peroxide. The formation of peroxides on storage may be inhibited by immersing copper or iron wire in the ether and keeping it in dark glass bottles in a cool place. (See J .S. C. I., 1949, 362).

The following peroxides have been identified in ether:



$$\underset{\text{OH}}{\mathrm{CH_3CH}}.\mathrm{O{-}O}\underset{\text{OH}}{\mathrm{CH}}.\mathrm{CH_3}$$

and



$$\left(\mathrm{CH_3CH}\langle\mathrm{O_2}\rangle\right)_n$$

Reaction LXXVIII. Action of Alkyl Halides on Alkali Alcoholates or Phenates. (P. R. S., 7, 135; J. C. S., 2, 198; A., 78, 226; 152, 164; B., 12, 116.)—This method is of importance as indicating the structure of ethers.

$$R_1I + NaOR_2 = R_1OR_2 + NaI.$$

It is applicable both in the aromatic and aliphatic series, and can be used to obtain the ethers corresponding to the hypothetical di- and trihydric-alcohols, in which more than one hydroxyl group is attached to the same carbon.

$$CH_2Cl_2 + 2C_2H_5ONa = CH_2(OC_2H_5)_2 + 2NaCl.$$

PREPARATION 144.—**Phenetole** (*Ethoxybenzene*).

$C_6H_5.O.C_2H_5.$ $C_8H_{10}O.$ 122.

A 500-c.c. round flask containing 200 c.cs. (excess) of absolute ethyl alcohol is attached to a reflux condenser, and 8 gms. (1 mol.) of sodium in thin slices or in small pieces of wire are added. When it has completely dissolved 31 gms. (1 mol.) of phenol and 75 gms. (excess) of dry ethyl iodide are added, and the whole refluxed on a water bath until the solution is no longer alkaline (4 hours). The alcohol and excess of ethyl iodide are distilled off on a water bath, the residue treated with water to dissolve sodium iodide, and extracted with ether. After drying over calcium chloride ether is removed on a water bath, and the phenetole distilled over the naked flame, the distillate being collected between 168°–173°.

$$C_6H_5OH + C_2H_5ONa = C_6H_5ONa + C_2H_5OH.$$

$$C_6H_5ONa + C_2H_5I = C_6H_5.O.C_2H_5 + NaI.$$

Yield.—Almost theoretical (40 gms.). Colourless liquid; pungent smell; insoluble in water; B.P. 172°; D. $^{15}_{4}$ 0·973. (A., 78, 226.)

It should be noted that owing to the great affinity of the phenol for sodium, no sodium alcoholate remains to react with the ethyl iodide. Diethyl ether, however, may be prepared in a similar manner, using the same quantities of sodium, alcohol and ethyl iodide as above. The ether and excess of alcohol are distilled off, and the ether separated from the alcohol by the addition of salt solution. Anisole (phenylmethyl ether, B.P. 154°, see p. 221) can also be prepared in a similar way, using corresponding quantities of methyl alcohol and methyl iodide. The alkyl iodides give the best yields, but alkyl chlorides can also be employed.

PREPARATION 145.—**Ethyl Orthoformate** (*Triethoxymethane*).

$CH(OC_2H_5)_3.$ $C_7H_{16}O_3.$ 148.

58·5 gms. (3 mols.) of metallic sodium, well pressed between filter paper and cut into thin slices or pressed into wire (see p. 515), are placed in a dry flask of about 1½ litres capacity, and covered with a layer of anhydrous ether (see p. 219). The flask is connected to a condenser. A mixture of 117 gms. (3 mols.) of absolute alcohol and 100 gms. (1 mol.) of anhydrous chloroform is added drop by drop from a tap funnel. At the beginning the reaction is violent, and the flask must be well cooled with ice; sodium chloride separates and the liquid gradually changes to a brown colour. To complete the reaction the mass is warmed on a water bath until all the sodium present is converted into sodium chloride. The contents of the flask are poured into water, the ethereal solution of ethyl orthoformate which separates is removed, washed three times with water, dehydrated over calcium chloride, the ether removed on a water bath, and the residue distilled over a bare flame. That portion of the distillate which passes over above 100° is collected separately and redistilled, the fraction 143°–150° being retained.

$$CHCl_3 + 3C_2H_5ONa = CH(OC_2H_5)_3 + 3NaCl.$$

Yield.—70% theoretical (85 gms.). Colourless liquid; insoluble in water; soluble in ether; B.P. 145°–147°; D. $^{4}_{0}$ 0·8946. (P. R. S., 7, 135; J. C. S., 2, 198; A., 152, 164; B., 12, 116; O. S., V, 55.)

Reaction LXXIX. Action of Dimethyl Sulphate on Hydroxy Compounds. (A., 327, 114.)—Dimethyl sulphate is a valuable methylating agent, and can be used generally in place of methyl iodide. It reacts with greater readiness and gives better yields. The substance to be treated is dissolved or suspended in cold conc. caustic potash solution and a slight excess of dimethyl sulphate added. Great care must be taken in working with dimethyl sulphate, as it is excessively poisonous (see p. 75).

$$RONa + (CH_3)_2SO_4 = ROCH_3 + NaCH_3SO_4.$$

This reagent has proved especially important in the study of the constitution of the sugars, and of cellulose. A series of methyl-celluloses has been obtained, and by the study of their hydrolysis, or decomposition in a vacuum, much light has been thrown on the structure of the cellulose molecule and its derivatives. In the laboratory dimethyl sulphate is much employed in the methylation of phenols and naphthols. Diethyl sulphate is not so suitable for such alkylations as its lower homologue.

PREPARATION 146.—**Anisole** (*Phenyl methyl ether*).

$$C_6H_5.O.CH_3. \qquad C_7H_8O. \qquad 108.$$

Caution !—*Dimethyl sulphate is very poisonous and this preparation must be carried out in a good fume cupboard.* (See p. 266).

30 gms. (1 mol.) of phenol dissolved in 160 gms. (excess) of 10% aqueous caustic soda solution in a ½-litre round-bottomed flask are *carefully* treated with 50 c.cs. of commercial dimethyl sulphate, and the whole continually shaken. The flask is closed by a cork through which passes a thermometer and a glass tube, bent in a spiral to prevent liquid spurting. The beginning of the reaction is shown by the separation of an upper layer of oil, and by the evolution of heat. The temperature must be kept between 40°–50°. When no more heat is evolved, excess of dimethyl sulphate is destroyed by boiling under a reflux condenser with frequent shaking. The liquid is cooled and caustic soda added until an alkaline reaction is obtained; the whole is extracted with ether and the extract dried by shaking with anhydrous potassium carbonate and filtered. The ether is removed on a water bath and the residue distilled, the fraction 150°–156° being retained.

$$C_6H_5OH + NaOH = C_6H_5ONa + H_2O.$$

$$C_6H_5ONa + (CH_3)_2SO_4 = C_6H_5.O.CH_3 + Na.CH_3.SO_4.$$

$$(CH_3)_2SO_4 + 2NaOH = 2CH_3OH + Na_2SO_4.$$

Yield.—90% theoretical (32 gms.). Colourless oil; pleasant odour; insoluble in water; soluble in ether; B.P. 154°; D. $^{15}_{4}$ 0·991. (A., 41, 71; 48, 65; 78, 226; 327, 114; O. S., IX, 12.)

Other methyl ethers may be prepared in a similar manner; e.g., β-naphthyl methyl ether (M.P. 71°) is formed in good yield from β-naphthol.

The next preparation illustrates the preparation of the ethers of the polyhydric phenols.

PREPARATION 147.—**Pyrogalloltrimethyl Ether** (1 : 2 : 3-*Trimethoxybenzene*).

$C_6H_3(OCH_3)_3[1:2:3]$. $C_9H_{12}O_3$. 168.

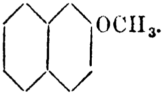
Caution !—*Dimethyl sulphate is very poisonous.* (*See note to previous preparation.*)

20 gms. (1 mol.) of pyrogallol are dissolved in 30 gms. (excess) of 35% aqueous caustic soda in a 1-litre, round-bottomed flask closed with a cork, through which pass a thermometer and an open tube bent in a spiral to prevent spurting. 50 c.cs. (excess) of commercial dimethyl sulphate are gradually added with continuous shaking, the cork being momentarily removed. The temperature is not allowed to rise above 45°. When heat is no longer evolved, the mixture is boiled under a reflux condenser, cooled, made alkaline with caustic soda if necessary, the dark-coloured precipitate filtered at the pump, and well washed with water. It is dissolved in ether, filtered, the ether removed on a water bath, and the residue recrystallised from dilute alcohol.

$$C_6H_3(ONa)_3[1:2:3] \xrightarrow{(CH_3)_2SO_4} C_6H_3(OCH_3)_3[1:2:3].$$

Yield.—70% theoretical (19 gms.). Colourless crystals ; insoluble in water ; soluble in alcohol and ether ; M.P. 47° ; B.P. 235°. (B., 21, 607, 2020, R., 126.)

PREPARATION 148.—**β-Naphthylmethyl Ether** (2-*Methoxynaphthalene*).



$C_{11}H_{10}O$. 158

(*See cautions to previous two preparations.*)

10 gms. (1 mol.) of β-naphthol are dissolved in 40 gms. (excess) of 10% caustic soda solution, and the cooled liquid mixed with 8 c.cs. of commercial dimethyl sulphate, as described in the two previous preparations. Gentle warming may be needed to start the reaction. The required ether separates as a solid which is filtered off after boiling and making alkaline if necessary, as before. The precipitate is washed with water and recrystallised from alcohol.

$$C_{10}H_7OH[2] \xrightarrow[NaOH]{(CH_3)_2SO_4} C_{10}H_7.OCH_3[2].$$

Yield.—Almost theoretical (11 gms.). Lustrous plates ; insoluble in water ; soluble in ether and in hot alcohol ; M.P. 71°. (B., 26, 2706.)

The following preparations indicate how cellulose $[C_6H_7O_2(OH)_3]_n$, can be methylated to give compounds having the empirical composition :

$$[C_6H_7O_2(OH)_2(OCH_3)]_n,\ [C_6H_7O_2(OH)(OCH_3)_2]_n \text{ and } [C_6H_7O_2(OCH_3)_3]_n.$$

These compounds are known respectively as monomethyl-, dimethyl-, and trimethyl-cellulose.

PREPARATION 149.—**The Methyl-celluloses.**—(i) ***Mono*methylcellulose.**

$$[C_6H_7O_2(OH)_2(OCH_3)]_n. \qquad (C_7H_{12}O_5)_n. \qquad 176_n.$$

50 gms. (1 mol.) of well-picked sliver cotton are shaken in a 2-litre flask closed as described in Preparation 147, with 180 c.cs. (excess) of 23% caustic soda; after standing for 1 hour the cotton is "pounded" in a glass mortar. It is returned to the flask, and 110 c.cs. (excess) of dimethyl sulphate gradually added (*caution!* see p. 75), the flask being shaken for ½ hour between each addition. When no further evolution of heat occurs, the flask is filled with water and the contents poured through a 100-mesh copper gauze. The methyl cotton is well washed with water and dried in an air oven.

$$[C_6H_7O_2(OH)_3]_n \longrightarrow [C_6H_7O_2(OH)_2(OCH_3)]_n.$$

Yield.—Almost theoretical (53 gms.). The methyl cotton is best characterised by its methoxyl content (see p. 490), which should be about 17·6% OCH_3.

(ii) ***Di*methylcellulose.**

$$[C_6H_7O_2(OH)(OCH_3)_2]_n. \qquad (C_8H_{14}O_5)_n. \qquad 190_n.$$

50 gms. (1 mol.) of monomethyl cellulose, prepared as above, are treated as before with 175 c.cs. (excess) of 20% caustic soda solution and 120 c.cs. of dimethyl sulphate added. The subsequent operations are as above. The dried product contains about 20% OCH_3. 50 gms. of this latter product are treated with 400 gms. of water, and 100 c.cs. of 75% caustic soda solution added slowly and with shaking. 100 c.cs. of dimethyl sulphate are added under cooling. The subsequent operations are as in (i).

$$[C_6H_7O_2(OH)_2(OCH_3)]_n \text{ —— } [C_6H_7O_2(OH)(OCH_3)_2]_n.$$

Yield.—90% theoretical (48 gms).

The product should contain about 32·6% OCH_3.

(iii) ***Tri*methylcellulose.**

$$[C_6H_7O_2(OCH_3)_3]_n. \qquad (C_9H_{16}O_5)_n. \qquad 204_n.$$

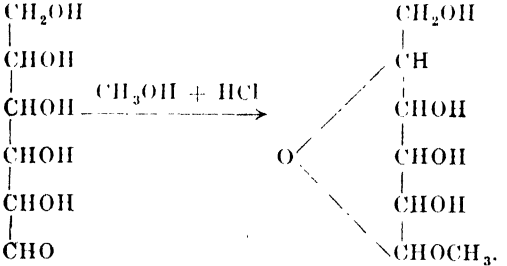
50 gms. (1 mol.) of dimethyl cellulose are treated with 100 gms. of water, and 140 c.cs. of 75% aqueous caustic soda solution slowly poured in, with good shaking and cooling. 120 c.cs. of dimethyl sulphate are added, and the whole allowed to stand overnight and filtered. 100 c.cs. of 75% aqueous caustic soda are poured in, and 120 c.cs. more of dimethyl sulphate added, as before. The subsequent operations are as in (ii).

$$[C_6H_7O_2(OH)(OCH_3)_2]_n \text{ —— } [C_6H_7O_2OCH_3)_3]_n.$$

Yield.—80% theoretical (45 gms.). The product contains about 42·5% methoxyl; the theoretical percentage for a trimethyl cellulose is 45·6%, but so far cellulose has not been completely methylated. It will be noted how the strength of the caustic soda used varies with the percentage of methoxyl required in the product. (J. C. S., 103, 1735.)

By repetitions of the above procedures, methoxyl contents of 20·4% in (i), 39·5% in (ii), and 44·6% in (iii) have been obtained. (J. C. S., 119, 77.)

Reaction LXXX. Action of very Dilute Methyl Alcoholic Hydrogen Chloride on the Sugars. (B., 28, 1151.)—When the hexoses are heated for several hours at 100° with dilute methyl alcoholic hydrogen chloride, methyl glucosides are produced. This synthesis is important, as it indicates methods for the synthesis of the higher sugars which are themselves of the glucoside type.



Glucose. Methyl-glucoside.

Each sugar can yield two glucosides (α and β), since the carbon to which the methoxyl group becomes attached is in that way rendered asymmetric. It is assumed that each sugar first forms a dimethyl-acetal, which loses alcohol to yield the glucoside. In the following preparation, it is the α-glucoside which preponderates in the product.

PREPARATION 150.—**α-Methyl-*d*-glucoside** (1-*Methoxy-pentol-hexan*).

$C_6H_{11}O_5.OCH_3$. $C_7H_{14}O_6$. 194.

Dry hydrogen chloride is passed into 200 gms. of anhydrous methyl alcohol contained in a flask under a reflux protected with an anhydrous calcium oxide or silica gel tube, the flask being ice-cooled to prevent loss by evaporation, until a gain in weight of 6 gms. has taken place. 100 gms. of powdered *pure anhydrous* dextrose are then added and the mixture boiled under the protected reflux for 4½ to 12 hours, the longer period giving only slightly better yields. 3 gms. decolourising carbon are added and boiling continued for 15 minutes. The solution is rapidly filtered and cooled in ice-water with occasional stirring. After about an hour the thick paste of α-methyl glucoside is filtered, washed with a little methyl alcohol and dried in air. A second crop may be obtained by concentrating the mother liquor to one-half its bulk in presence of decolourising carbon. The combined crude yields when recrystallised from 2½ parts of methyl alcohol yield the pure glucoside.

For equation, see above.

Yield.—40% theoretical (46 gms.). Colourless needles ; soluble in hot alcohol; M.P. 165°–166° ; $[\alpha]_D^{12.5} = +157{\cdot}9°$. For the recovery of β-methyl glucoside from the original mother liquors, see J. C. S., 1929, 301.

Reaction LXXXI. Action of Hydrogen Chloride on a Mixture of an Aldehyde and an Alcohol. (B., 30, 3053 ; 31, 545.)—The reaction is of the same type as the preceding. Under the influence of condensing agents, calcium chloride, hydrogen chloride, etc., aldehydes combine with alcohols to yield the ethers (acetals) of the hypothetical dihydroxy compounds from which the aldehydes are derived. Ketones form these compounds only with difficulty.

$$RCHO + 2R_1CH_2OH \longrightarrow RCH(OCH_2R_1)_2 + H_2O.$$

PREPARATION 151.—**Diethylacetal** (1 : 1-*Diethoxyethane*).

$CH_3CH(OC_2H_5)_2$. $C_6H_{14}O_2$. 118.

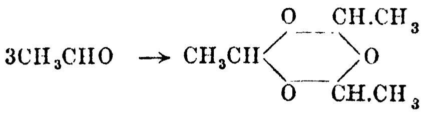
15 gms. anhydrous calcium chloride and a few drops dilute hydrochloric acid are added to a mixture of 44 gms. freshly-distilled acetaldehyde and 100 gms. alcohol. The whole is allowed to stand with occasional shaking for 1 hour, when the lower aqueous layer which has separated is siphoned off. The upper layer is placed over other 15 gms. of anhydrous calcium chloride, and after standing for 5 hours with constant shaking the separated aqueous layer is again siphoned off, and the upper layer added to a third 15 gms. of calcium chloride. This operation is once more repeated after 12 hours' standing, and the last lot allowed to act for 24 hours. It is filtered off and the filtrate fractionally distilled. The fraction 102°–108° is collected separately. The fraction below 102° is again allowed to stand over calcium chloride for 24 hours, and again fractionated as before ; if preferred the fractionation may be performed under reduced pressure.

$$CH_3.CHO + 2C_2H_5OH = CH_3CH(OC_2H_6)_2 + H_2O.$$

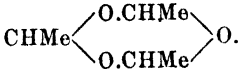
Yield.—60% theoretical (70 gms.). Colourless liquid ; soluble in 18 volumes of water at 25° ; miscible with alcohol ; B.P. ^{760} 104° ; D. $^{20}_{4}$ 0·831. (J., (1880), 694 ; B., 30, 3053 ; C. V., 1, 1.)

The same compound may be obtained by dissolving 10 gms. of acetaldehyde in 50 gms. of a 1% absolute alcoholic solution of hydrogen chloride, and in 24 hours extracting the solution with ether after neutralisation with potassium carbonate. The extract is dried and purified by distillation as before.

Reaction LXXXII. Condensation of an Aldehyde with itself under the Action of Mineral Acids or of Calcium Chloride. (A., 27, 319 ; 162, 143 ; 203, 26, 43.)—If acetaldehyde is treated with calcium chloride or mineral acids, such as conc. sulphuric or gaseous hydrogen chloride, polymerisation occurs and paraldehyde is formed. A certain amount of metaldehyde is also obtained ; its quantity increases with reduction in the temperature of polymerisation.



PREPARATION 152.—**Paracetaldehyde.**



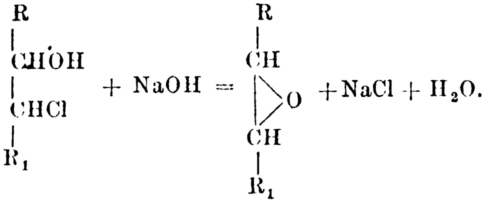
$C_6H_{12}O_3$. 132.

132 gms. (3 mols.) of freshly-distilled *absolute* acetaldehyde are placed in a flask fitted with a thermometer, reflux condenser, and gas delivery

tube, and the whole cooled to 5°. Dry hydrogen chloride is led in until an absorption of 6% (8 gms.) has taken place. The mixture is then allowed to stand for several hours at room temperature, and until the temperature has risen to the boiling point of acetaldehyde, 21°, when it is recooled to 5° and allowed to stand for 15 hours. Some metaldehyde has by then separated, and is filtered off. The liquid is shaken with a saturated solution of sodium carbonate to remove acid, and then washed with water. It is dried with anhydrous potassium carbonate and fractionated, the fraction 122°–128° being retained. The distillation can be carried out under reduced pressure.

Yield.—70% theoretical (90 gms.). Colourless liquid; sparingly soluble in water; M.P. 12·5°; B.P. 124°; metaldehyde forms bright feathery crystals which readily sublime. (A., 27, 319; 162, 143; 203, 26, 43.)

Reaction LXXXIII. Action of Caustic Alkali on the $\alpha\beta$-chlorohydrins. (A. Spl., (1861), 1, 221; J., 13, 456.)—When the chlorohydrins which contain chlorine and hydroxyl attached to adjacent carbons are heated with caustic alkali, elimination of hydrochloric acid occurs and an inner ether or oxide is obtained.

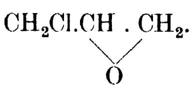


$$R.CHOH.CHCl.R_1 + NaOH = R.CH.CH.R_1 \; (>O) + NaCl + H_2O.$$

These oxides are unstable, reacting with water to form glycols, with hydrochloric acid to regenerate the chlorohydrin, and so on. The simplest member of this group, ethylene oxide is an important organic intermediate.

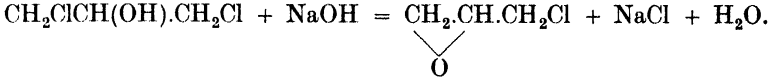
For preparation of cyclohexene oxide, see C. V., I, 185.

Preparation 153.—**Epichlorohydrin.**



$CH_2Cl.CH\,.\,CH_2$ (>O). C_3H_5OCl. 92·5.

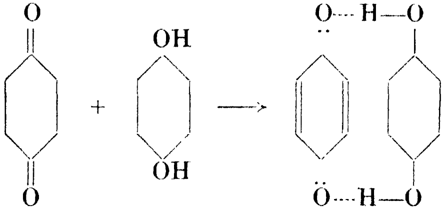
The dichlorohydrin (Preparation 317) is added to a slight excess of hot caustic soda (D. 1·5) solution contained in a distillation apparatus at reduced pressure, and is dropped in at approximately the same rate as the epichlorohydrin distils over when the pressure is maintained below 100 mms. The distillate is separated, dried over anhydrous sodium sulphate, and systematically fractionated (p. 23). The fraction B.P. ^{760} 116°–117° is pure epichlorohydrin. Some dichlorohydrin is recovered.



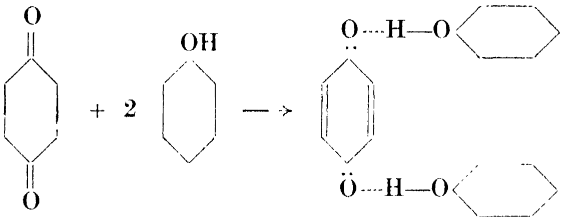
$$CH_2ClCH(OH).CH_2Cl + NaOH = CH_2.CH.CH_2Cl \; (>O) + NaCl + H_2O.$$

Yield.—90% theoretical. Colourless mobile liquid; ethereal smell; B.P. 117°; D. $^{0}_{4}$ 1·203. (C. V., II, 256.)

Reaction LXXXIV. Addition of Phenols to Quinones. (A., 200, 251; 215, 134; B., 24, 1341.)—Quinones readily react with 1 mol. of *p*-di-hydric phenols and 2 mols. of other phenols to form the highly-coloured ether compounds, quinhydrones and phenoquinones respectively.



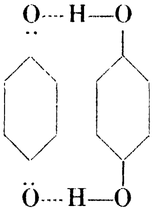
Quinhydrone.



Phenoquinone.

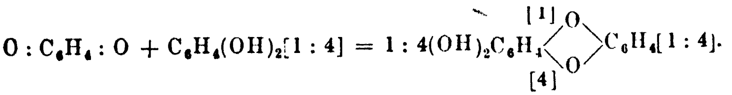
Quinhydrone can be prepared from quinone or quinol by partial reduction or oxidation respectively (see Preparation 154).

PREPARATION 154.—**Quinhydrone.**



$C_{12}H_{10}O_4$. 218.

Method I.—10 gms. (1 mol.) of quinone and 10 gms. (1 mol.) of quinol are separately dissolved in the minimum quantity of water, and the solutions mixed and warmed. After cooling, the precipitate is filtered off and washed with water.



$$O:C_6H_4:O + C_6H_4(OH)_2[1:4] = 1:4(OH)_2C_6H_4\overset{[1]}{\underset{[4]}{<}}\begin{matrix}O\\O\end{matrix}>C_6H_4[1:4].$$

Yield.—Almost theoretical (20 gms.).

Method II.—10 gms. (1 mol.) of quinol are dissolved in water and heated with an aqueous solution of 14·5 gms. (2 mols.) of ferric chloride.

The quinhydrone rapidly separates. It is filtered off and washed with water.

$$C_6H_4(OH)_2 + 2FeCl_3 = C_6H_4O_2 + 2FeCl_2 + 2HCl.$$

$$C_6H_4O_2 + C_6H_4(OH)_2 = (OH)_2C_6H_4.O_2.C_6H_4.$$

Yield.—Almost theoretical (10 gms.). Lustrous green prisms or leaflets; quinone-like odour; soluble in warm petroleum ether; insoluble in cold water; M.P. 171°. (B., 24, 1341; 28, 1615.)

PREPARATION 155.—**Phenoquinone.**

$$C_6H_5OH \cdots OC_6H_4O \cdots HOC_6H_5. \qquad C_{18}H_{16}O_4. \qquad 296.$$

20 gms. (1 mol.) of phenol and 12 gms. (1 mol.) of quinone are dissolved in petroleum ether or benzene and refluxed for 10 minutes. The solution is then concentrated on a water bath until crystals separate on cooling. They are filtered off and washed with water.

Yield.—Almost theoretical (32 gms.). Red acicular crystals; insoluble in water; somewhat soluble in warm petroleum ether; M.P. 71°; sublimes on heating. (A., 204, 251; 215, 134.)

The above preparation can also be performed in aqueous solution.

Resorcinolquinone and pyrogallolquinone are similarly prepared; they decompose at 90° and above 120° respectively.

CHAPTER XV

OXYGEN TO CARBON

OXY COMPOUNDS

Aldehydes, Ketones, and Quinones

ALDEHYDES, ketones and quinones are important ; most of the methods of preparing them come into this section. The reactions on which these methods are based are chiefly of two kinds—purely oxidising reactions (Preparation 440), and reactions involving hydrolysis followed by oxidation (Preparation 156).

Reaction LXXXV. Simultaneous Hydrolysis and Oxidation of Monohalogen Compounds. (A., 22, 1 ; 143, 186.)—When benzyl chloride and its derivatives are heated with an aqueous solution of a mild oxidising agent, such as copper nitrate, lead nitrate, etc., combined hydrolysis and oxidation occurs, and benzaldehyde and its derivatives are obtained.

$$C_6H_5CH_2Cl \xrightarrow{H_2O} C_6H_5CH_2OH \xrightarrow{O} C_6H_5CHO.$$

PREPARATION 156.—**Benzaldehyde** (*Phenyl-methanal*).

$$C_6H_5CHO. \qquad C_7H_6O. \qquad 106.$$

50 gms. (1 mol.) of benzyl chloride (see p. 357), 50 gms. (excess) of copper nitrate and 300 c.cs. of water are refluxed together in a current of carbon dioxide for about 8 hours, and until a sample of the oil present contains very little chlorine (test). The mixture is extracted with ether, the ether removed on a water bath, and the residual oil mechanically shaken for 1 hour with a saturated solution of sodium bi-sulphite. After standing for 2 hours, the crystals which have separated are filtered at the pump and washed first with a little alcohol and then with ether. They are warmed with excess of 10% sulphuric acid ; the aldehyde which separates is extracted with ether, the extract dried over anhydrous sodium sulphate, the ether removed on a water bath and the residue distilled in a current of carbon dioxide. The fraction 176°–181° is retained.

$$2C_6H_5CH_2Cl + Cu(NO_3)_2 = 2C_6H_5CHO + CuCl_2 + 2HNO_2.$$

Yield.—40% theoretical (17 gms.). Colourless oil ; characteristic odour ; B.P. 179° ; D. $^{15}_{4}$ 1·0504. (A., 22, 1 ; 143, 186.)

Reaction LXXXVI. Hydrolysis of certain Dihalogen Compounds. (A. Spl., 2, 253 ; A., 139, 319 ; D.R.P., 82927 ; 85493.)—When dihalogen compounds containing two halogen atoms attached to the same carbon atom are boiled with water in presence of an alkali or certain metals, hydrolysis occurs, and an aldehyde or ketone is obtained.

$$R.CCl_2R_1 \xrightarrow{2H_2O} R.C(OH)_2R_1 \longrightarrow RCOR_1.$$

The process is used on a commercial scale to prepare benzaldehyde by heating benzal chloride with an aqueous suspension of chalk or milk of lime under pressure. Water is sufficient to bring about hydrolysis. Alkali is added to remove the hydrogen chloride formed, and so prevent the reverse reaction taking place. In place of an alkali, a trace of iron powder can be used; the reaction then takes a slightly different course, only 1 mol. of water being required for 1 mol. of the dichloride.

PREPARATION 157.—**Benzaldehyde** (*Phenyl-methanal*).

$$C_6H_5CHO. \qquad C_7H_6O. \qquad 106.$$

Method I.—20 gms. (1 mol.) of benzal chloride (see p. 357) are refluxed for 4 hours in an atmosphere of carbon dioxide with 200 c.cs. of water and 40 gms. of precipitated chalk in a round flask heated on an oil bath which is kept at 130°. The whole is then steam distilled in an atmosphere of carbon dioxide (see p. 34). The distillate is extracted with ether, the ether removed on a water bath and the residual benzaldehyde purified by means of its bisulphite compound, as described in Preparation 156.

$$C_6H_5CHCl_2 \xrightarrow{H_2O} C_6H_5CH(OH)_2 \longrightarrow C_6H_5CHO.$$

Yield.—70% theoretical (9 gms.). (A. Spl., 2, 253; 139, 319.)

Method II.—150 gms. (1 mol.) of benzal chloride (see p. 357) are heated in a round-bottomed flask to 30° with agitation; 0·5 gms. of iron powder and 25 gms. (excess) of water are then added, and the mixture cautiously heated until hydrogen chloride is evolved (about 100°). Heating may be discontinued until the action subsides, when more heat is applied. About 20 gms. sodium carbonate are added to give an alkaline reaction, and the benzaldehyde distilled in steam in an atmosphere of carbon dioxide and purified as described in Preparation 156.

$$C_6H_5CHCl_2 + H_2O \longrightarrow C_6H_5CHO + 2HCl.$$

Yield.—80% theoretical (75 gms.). Colourless oil; characteristic odour; insoluble in water; soluble in ether; B.P. 179°; D. $^{15}_{4}$ 1·0504. (D.R.P., 82927; 85493.)

In all these preparations of benzaldehyde the chief loss is due to oxidation of the aldehyde to benzoic acid. The acid may be removed from the reaction mixture from which the benzaldehyde has been steam distilled by filtration while still hot, and acidification with much concentrated hydrochloric acid. Benzoic acid separates on cooling.

Reaction LXXXVII. Hydrolysis of certain Anils. (B., 35, 1228; D.R.P., 121745.)—When derivatives of toluene which contain negative groups in the *o*- and *p*-positions are treated with *p*-nitrosodimethylaniline, owing to the activation of the methyl group by the presence of the two negative groups, condensation to an anil occurs.

$$C_6H_3(NO_2)_2(CH_3)[2:4:1] + C_6H_4(NO).N(CH_3)_2[1:4]$$
$$= C_6H_3(NO_2)_2CH:N.C_6H_4N(CH_3)_2 + H_2O.$$

These anils are readily hydrolysed by acids to yield derivatives of benzaldehyde.

$$C_6H_3(NO_2)_2CH : N.C_6H_4N(CH_3)_2 \xrightarrow{H_2O} C_6H_3(NO_2)_2CHO + H_2N.C_6H_4N(CH_3)_2.$$

PREPARATION 158.—**2 : 4-Dinitrobenzaldehyde.**

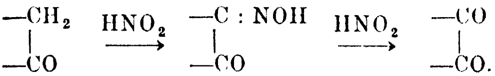
$C_6H_3(NO_2)_2(CHO)[2:4:1]$. $C_7H_4O_5N_2$. 196.

50 gms. (1 mol.) of 2 : 4-dinitrotoluene, 50 gms. (excess) of *p*-nitroso dimethylaniline and 90 gms. of crystallised sodium carbonate are refluxed on a water bath for 6 hours with 300 c.cs. of alcohol. The anil which separates is filtered off, washed with boiling water, and recrystallised from acetone. The whole is then mechanically shaken for 4 hours with 350 gms. (excess) of nitric acid (D. 1·17) and 300 c.cs. of benzene, filtered, the benzene layer separated and the solvent removed on a water bath. The residue is recrystallised from alcohol, with the addition of decolorising carbon being precipitated from the alcoholic solution by dilution with water. The crystals which separate contain 1 mol. of alcohol of crystallisation ; this they lose at 90°. The aqueous layer above is re-shaken with benzene and nitric acid, and worked up for further aldehyde as above.

$$C_6H_3(NO_2)_2(CH_3)[2:4:1] + NOC_6H_4N(CH_3)_2[1:4] \longrightarrow$$
$$C_5H_3(NO_2)_2CH : NC_6H_4N(CH_3)_2 \xrightarrow{H_2O}$$
$$C_6H_3(NO_2)_2CHO[2:4:1] + H_2NC_6H_4N(CH_3)_2.$$

Yield.—80% theoretical (42 gms.). Yellowish crystals ; insoluble in water ; soluble in alcohol and benzene ; M.P. 72° ; B.P. ^{10} 190° ; B.P. ^{20} 210°. (B., 35, 1228 ; D.R.P., 121745 ; C. V., II, 223.)

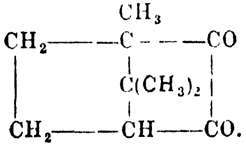
Reaction LXXXVIII. Action of Nitrous Acid on the Monoximes of α-Diketones. (A., 274, 71.)—When compounds containing the group —CH_2—CO—are treated with nitrous acid in presence of sodium, an "*iso*-nitroso compound" identical with the monoxime of the corresponding α-diketone is obtained (see p. 118). From the monoxime by the further action of nitrous acid in the presence of glacial acetic acid, the diketone itself is formed. See also p. 315.



$$\begin{array}{l} —CH_2 \\ \ | \\ —CO \end{array} \xrightarrow{HNO_2} \begin{array}{l} —C : NOH \\ \ | \\ —CO \end{array} \xrightarrow{HNO_2} \begin{array}{l} —CO \\ \ | \\ —CO. \end{array}$$

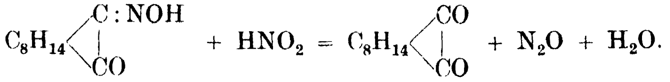
It may be noted that aldehydes and ketones can usually be obtained from the corresponding oximes, phenyl-hydrazones, semi-carbazones, etc., by hydrolysis with dilute mineral acids.

PREPARATION 159.—**Camphorquinone.**



$C_{10}H_{11}O_2$. 166.

To 20 gms. (1 mol.) of *iso*-nitroso-camphor dissolved in 35 c.cs. of glacial acetic acid, 9 gms. (excess) of sodium nitrite in 20 c.cs. of water are slowly added with mechanical stirring. Initially the temperature must not be allowed to rise above 20°, but when the evolution of gas ceases, the mixture is heated until no more gas is evolved. When cool, the whole is poured into an excess of cold water, and the precipitate filtered off at the pump, well washed with cold water, and dried on a porous plate. It is then sublimed at 60° (see p. 35).



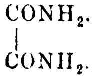
$$C_8H_{14}\left\langle\begin{array}{l}C:NOH\\ |\\ CO\end{array}\right. + HNO_2 = C_8H_{14}\left\langle\begin{array}{l}CO\\ |\\ CO\end{array}\right. + N_2O + H_2O.$$

Yield.—50% theoretical (9 gms.). Yellow needles; sweet odour; insoluble in water; sublimes when heated; M.P. 198°. (A., 274, 71.)

Reaction LXXXIX. Hydrolysis of Nitriles to Amides. (B., 18, 355.)—When nitriles are heated with acids or alkalis they are hydrolysed to the corresponding acids passing intermediately through the amides. It is possible only in a few instances (e.g. oxamide) to stop the hydrolysis at this intermediate stage, unless alkaline hydrogen peroxide is employed, when the amide, if aromatic, is obtained in almost theoretical yield. Both methods of hydrolysis are illustrated in the following preparations.

$$R.C\vdots N \xrightarrow{H_2O} R.CO.NH_2.$$

PREPARATION 160.—**Oxamide** [*Diamide of ethan-diacid*].

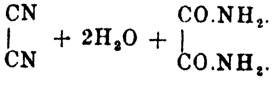


$$\begin{array}{l}CONH_2.\\ |\\ CONH_2.\end{array}$$

$C_2H_4O_2N_2$. 88.

(To be carried out in a *good* fume cupboard.)

25 gms. (1 mol.) of crystallised copper sulphate are dissolved in 75 c.cs. of water in a distilling flask heated on a water bath, and a warm solution of 13 gms. (2 mols.) of 98% potassium cyanide in 25 c.cs. of water is added (*caution! cyanogen is extremely poisonous*). The evolved cyanogen is led into 20 c.cs. of cold conc. hydrochloric acid. When all the cyanide has been added, the second equivalent of cyanogen is expelled by adding, in the same way, a solution of 16 gms. (1 mol.) of ferric chloride in 20 c.cs. of water. Oxamide separates out, provided the hydrochloric acid is kept quite cool. It is washed with water.



$$\begin{array}{l}CN\\ |\\ CN\end{array} + 2H_2O + \begin{array}{l}CO.NH_2.\\ |\\ CO.NH_2.\end{array}$$

Yield.—50% theoretical (4·5 gms.). White crystalline solid; partly sublimes on heating, but for the most part decomposes; sparingly soluble in water and in alcohols. (B., 18, 355.)

PREPARATION 161.—**Benzamide** (*Amide of phenylmethan acid*).

$C_6H_5.CO.NH_2$. C_7H_7ON. 121.

20 gms. (1 mol.) of benzonitrile are added to 300 c.cs. (excess) of 3% (10 volumes) aqueous hydrogen peroxide containing 5 c.cs. of 2N caustic soda. The mixture is warmed on a water bath to 40°, and then shaken in an uncorked bottle until the oil has completely disappeared. The precipitate which forms is filtered off at the pump, and recrystallised from alcohol or hot water.

$$2C_6H_5CN + 2H_2O_2 = 2C_6H_5CO.NH_2 + O_2.$$

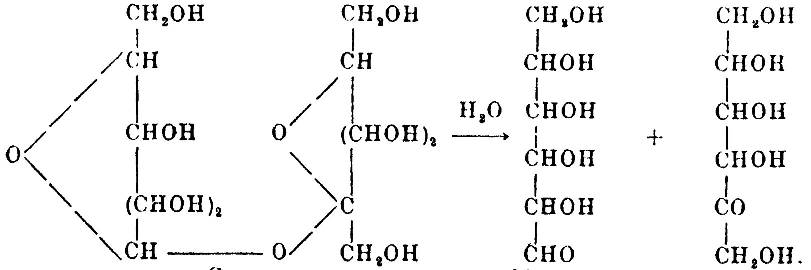
Yield.—Theoretical (24 gms.). White crystalline powder; soluble in hot water; M.P. 128°. (B., 18, 355.) See also O. S., XIII, 94.

Reaction XC. Hydrolysis of Polysaccharides. (J. pr., [2] 2, 1, 245; B., 13, 1761; 28, 1429.)—When polysaccharides are heated with mineral acids, hydrolysis to the component monosaccharides takes place. Glycosides are similarly hydrolysed to monosaccharides and alcohols.

In this way

cane sugar yields glucose and fructose,
lactose yields glucose and galactose,
maltose yields glucose,
methyl glucoside yields glucose and methyl alcohol.

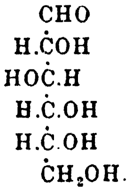
These hydrolyses can also be brought about by means of various enzymes, e.g. invertase will hydrolyse cane sugar, maltase maltose, and so on. (See Haworth, "The Constitution of Sugars" (Arnold & Co., 1929).)



Cane sugar. Glucose. Fructose

More complicated compounds can be brought within the scope of the reaction; thus starch can be hydrolysed to glucose in this way.

Preparation 162.—**Glucose** (*Pentolhexanal*, + − + +).



$$\begin{array}{l} CHO \\ H.\dot{C}OH \\ HO\dot{C}.H \\ H.\dot{C}.OH \\ H.\dot{C}.OH \\ \dot{C}H_2OH. \end{array} \qquad C_6H_{12}O_6. \quad 180.$$

70 gms. of fuming hydrochloric acid (38%) are mixed with 1,500 c.cs. of 95% alcohol, and the whole warmed on a water bath; 500 gms. of

finely-powdered cane sugar are gradually added with mechanical stirring, the temperature being kept at 50° throughout. When all the sugar has dissolved, the liquid is filtered, cooled, seeded with 0·5 gm. of glucose crystals, and allowed to stand for a week at ordinary temperature. The crystals which separate are filtered off at the pump, washed with absolute alcohol, and recrystallised by dissolving in a very little hot water to form a syrup, and adding hot methyl or ethyl alcohol until the solution becomes turbid. On cooling, the sugar which separates is filtered off at the pump, and washed with absolute alcohol.

$$\underset{\text{Cane sugar}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Glucose}}{C_6H_{12}O_6} + \underset{\text{Fructose}}{C_6H_{12}O_6}.$$

Colourless crystals ; very soluble in water ; sparingly soluble in alcohol ; M.P. 86° ($\cdot 1H_2O$) ; 146° (anhydrous). (J. pr., [2], 21, 245.)

Reaction XCI. (*a*) **Oxidation of Aromatic Hydrocarbons to Aldehydes by the action of Chromyl Chloride in Carbon Disulphide Solution.** (Etard.) (A. Ch., [5], 22, 225.)—In this reaction the hydrocarbon and chromyl-chloride are both dissolved in carbon disulphide, and the solutions carefully mixed. An explosive intermediate compound is precipitated, and this is separated and decomposed with water to give the aldehyde. The yields are very good, but the method is not often used owing to the inconvenience of working with carbon disulphide and the dangerous nature of the intermediate compounds.

$$RCH_3 + 2CrO_2Cl_2 = RCH.(OCr.Cl_2OH)_2.$$

$$R.CH.(OCrCl_2OH)_2 + 3H_2O = RCHO + 2CrO(OH)_2 + 4HCl.$$

PREPARATION 163.—**Benzaldehyde** (*Phenyl-methanal*).

$C_6H_5.CHO$. C_7H_6O. 106.

(*Great caution must be observed in performing this experiment. No flame must be brought near the apparatus.*)

10 gms. (excess) of toluene and 30 gms. (2 mols.) of chromyl chloride (see p. 521) are each dissolved in anhydrous carbon disulphide, the former in 50 gms., and the latter in 120 gms. ; the former solution is placed in a litre flask fitted with a thermometer and long reflux condenser, and the latter is added in 10 c.cs. quantities, the reaction each time being allowed to moderate before further addition. Should no reaction occur on the first addition, the mixture is allowed to stand for 15 minutes before further addition. The reaction is very vigorous, and the flask must be cooled by immersing in a bath of ice-water, so that the temperature of the mixture never rises above 45°. When addition is complete, the mixture is allowed to stand for 3 hours, the explosive intermediate compound which appears as a precipitate is filtered off at the pump, well washed with anhydrous carbon disulphide, dried by blowing air through it, and decomposed by adding in small quantities to 1 litre of cold water. The chromic acid formed is reduced with gaseous sulphur dioxide, and the liquid steam distilled in a current of carbon dioxide to remove benzaldehyde, which is extracted from the distillate with ether. The extract is dried over calcium chloride, the ether removed on a water bath, and the residue distilled in a

current of carbon dioxide, the fraction 177°–182° being retained. (For the purification of the aldehyde by means of its bisulphite compound, see p. 229.)

Colourless oil; pleasant odour; insoluble in water; B.P. 179°; $D. {}^{15}_{4}$ 1·0504. (J. C. S., 91, 261.)

Benzaldehyde may be prepared from benzene by the direct action of carbon monoxide, see J. Eng., 25, 495.

Reaction XCI. (*b*) **Oxidation of Aromatic Hydrocarbons to Aldehydes by the action of Chromic Acid in Acetic Anhydride Solution.** (A., 311, 353; D.R.P., 121788.)—In the ordinary way, chromic acid oxidises hydrocarbons to aldehydes and then to acids. But if acetic anhydride and conc. sulphuric acid are present, the di-acetyl derivative of the aldehyde is formed and this does not undergo further oxidation. The aldehyde is obtained from the di-ester by hydrolysis. (Cf. the preparation of salicylaldehyde, p. 112.) For mechanism of oxidation, see Ann. Rep., 1945, 130; J. C. S., 1946, 1151.

$$RCH_3 \xrightarrow{O_2} RCHO \xrightarrow{(CH_3CO)_2O} R.CH.(OCOCH_3)_2 \xrightarrow{HCl} R.CHO.$$

PREPARATION 164.—*Iso*-Phthalaldehyde (*m-Phthalaldehyde*).

$C_6H_4(CHO)_2[1:3]$. $C_8H_6O_2$. 134.

60 gms. (excess) of chromic acid are slowly added, with good agitation and cooling in a freezing mixture, to 15 gms. (1 mol.) of *m*-xylene mixed with 250 gms. glacial acetic acid, 500 gms. (excess) acetic anhydride, and 10 c.cs. conc. sulphuric acid. When all has been added, the mixture is kept at 0° until a sample gives a bulky white precipitate when shaken with cold water to decompose the anhydride. It is then poured on to powdered ice and stirred, until the oil formed solidifies. The *iso*-phthalaldehyde tetracetate is filtered off and recrystallised from methyl alcohol (M.P. 101°). The crystallised product is now heated under a reflux for 15 minutes with 150 c.cs. of 5% hydrochloric acid. On cooling, the aldehyde separates, is filtered and recrystallised from hot water.

$$C_6H_4(CH_3)_2 \longrightarrow C_6H_4[CH(OCOCH_3)_2]_2 \longrightarrow C_6H_4(CHO)_2.$$

Yield.—80% theoretical (15 gms.). Colourless needles; soluble in hot water; M.P. 89°. (A., 311, 353; D.R.P., 121788.)

Reaction XCI. (*c*) **Oxidation of Aromatic Hydrocarbons to Aldehydes by the action of Cerium Dioxide in presence of Concentrated Sulphuric Acid.** (D.R.P., 158609.)—Cerium dioxide has the property of oxidising aromatic hydrocarbons to aldehydes and no further. The addition of a reagent to combine with the aldehyde group as formed is unnecessary.

$$RCH_3 \xrightarrow{CeO_2} R.CHO.$$

PREPARATION 165.—Benzaldehyde (*Phenyl-methanal*).

C_6H_5CHO. C_7H_6O. 106.

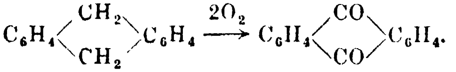
30 gms. (1 mol.) of toluene are heated to 60° with 1,500 gms. (excess) of sulphuric acid (D. 1·5) in a 2-litre round-bottomed flask fitted with a

reflux condenser and mechanical stirrer (see Fig. 36). 250 gms. (excess) of cerium dioxide are gradually added, and the temperature allowed to rise to 90°. When no more dioxide remains, the whole is steam-distilled until all the benzaldehyde passes over. Benzaldehyde is then recovered from the distillate as in Preparation 163.

$$C_6H_5CH_3 + O_2 = C_6H_5CHO + H_2O.$$

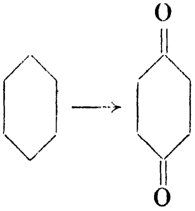
Yield.—70% theoretical (25 gms.). See p. 235. (D.R.P., 158609; J. S. C. I., 51, 159.)

Reaction XCII. (*a*) **Action of Oxidising Agents on Methylene Groups in Aromatic Compounds.** (B., 6, 1347; A. Spl., (1869), 7, 284; A., 279, 258.)—When compounds containing methylene groups attached to two aromatic residues are heated with oxidising agents—chromic acid is usually employed—the two hydrogens of each methylene group are replaced by oxygen to yield carbonyl compounds, which have some or all of the properties of ketones and of quinones. Thus diphenylmethane yields benzophenone, and 9 : 10-dihydroanthracene yields anthraquinone.

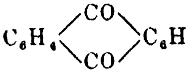


$$C_6H_4\begin{matrix}\diagup CH_2 \diagdown \\ \diagdown CH_2 \diagup\end{matrix}C_6H_4 \xrightarrow{2O_2} C_6H_4\begin{matrix}\diagup CO \diagdown \\ \diagdown CO \diagup\end{matrix}C_6H_4.$$

Reaction XCII. (*b*) **Oxidation of Aromatic Hydrocarbons to Quinones.** (J. C. S., 37, 634; A., 167, 139, 357.)—Although benzene does not react in this way polynuclear aromatic hydrocarbons can be oxidised directly to give quinones analogous to both *o*- and *p*-quinones. The oxidising agent used is chromic acid in glacial acetic or sulphuric acid. Amino-compounds, however, give better yields (see Reaction XCIII).



PREPARATION 166.—**Anthraquinone.**



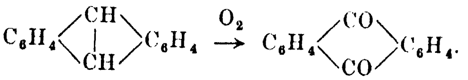
$$C_6H_4\begin{matrix}\diagup CO \diagdown \\ \diagdown CO \diagup\end{matrix}C_6H_4.$$

$C_{14}H_8O_2$. 208.

Anthracene is sublimed with superheated steam (see p. 29) at 200°. This reduces it to a fine state of division.

100 gms. (1 mol.) of moist sublimed anthracene are stirred up with 2 litres of water in a lead-lined pot, fitted with a glass agitator; 200 gms. (excess) of sodium dichromate are added at the same time. The mixture is heated to 80° and 600 gms. (excess) of 50% sulphuric acid are added from a dropping funnel during 10 hours. The presence of chromic acid must always clearly be shown (test with hydrogen peroxide). The mixture is then boiled for 2 hours, evaporated water being replaced at intervals.

The product is filtered off, thoroughly washed and dried. It is heated in 2½ times its weight of conc. sulphuric acid at 120° as long as SO_2 is evolved. After 3 hours it is poured into 3 times its weight of water, and the anthraquinone, which is precipitated, filtered off at the pump. It may be further purified by sublimation at 250°.

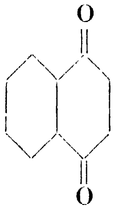


$$C_6H_4\left\langle\begin{array}{c}CH\\|\\CH\end{array}\right\rangle C_6H_4 \xrightarrow{O_2} C_6H_4\left\langle\begin{array}{c}CO\\ \\CO\end{array}\right\rangle C_6H_4.$$

Yield.—90% theoretical (105 gms.). Yellow needles; insoluble in water; soluble in glacial acetic acid; sublimes on heating at 250°; M.P. 277°; an important intermediate for vat dyes. C. V., II, 554, uses as oxidant vanadium pentoxide and sodium chlorate.

Anthraquinone does not possess the properties of a true quinone.

PREPARATION 167.—**α-Naphthaquinone.**



$C_{10}H_6O_2$. 158.

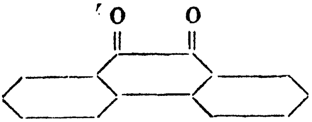
10 gms. (1 mol.) of naphthalene dissolved in 100 c.cs. glacial acetic acid are gradually added with good agitation to 10 gms. (excess) of chromic acid dissolved in 70 c.cs. of 80% acetic acid, the whole being kept at 0°. After standing for 4 days at the ordinary temperature with occasional shaking, the liquid is poured into a litre of water. The precipitated naphthaquinone is then filtered, washed with water and recrystallised from alcohol.

$$C_{10}H_8 + 3O \longrightarrow C_{10}H_6O_2 + H_2O.$$

Yield.—15% theoretical (2 gms.) (cf. yield in Preparation 171). Yellow plates with sharp odour; insoluble in water; soluble in hot alcohol; volatile in steam; M.P. 125°. (J. C. S., 37, 634; A., 167, 357.)

(Cf. *p*-benzoquinone, p. 239).

PREPARATION 168.—**Phenanthraquinone.**



$C_{14}H_8O_2$. **208.**

30 gms. (1 mol.) of phenanthrene are dissolved in 150 gms. of warm glacial acetic acid, and 80 gms. (excess) of chromic acid dissolved in about 250 gms. of glacial acetic acid are gradually added. This latter solution is prepared by dissolving the chromic acid in the *minimum* quantity of water, and pouring into glacial acetic acid. The addition is regu-

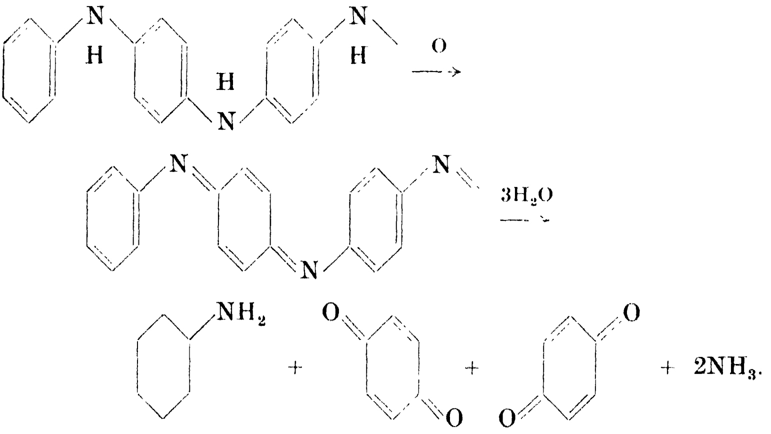
lated so that the heat of reaction keeps the mixture just on the boil throughout. When addition is complete most of the acetic acid is distilled off, and the residue treated with much water. The precipitate is filtered at the pump, washed with a little hot water, shaken with a warm dilute sodium bisulphite solution and filtered ; the filtrate is warmed on a water bath, and the quinone precipitated by addition of sulphuric acid. This precipitate is recrystallised from an excess of boiling alcohol.

$$C_{14}H_{10} + 3O = C_{14}H_8O_2 + H_2O.$$

Yield.—Almost theoretical (35 gms.). Orange needles ; odourless ; not volatile in steam ; insoluble in water and in cold alcohol ; soluble in glacial acetic acid ; M.P. 198°. (A., 167, 139.)

Reaction XCIII. Oxidation of Primary Aromatic Amines and their *para*-substituted Derivatives to Quinones. (A., 27, 268 ; 194, 202 ; 211, 49 ; 215, 125 ; B., 19, 1467 ; 20, 2283 ; 25, 982 ; 36, 4390.)—Many primary aromatic amines, when oxidised with chromic acid, or with sulphuric acid and sodium chlorate in presence of vanadium pentoxide, readily yield *p*-quinones, aniline, for example, giving *p*-benzoquinone. The mechanism of this reaction is believed to be as follows :

$$C_6H_5NH_2 \xrightarrow{O} C_6H_5\dot{N}H \xrightarrow{C_6H_5NH_2}$$



With aminophenols or diamines (*o*- or *p*-) the mechanism of reaction is as follows :

$$OHC_6H_4NH_2 \xrightarrow{O} O:C_6H_4:NH \xrightarrow{H_2O} O:C_6H_4:O$$

$$NH_2C_6H_4NH_2 \xrightarrow{O} NH:C_6H_4:NH \xrightarrow{H_2O} O:C_6H_4:O.$$

p-Amino-phenols, most *p*-substituted primary amines, e.g. *p*-diamines, *p*-alkylamines, such as *p*-toluidine, sulphanilic acid and its derivatives, also yield quinones. In fact, the reaction can be used as a test for *p*-substituted primary amines. *p*-Benzoquinone is usually made from aniline or hydroquinone ; for the other *p*-quinones the *p*-amino-phenols, which are easily obtained by reduction of the *p*-nitroso-phenols and of azo-phenols, are employed. These reactions also apply, but not so widely in the naphthalene series.

PREPARATION 169.—*p*-**Benzoquinone** (*Quinone*).

$O : C_6H_4 : O.$ $C_6H_4O_2.$ 108.

To 50 gms. (1 mol.) of aniline dissolved in 1,300 gms. (excess) of 25% sulphuric acid, a cold 20% solution of 50 gms. of sodium dichromate is slowly added in 3 hours, with good cooling and mechanical stirring. The temperature must throughout be kept below 4°. When all the dichromate has been dropped in the whole is allowed to stand for 24 hours, and 100 gms. of sodium dichromate added in the same manner as before. After 6 hours the liquid is extracted 6 times with its own volume of ether, the latter being recovered each time by distillation and used again. The shaking must not be too vigorous as the mixture tends to emulsify very readily. The crude product from the ether extraction is distilled in steam (see p. 28).

If sodium dichromate is not available the potassium salt may be employed. Equivalent quantities are taken as for the sodium salt, but the potassium salt is added in the form of powder, and not in aqueous solution.

It is usual to treat half the solution, after oxidation is complete, with sulphur dioxide to obtain quinol (see p. 193). As quinone is more difficult to extract with ether from water than quinol, the whole resulting solution may be worked up from quinol, and the latter, when purified, oxidised with sodium dichromate solution to quinone.

$$C_6H_5NH_2 \longrightarrow O : C_6H_4 : O.$$

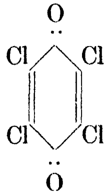
Yield.—70% theoretical (40 gms.). Yellow, acicular crystals ; penetrating odour ; slightly soluble in water ; soluble in alcohol and ether ; sublimes on heating ; M.P. 116°. (A., 27, 268 ; 45, 354 ; 200, 240 ; 215, 125 ; B., 19, 1467 ; 20, 2283 ; O. S., VIII, 122.)

Similarly *o*-tolu-*p*-quinone (M.P. 67°) may be prepared from *o*-toluidine.

C. V., I, 482, and C. V., II, 553, describe preparation of quinone from quinol.

For electrolytic oxidation of benzene to *p*-benzoquinone and quinol, see E. P., 430572.

PREPARATION 170.—**Chloranil** (*Tetrachloro-p-benzoquinone*).



$C_6O_2Cl_4.$ 246.

20 gms. (1 mol.) of 2 : 6-dichloro-4-nitroaniline are reduced to 2 : 6-dichloro-1 : 4-diaminobenzene by refluxing with 800 c.cs. (excess) of conc.

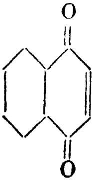
hydrochloric acid and 30 gms. of tin until the metal dissolves. 20 gms. (excess) of potassium chlorate are gradually added, the liquid being maintained at the boil for 15 minutes after all the chlorate has been added. The liquid is diluted with much water and filtered ; the precipitate is well washed with water, dried and recrystallised from boiling toluene.

$$C_6H_2Cl_2(NH_2)_2[2:6:1:4] \xrightarrow{O_2+Cl_2} C_6Cl_4O_2.$$

Yield.—90% theoretical (22 gms.). Yellow leaflets ; characteristic odour ; insoluble in water ; sublimes on heating. (B., 36, 4390.)

The potassium chlorate both oxidises and chlorinates. If chromic acid, or even weaker oxidising agents, is employed the dichloro-quinone is obtained. The oxidation of aminophenols is illustrated in the following, in which nitrous acid serves as oxidising agent.

PREPARATION 171.—**α-Naphthaquinone.**



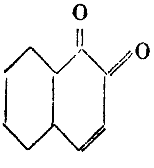
$C_{10}H_6O_2$. 158.

To 20 gms. of finely-powdered 1 : 4-aminonaphthol, or an equivalent amount of one of its salts suspended in 100 c.cs. (excess) of hydrochloric acid (D. 1·05), 20 gms. (excess) of sodium nitrite are slowly added. The precipitate formed is well washed with water, filtered, and dried on a porous plate. The filtrate is extracted with ether, the extract dried over calcium chloride, filtered, and the ether removed on a water bath at 60°. The residue and the dried precipitate are recrystallised from petroleum ether.

$$C_{10}H_6(OH)(NH_2)[1:4] \xrightarrow{O_2} C_{10}H_6O_2[1:4].$$

Yield.—80% theoretical (16 gms.). Yellowish plates ; characteristic odour ; soluble in hot alcohol ; volatile in steam ; sublimes at 100° ; M.P. 125°. (A., 183, 242 ; C. V., I, 383.)

PREPARATION 172.—**β-Naphthaquinone.**



$C_{10}H_6O_2$. 158.

50 gms. (1 mol.) of finely-powdered 1 : 2-aminonaphthol (see p. 373) are suspended in 250 c.cs. of 30% sulphuric acid, and 30 gms. (excess) of 10% aqueous potassium or sodium dichromate solution slowly added with mechanical stirring, the temperature being maintained at 0°. The

precipitate is filtered off, well washed with water, dried on a porous plate, and recrystallised from petroleum ether.

$$C_{10}H_6(OH)(NH_2)[1:2] \longrightarrow C_{10}H_6O_2[1:2].$$

Yield.—75% theoretical (35 gms.). Red acicular crystals; odourless; non-volatile in steam; M.P. 115°. (A., 189, 153; 194, 202; 211, 49; B., 25, 982; C. V., II, 430.)

The preparations of α- and β-naphthaquinone should be compared with those of phenanthraquinone, and the corresponding benzoquinones (see p. 239).

Reaction XCIV. Conversion of Nitriles to Aldehydes by the action of Hydrochloric Acid and Stannous Chloride followed by Hydrolysis of the Aldime-Stannichloride so formed (Stephen). (J. C. S., 127, 1874.)—When a nitrile is added to anhydrous stannous chloride (p. 521) in dry ether saturated with hydrogen chloride, a white crystalline aldime-stannichloride separates, owing to the reduction of the imino-chloride first formed:

$$R.C \vdots N + HCl \longrightarrow R.CCl:NH.$$

$$R.CCl:NH + SnCl_2 + 2HCl \longrightarrow R.CH:NH.HCl + SnCl_4.$$

Two hours is usually sufficient time for the completion of the reaction and the separation of these salts. The products are readily hydrolysed by warm water. The yields from aliphatic and aromatic (other than *o*-substituted) nitriles are usually quantitative. The method has found an important application in the synthesis of thyroxine (Ann. Rep., 1926, 236.) The details of the following preparation constitute a general method of procedure. See Chem. Rev., 38, 243.

PREPARATION 173.—*p*-**Tolualdehyde.**

$CH_3C_6H_4CHO$. C_8H_9O. 120.

30 gms. anhydrous stannous chloride (see p. 521) and 100 c.cs. anhydrous ether are placed in a 500-c.c. three-necked flask fitted with reflux and calcium chloride tube, tap-funnel and inlet tube leading to the bottom of the flask. The flask is cooled in ice-water and dry hydrogen chloride passed in until the stannous salt has formed a heavy oily layer, or homogeneous solution. 12 gms. *p*-toluonitrile (Prep. 82) in 30 c.cs. anhydrous ether are added during 10 minutes with gentle shaking. After keeping for one hour at room temperature, aldimine stanni-chloride separates, and is filtered (use a fume cupboard) and washed with a little anhydrous ether. The product is dissolved in 100 c.cs. water and heated on a steam bath. The aldimine is then hydrolysed to the oily *p*-tolualdehyde, which is extracted with ether, the extract dried over anhydrous sodium sulphate, and the product obtained by evaporation of the ether. It is then distilled under reduced pressure, the fraction B.P. 106° at 10 m.m. being collected.

***Yield.*—80% theoretical (10 gms.). Colourless liquid. B.P. 205°.**

CHAPTER XVI

OXYGEN TO CARBON

HYDROXY-OXY COMPOUNDS

Acids

VARIOUS hydrolytic and oxidation reactions give rise to acids—the hydroxy-oxy compounds which have the hydroxy and oxy (carbonyl) groups attached to the same carbon. In none of the reactions is the product necessarily a hydroxy-oxy compound with these groups attached to different carbons.

Reaction XCV. Hydrolysis of Nitriles. (B., 19, 1950 ; 20, 241, 592 ; A., 258, 10.)—On heating with aqueous solutions of mineral acids or alkalis, the nitriles are converted respectively into the corresponding acids or into the alkali salts of the latter. Aqueous solutions of sodium carbonate can also be employed if the heating is performed under pressure. The reaction occurs in two stages.

$$RC:N \xrightarrow{H_2O} R.CO.NH_2 \xrightarrow{HOH} R.COOH.$$

It is difficult to stop the hydrolysis at the intermediate amide stage (see p. 232).

It is not always necessary to isolate the nitriles on their formation in order to hydrolyse them to acids (see p. 164). Also without isolation, the acid formed can be simultaneously esterified by using for hydrolysis aqueous alcoholic solutions of sulphuric acid (see p. 260 ; cf. also p. 261).

In all these reactions water is the hydrolysing agent, the acid or alkali acting as catalyst.

PREPARATION 174.—**Mandelic Acid** (*Phenylglycollic Acid*).

$$C_6H_5CH(OH)COOH. \qquad C_8H_8O_3. \qquad 152.$$

(*This preparation should be conducted in a fume cupboard.*)

65 gms. freshly-prepared mandelonitrile (p. 162) and 85 c.cs. conc. hydrochloric acid are placed in an evaporating basin and the mixture allowed to stand for 12 hours. It is then heated on a steam bath to remove excess water and hydrochloric acid. The mixture, after heating for 6 hours, is cooled, with stirring, and the mandelic acid and ammonium chloride which separate filtered off. The filtrate is evaporated to dryness. The total residue is dried in air and ground in a mortar. The mixture is then washed twice in a flask with 150-c.c. portions of cold benzene and again filtered. The mandelic acid is separated by extracting in a Soxhlet apparatus with hot benzene and crystallising.

$$C_6H_5CH(OH)CN \longrightarrow C_6H_5CH(OH)COOH.$$

Yield.—60% theoretical (45 gms.). Rhombic crystals ; M.P. 118°. (J. C. S., 113, 12 ; O. S., VI, 59 ; XXIII, 48.)

PREPARATION 175.—*p*-**Toluic Acid** (1-*Methyl*-4-*carboxy-benzene*).

$C_6H_4(CH_3)(COOH)[1:4]$. $C_8H_8O_2$. 136.

20 gms. (1 mol.) of *p*-toluonitrile (see p. 160) are refluxed with 160 gms. (excess) of 85% sulphuric acid, until crystals appear in the condenser. The well-cooled mixture is diluted with two volumes of water, and the precipitate filtered, well washed with cold water, and recrystallised from hot water or aqueous alcohol with the addition of charcoal.

$$C_6H_4(CH_3)(CN)[1:4] \xrightarrow{H_2O} C_6H_4(CH_3)(COOH)[1:4].$$

Yield.—85% theoretical (20 gms.). Colourless crystals ; soluble in hot water and in alcohol ; M.P. 178°. (A., 258, 10.) See also J. Eng., 23, 1129.

PREPARATION 176.—**Phenylacetic Acid** (*Phenylethan acid*).

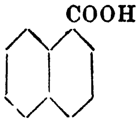
$C_6H_5CH_2COOH$. $C_8H_8O_2$. 136.

50 gms. (1 mol.) of benzyl cyanide and 150 gms. (excess) of 80% sulphuric acid are placed in a ½-litre round-bottomed flask connected by a glass tube bent twice at right angles with a second ½-litre round-bottomed flask fitted with a two-holed cork. The end of the tube is flush with the cork in one hole. Through the second hole passes a vertical glass tube, 50 cms. long, dipping just below the surface of 250 c.cs. of water in the flask. In the middle of this tube a large bulb is blown. The whole apparatus is fitted up in a fume cupboard. The mixture is gently heated by a naked flame, until small bubbles are seen to rise from the surface of the lower layer of acid. In a few minutes a vigorous reaction begins, the liquid in the flask boils, and a small quantity of benzyl cyanide distils over into the second flask, some of the water in which is forced up into the bulb. When the reaction is over, the flask is again heated for 3 minutes and allowed to cool, its contents solidifying in so doing. The solid residue is washed with cold water, dissolved in hot water, the solution neutralised with sodium carbonate, filtered hot, the filtrate acidified with dilute sulphuric acid, and allowed to stand. The crystals which separate are filtered off, washed with cold water, and recrystallised from hot water.

$$2C_6H_5CH_2.CN + 4H_2O + H_2SO_4 = 2C_6H_5CH_2COOH + (NH_4)_2SO_4.$$

Yield.—80% theoretical (46 gms.). Colourless thin laminated crystals soluble in hot water ; M.P. 76·5° ; B.P. 262° ; K = 0·0056. (B., 19, 1950 20, 592 ; Bl., 37, 287 ; O. S., II, 63.)

PREPARATION 177.—α-**Naphthoic Acid** (1-*Carboxynaphthalene*).



$C_{11}H_8O_2$. 172.

15 gms. (1 mol.) of α-naphthonitrile, 10 gms. (excess) of caustic soda, and 75 c.cs. of 95% alcohol are heated in a sealed tube (see p. 47) at

170° for 5 hours. On opening, the contents of the tube are diluted with 5 volumes of water, and carefully acidified with conc. hydrochloric acid. The precipitate is filtered at the pump, washed with water, and recrystallised from alcohol.

$$C_{10}H_7CN + NaOH + H_2O = C_{10}H_7COONa + NH_3.$$

Yield.—90% theoretical (15 gms.). Colourless crystals ; insoluble in water ; soluble in alcohol ; M.P. 160°. (B., 20, 241.) See C. V., II, 425, for preparation of α- and β-naphthoic acids by Grignard reaction.

Reaction XCVI. Hydrolysis of Esters to Acids. (A., 186, 161 ; 204, 127 ; 215, 26 ; Ann. Rep., 1930, 146.)—When esters are heated with water, hydrolysis occurs, but does not go to completion, the reaction being reversible.

$$R.CO.OR_1 + H_2O \rightleftarrows RCOOH + HOR_1.$$

If, however, aqueous or alcoholic caustic alkali is used, by combining with the acid as formed, it shifts the equilibrium point of the reaction, and almost complete hydrolysis occurs. This reaction could also have been dealt with under Chapter XIII, since alcohols are simultaneously formed ; however, the hydrolysis is more usually undertaken to obtain the acid. Other special cases of hydrolysis have been dealt with elsewhere (see Reaction LXVII). The general method of procedure will be clear from the following.

PREPARATION 178.—Acetic Acid (*Ethan-acid*).

$CH_3.COOH.$ $C_2H_4O_2.$ 60.

20 gms. (1 mol.) of ethyl acetate (see p. 261) are refluxed with 80 gms. (excess) of 25% aqueous caustic potash for 1 hour, until the layer of ester has disappeared, and the mixture no longer smells of it. The whole is then distilled to 100° ; ethyl alcohol can be separated from the distillate by saturation with anhydrous potassium carbonate. The residue in the flask is neutralised with dilute sulphuric acid and evaporated to dryness on a water bath. The solid residue is powdered and distilled with 50 gms. of conc. sulphuric acid to 130°, and the distillate fractionated between 115° and 120°.

Cooling in ice until solidification takes place, and subsequently draining away the still-liquid portion, gives crystals of glacial acetic acid.

Yield.—90% theoretical (12 gms.). Colourless liquid or crystals ; characteristic odour ; miscible with water ; M.P. 16·7° ; B.P. 119° ; D. $^{15}_{4}$ 1·055. (Phil. Trans., 156, 37 ; Bl., 33, 350.)

PREPARATION 179.—Ethylmalonic Acid (*Ethylpropan diacid*).

$C_2H_5.CH(COOH)_2.$ $C_5H_8O_4.$ 132.

20 gms. of diethyl-ethylmalonate (see p. 143) are gradually added to 50 gms. (excess) of 50% aqueous caustic potash in a flask fitted with a reflux condenser, and cooled in water. The mixture so obtained is heated on a water bath with shaking until, after a vigorous reaction, complete

liquefaction has occurred (1 hour). The liquid is cooled, diluted with an equal volume of water, acidified with conc. hydrochloric acid, and extracted with ether. The extract is dried over anhydrous sodium sulphate, filtered, the ether removed on a water bath, and the residue recrystallised from benzene.

The ethylmalonic acid can also be worked up by precipitating its calcium salt from the neutralised solution by addition of a concentrated solution of calcium chloride, and treating the solid salt with conc. hydrochloric acid, extracting the liberated acid with ether, and proceeding as above.

$$C_2H_5CH(COOC_2H_5)_2 + 2KOH = C_2H_5CH(COOK)_2 + 2C_2H_5OH.$$

Yield.—85% theoretical (12 gms.). Colourless prisms; soluble in water, alcohol and ether; M.P. 112°. (A., 204, 134.)

Like all the malonic acids, this acid loses carbon dioxide on heating. yielding butyric acid, B.P. 163°. The reaction is carried out by heating 10 gms. of the acid in a reflux apparatus to 180° until carbon dioxide is no longer evolved (½ hour). The residue is fractionated for butyric acid between 160° and 165°.

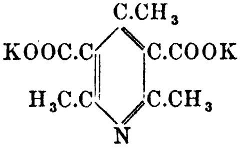
Preparation 180.—**Soap from Olive Oil.**

100 gms. of olive oil are heated in a beaker with 7 gms. of solid caustic soda and a little piece of soap in 75 c.cs. water for about 20 minutes. Another portion of 7 gms. caustic soda in 20 c.cs. of water is now added and heating continued for a further 20 minutes. Vigorous agitation should be maintained throughout the whole of this saponification, which should now be complete. A sample of the soap should be soluble in much water on heating; if not, a little more alkali solution should be added and heating continued. 100 gms. of common salt are added, stirred to dissolve, and the mixture allowed to cool. The cake which separates on the top is filtered and pressed (p. 37). Glycerine can be obtained from the filtrate by acidification, concentration, removal of the common salt, and vacuum distillation.

Olive oil is a mixture of glycerides, chiefly olein.

$$C_3H_5(O.COC_{17}H_{33})_3 + 3NaOH \longrightarrow C_3H_5(OH)_3 + 3NaOOC.C_{17}H_{33}.$$

Preparation 181.—**Potassium Collidine Dicarboxylate** (*Dipotassium-2 : 4 : 6—trimethyl-pyridine-3 : 5-dicarboxylate*).



$C_{10}H_9O_4NK_2$. 285.

10 gms. of diethyl-collidine dicarboxylate (p. 419) are refluxed on a water bath for 4 hours with about 10 times the volume (excess) of alcoholic potash (2·5 N approx.). The alcoholic solution is decanted from the separated potassium salt, a further yield of which is obtained by

adding ether to the alcoholic solution. The total product is washed with alcohol, then with ether and dried.

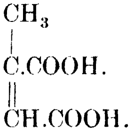
$$C_5N(CH_3)_3(COOC_2H_5)_2 + 2KOH = C_5N(CH_3)_3(COOK)_2 + 2C_2H_5OH.$$

Yield.—Almost theoretical (11 gms.). White crystalline mass; insoluble in ether. (A., 215, 26.)

Reaction XCVII. Hydrolysis of Amides, Acid Chlorides and Acid Anhydrides. (A., 188, 73; B., 26, R., 773; 28, R., 917, 32, 1118.)—All these compounds on hydrolysis yield acids. The anhydrides are hydrolysed by treatment with water or dilute alkali, the acid chlorides are usually very rapidly hydrolysed by water, but in the aromatic series 10% caustic alkali is sometimes necessary. The amides are boiled with caustic alkali solution (10%) or with conc. hydrochloric or sulphuric acid. They are, especially the substituted aromatic amides, very resistant to the action of acids, so that the former method is better. Another method is to dissolve the amide in conc. sulphuric acid, and add sodium nitrite in the cold, afterwards gently warming. Dilute sulphuric acid and addition of the nitrite in the warm sometimes gives better results.

$$C_6H_5CONH_2 + O:NOH = C_6H_5COOH + N_2 + H_2O.$$

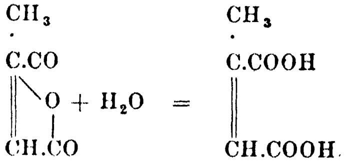
PREPARATION 182.—**Citraconic Acid** (*Cis-3-carboxy-2-buten acid*).



$$\begin{array}{l} CH_3 \\ | \\ C.COOH. \\ \| \\ CH.COOH. \end{array}$$

$C_5H_6O_4$. 130.

3·2 gms. (1 mol.) of water are added to 20 gms. (1 mol.) of citraconic anhydride (p. 422), and the mixture well stirred. The whole solidifies, on standing, to a mass of crystals which are dried on a porous plate.



Yield.—Theoretical (23 gms.). Colourless crystals; soluble in ether and chloroform; very soluble in water; M.P. 85°; K = 0·340. (A., 188, 73.)

Reaction XCVIII. Simultaneous Hydrolysis and Oxidation of Benzyl and Benzylidene Chlorides and their Derivatives. (B., 7, 100; B., 10, 1275.)—If benzyl or benzylidene chloride, or derivatives, are refluxed with an aqueous solution containing sodium carbonate and potassium permanganate, simultaneous hydrolysis and oxidation occurs, and benzoic acid or one of its derivatives is produced.

$$C_6H_5.CH_2.Cl \xrightarrow{Na_2CO_3} C_6H_5CH_2OH \xrightarrow{O_2} C_6H_5COOH.$$

$$C_6H_5.CH.Cl_2 \xrightarrow{Na_2CO_3} C_6H_5.CHO \xrightarrow{O_2} C_6H_5COOH.$$

PREPARATION 183.—**Benzoic Acid** (*Phenylmethan acid*).

C_6H_5COOH. $C_7H_6O_2$. 122.

To a mixture of 10 gms. (6 mols.) of benzyl chloride, 8 gms. (excess) of anhydrous sodium carbonate, and 15 c.cs. of water boiling under a reflux condenser, 17 gms. (8 mols.) of potassium permanganate in 250 c.cs. of water are added gradually, and the boiling continued until the colour of the permanganate has been discharged. Sulphur dioxide is then bubbled through the warm liquid until the precipitated manganese dioxide has dissolved. On cooling benzoic acid separates ; it is filtered at the pump, washed with a little cold water, and recrystallised from hot water.

Yield.—Theoretical (9 gms.). Colourless needles ; soluble in hot water, alcohol and ether ; volatile in steam ; M.P. 121°. (B., 10, 1275.)

Reaction XCIX. Oxidation of certain Carbon Compounds to less complex Compounds.—Complex compounds under vigorous oxidation yield simpler compounds, usually highly oxygenated. Such reactions are of value in determining the structure of certain compounds.

Oxalic is formed from the sugars, especially under the influence of V_2O_5, whereas in the presence of manganese salts tartaric acid is formed. (J. pr., 75, 146 ; U.S.P., 1,870,472.)

The preparation of maleic anhydride (U.S.P., 1,515,299) by the oxidation of benzene in presence of V_2O_5 constitutes an important industrial development, the anhydride being converted into succinic acid by reduction with hydrogen and nickel (U.S.P., 1,491,465), and into malic acid by hydration. It is important in Diels-Alder reactions (A., 460, 119). See Reaction XXXIX.

PREPARATION 184.—**Oxalic Acid** (*Ethan diacid*).

$(COOH)_2.2H_2O$. $C_2H_2O_4(+H_4O_2)$. 90(+36).

140 c.cs. (excess) of conc. nitric acid and ·01 gm. of vanadium pentoxide are gently warmed in a 1-litre round-bottomed flask on a water bath. The flask is then removed to a fume cupboard, and 22 gms. (1 mol.) of cane sugar are added all at once. As soon as brown fumes are evolved in large quantities, the flask is placed in cold water, and allowed to stand 24 hours, when the crystals which have separated are filtered off. A further small quantity may be obtained by allowing the mother liquors to stand. The crystals are drained on a small porcelain funnel without filter paper, and recrystallised from a very small quantity of water.

$$C_{12}H_{22}O_{11} + 9O_2 = 6(COOH)_2 + 5H_2O.$$

Yield.—25% theoretical (8 gms.). Colourless needles ; soluble in water and alcohol ; sparingly soluble in ether ; water of crystallisation given off at 100°–105° ; M.P. 101·5°. K = 10. (J. pr., 75, 146.)

Reaction C. Oxidation of the Side Chains in Aromatic Compounds. (A., 122, 184 ; 133, 41 ; 137, 308 ; 141, 144 ; 147, 292 ; Ann. Rep., 1945, 130 ; J. C. S., 1946, 1151.)—When aromatic compounds containing aliphatic side chains attached to the nucleus are treated with certain oxidising agents (potassium permanganate, dilute, nitric acid, and chromic acid), the side chain is oxidised until only a carboxylic group attached to the nucleus remains ; the end methyl group, if there are several carbon atoms present, being first oxidised to carboxyl and split off, and so on down to the first. If several side chains are present the results vary with the reagent, and the orientation of the side chains. Thus, if there are two, dilute nitric acid and potassium permanganate oxidise only one side chain, while chromic acid oxidises both, unless they are in the *ortho*-position to one another, when the compound is either not attacked or destroyed. Somewhat the same applies to nuclear substituted benzenes with one side chain ; the *ortho*-compound is often unattacked or destroyed, whereas the *para*- and *meta*-compounds yield the corresponding acids. Nitro groups in the *ortho*-position hinder oxidation ; with halogen groups the *meta*-compound is least, and the *para* most readily attacked. The methods for the employment of the various reagents mentioned will be clear from the following preparations. Particular attention should be paid to the method of oxidation of the side chains in phenols and amines. Before such oxidation can be carried out these substituting groups must be protected, the phenol by forming its sulphuric or phosphoric acid ester, the amine by benzoylation or acetylation. For the protected amines, potassium permanganate in presence of magnesium sulphate is used ; alkaline permanganate is the best oxidising agent for phenol esters.

PREPARATION 185.—**3 : 5-Dimethylbenzoic** (*Mesitylenic Acid*).

$C_6H_3.(CH_3)_2(COOH)[1:3:5]$. $C_6H_{10}O_2$. 150.

1-Methyl-3 : 5-dicarboxybenzene (*Uvitic Acid*).

$C_6H_3(CH_3)(COOH)_2[1:3:5]$. $C_9H_8O_4$. 180.

20 gms. (1 mol.) of mesitylene are refluxed with 80 gms. (excess) of 30% nitric acid in a 250-c.c. round-bottomed flask, on a sand bath in a fume cupboard for 18 hours. The white residue is filtered off on cooling. washed with cold water, dissolved in sodium carbonate solution, unattacked mesitylene and nitromesitylene separated, and the mixed acids reprecipitated by acidification with dilute hydrochloric acid. The white precipitate is filtered off, washed with cold water, and heated on a water bath with tin and excess of strong hydrochloric acid for 2 hours with constant shaking in a capacious flask (*caution!* hydrogen evolved). Nitromesitylenic acid, a by-product in the reaction, is thus reduced and brought into solution. On cooling, the undissolved portion is filtered off, washed with cold water, dissolved in dilute caustic soda, and reprecipitated from the hot filtered solution with dilute hydrochloric acid. The precipitate is a mixture of mesitylenic and uvitic acids. It is filtered off, washed with cold water and distilled in steam, till after several hours no further trace of mesitylenic acid appears in the condenser, and the distillate ceases to have an acid reaction. The greater portion of the mesitylenic acid, free from uvitic acid, is suspended in the distillate. It is filtered off and the filtrate neutralised with caustic soda solution, evaporated to small bulk, acidified with dilute hydrochloric acid, and the usually somewhat yellow-coloured acid thus obtained united to the first portion. The whole is redissolved in caustic soda solution, filtered boiling hot, precipitated by addition of dilute hydro-

chloric acid, washed with cold water, and recrystallised from alcohol. It is then pure mesitylenic acid. Uvitic acid containing slight traces of mesitylenic acid separates from the residual liquid in the distilling flask on cooling. It is recrystallised from hot alcohol after precipitation by acid from alkaline solution.

$$C_6H_3(CH_3)_3 + 3O = C_6H_3(CH_3)_2COOH + H_2O.$$

$$C_6H_3(CH_3)_2.COOH + 3O = C_6H_3(CH_3)(COOH)_2 + H_2O.$$

Yield.—*Mesitylenic acid* 50% theoretical (12 gms.). *Uvitic acid* 40% theoretical (12 gms.). *Mesitylenic acid* forms colourless monoclinic crystals; difficultly soluble in hot water; easily soluble in cold alcohol; M.P. 166°. *Uvitic acid* forms colourless fine needles; insoluble in cold and hot water; readily soluble in alcohol and ether; M.P. 287°–288°. (A., 122, 184; 141, 144; 147, 292; Z. Ch., 4, 119.)

The above illustrates the action of nitric acid in oxidising only one or two, and not all of the alkyl groups present, unless the heating is very prolonged. The next preparation shows how chromic acid or alkali bichromate and sulphuric acid completely oxidises all the side chains present.

PREPARATION 186.—**Terephthalic Acid** (1 : 4-*Benzenedicarboxylic acid*).

$C_6H_4(COOH)_2[1:4]$. $C_8H_6O_4$. 166.

20 gms. (1 mol.) of *p*-xylene are refluxed in a flask for 24 hours with 80 gms. (excess) of sodium or potassium bichromate and 250 gms. of 50% sulphuric acid. The unoxidised hydrocarbon is removed by distillation in steam, and the cooled solution filtered. The precipitate is purified by reprecipitation with acid from its dilute solution in sodium carbonate or caustic alkali.

$$C_6H_4(CH_3)_2[1:4] \xrightarrow{O_3} C_6H_4(COOH)_2[1:4].$$

Yield.—90% theoretical (28 gms.). Colourless crystals; insoluble in water and in alcohol; sublimes without melting at 300°. (A., 133, 41.)

The next preparation proves how, even when two side chains form part of a ring, the oxidation follows the same course, and an *ortho*-dicarboxylic acid is obtained.

PREPARATION 187.—**Phthalic Acid** (1 : 2-*Dicarboxybenzene*).

$C_6H_4(COOH)_2[1:2]$. $C_8H_6O_4$. 166.

(This preparation must be carried out in a good fume cupboard.)

20 gms. (1 mol.) of naphthalene, 15 gms. of mercuric sulphate, and 350 gms. (excess) of conc. sulphuric acid are heated in a retort with its neck sealed to an air condenser acting as a reflux until all the naphthalene is dissolved. The retort is then lowered so that the air condenser slopes downwards and delivers into a receiver, cooled in water and containing 200 c.cs. of cold water. The contents of the retort are heated cautiously at first, and then vigorously at 300° until the residue in the retort is nearly

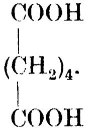
dry. Unchanged naphthalene, phthalic acid and anhydride, carbon dioxide, sulphur dioxide and water volatilise. The distillate is filtered, the precipitate well washed with cold water, dissolved in caustic soda, filtered from unchanged naphthalene, reprecipitated by acidification with hydrochloric acid, and crystallised from water, or aqueous alcohol.

$$C_{10}H_8 + 9H_2SO_4 = C_6H_4(COOH)_2 + 2CO_2 + 9SO_2 + 10H_2O.$$

Yield.—60% theoretical (16 gms.). Colourless plates slightly soluble in cold water ; soluble in alcohol and hot water ; M.P. 195° ; sublimes on heating to give phthalic anhydride (M.P. 128°). (D.R.P., 91202.)

The manufacture of phthalic anhydride (E.P., 249,973) from naphthalene, and maleic anhydride (U.S.P., 1,515,299) from benzene is carried out by oxidation with air or oxygen in presence of V_2O_5 as catalyst.

PREPARATION 187A.—**Adipic Acid** (*Tetramethylene dicarboxylic acid*) (*Hexan-diacid*).



$$\begin{array}{l} COOH \\ | \\ (CH_2)_4 \\ | \\ COOH \end{array}$$

$(CH_2)_4$. $C_6H_{10}O_4$. 146.

210 gms. nitric acid (50% ; D. 1·32) in a round-bottomed flask fitted with mechanical agitator and thermometer are heated to 85°–90° and 0·1 gm. ammonium vanadate added. From a funnel are gradually introduced 50 gms. commercial cyclohexanol, the reaction starting in about 5 minutes (evolution of oxides of nitrogen) after the addition of about 50 drops. The flask is then placed in ice-water, and when the temperature reaches 55°–60°, the remainder of the cyclohexanol is added at such a rate as to maintain the temperature between 55° and 60°. When the temperature begins to drop, heat is applied and stirring continued for 1 hour after the last addition of cyclohexanol. Adipic acid separates on cooling in ice, is filtered, washed with ice-water, and dried in air. It may be recrystallised from conc. nitric acid, alcohol or water.

$$C_6H_{11}OH + 4O \longrightarrow COOH(CH_2)_4COOH + H_2O.$$

Yield.—55% theoretical (40 gms.). White crystalline solid. M.P. 152°. (C. V., I, 18.)

PREPARATION 188.—*p*-**Hydroxybenzoic Acid** (1-*Hydroxy*-4-*carboxybenzene*).

$$C_6H_4(OH)(COOH)[1:4]. \quad C_7H_6O_3. \quad 138.$$

10 gms. (1 mol.) of *p*-cresol are dissolved in the minimum quantity of water, and the solution heated at 70° for 10 hours with 15 gms. (excess) of potassium pyrosulphate. The crude potassium *p*-cresyl sulphate formed is heated on a water bath with 25 gms. (excess) of potassium hydroxide dissolved in 20 c.cs. of water, and 30 gms. (excess) of potassium permanganate in 750 c.cs. water gradually added. The whole is heated for 6 hours. Sulphur dioxide is then passed through the mixture to remove excess of

permanganate, and the whole filtered hot. The filtrate is then boiled and acidified with hydrochloric acid, and heated to hydrolyse the sulphuric ester. On cooling, the acid crystallises out, the remainder being obtained by extracting with ether. It is recrystallised from ether.

$$C_6H_4OH.CH_3 + 2KMnO_4 \longrightarrow C_6H_4(OH)COOH + 2MnO_2 + 2KOH.$$

Yield.—90% theoretical (12 gms.). Colourless crystals; soluble in hot water and in ether; M.P. 210°. (B., 19, 705.) See also O. S., XIV, 48.

PREPARATION 189.—**Anthranilic Acid** (*1-Amino-2-carboxybenzene*).

$C_6H_4(NH_2)(COOH)[1:2]$. $C_7H_7O_2N$. 137.

20 gms. (1 mol.) of aceto-*o*-toluidide (cf. Preparation 274) and 50 gms. (excess) of magnesium sulphate crystals are dissolved in 2½ litres of water, the mixture heated to 80°, and 60 gms. (excess) of solid, finely-powdered, potassium permanganate, are added with mechanical stirring; this is continued for 2 hours, during which the temperature is maintained at 85°. Excess of permanganate is removed by the addition of alcohol, the hot solution filtered, and the filtrate acidified with dilute sulphuric acid. The acetanthranilic acid precipitated is purified by reprecipitation from alkaline solution (M.P. 185°). It is hydrolysed by boiling with excess of dilute hydrochloric acid or dilute alkali and recrystallised from hot water.

$$C_6H_4(NH.CO.CH_3)(CH_3)[1:2] + 2KMnO_4$$
$$= C_6H_4(NHCOCH_3)(COOH)[1:2] + 2MnO_2 + 2KOH.$$
$$2KOH + MgSO_4 = Mg(OH)_2 + K_2SO_4.$$
$$C_6H_4(NHCOCH_3)(COOH)[1:2] \longrightarrow C_6H_4(NH_2)(COOH)[1:2].$$

Yield.—80% theoretical (12 gms.). Colourless crystals; soluble in water and alcohol; sublimes on heating; M.P. 145°. (D.R.P., 94629.)

C. V., II, 341, gives preparation from salicylic acid.

Reaction CI. (*a*) **Oxidation of Primary Alcohols to the corresponding Carboxylic Acids.** (A., 106, 79, 95; 120, 226; B., 9, 1902.)—The primary alcohols are readily oxidised through the corresponding aldehydes to carboxylic acids containing the same number of carbon atoms.

$$R.CH_2OH \longrightarrow R.CHO \longrightarrow R.COOH.$$

Chromic acid or alkali dichromate and sulphuric acid is employed for the simpler alcohols; polyhydric alcohols are usually oxidised with moderately dilute nitric acid; if the acid be too concentrated the molecule may be attacked as a whole (cf. Preparation 184).

PREPARATION 190.—**Acetic Acid** (*Ethan-acid*).

CH_3COOH. $C_2H_4O_2$. 60.

To 80 gms. (excess) of finely-powdered potassium or sodium dichromate, and 100 gms. of 50% sulphuric acid placed in a reflux apparatus (see p. 216), 70 gms. (1 mol.) of 25% alcohol are slowly added. The mixture is heated for 30 minutes and distilled until only very little acid passes over. The distillate is neutralised with caustic potash, and evaporated to dryness on a water bath. The residue is powdered and distilled with conc. sulphuric acid to 139°, and the distillate fractionated between 115° and 120°.

$$3C_2H_5OH + 2K_2Cr_2O_7 + 8H_2SO_4$$
$$= 3CH_3COOH + 2K_2SO_4 + 2Cr_2(SO_4)_3 + 11H_2O.$$

Yield.—80% theoretical (18 gms.). Colourless liquid or crystals; pungent odour; miscible with water; M.P. 16·7°; B.P. 119°; D. $^{15}_{4}$ 1·055.

PREPARATION 191.—**Glyceric Acid** (2 : 3-*Diol-propan-acid*).

$OH.CH_2.CH(OH).COOH.$ $C_3H_6O_4$. 106.

50 gms. (1 mol.) of glycerol diluted with an equal volume of water are treated in a tall narrow glass cylinder with 50 gms. (excess) of 90% nitric acid, the latter being carefully run in below the surface of the glycerol from a funnel, the neck of which is drawn out into a fine tube, so that two layers are formed. The whole is allowed to stand at the ordinary temperature, till after some little time the liquid becomes homogeneous. The contents of several (six) such cylinders are slowly evaporated on a water bath to a syrup, 2 litres of water are added, and the solution (*a*) neutralised with lead carbonate and a small quantity of lead oxide. Towards the end of the operation the liquid is boiled and filtered hot. Crude lead glycerate separates on concentrating and cooling the filtrate. The salt which adheres firmly to the side of the vessel is detached by warming. A second crop of crystals slowly separates on concentrating the mother liquors. The finely-powdered salt made into a paste with water is treated with hydrogen sulphide in 2·5 gm. lots, and the solution, filtered from lead sulphide, evaporated on a water bath, when the acid remains as a thick syrup.

The aqueous solution (*a*) may also be worked up for glyceric acid by boiling it with excess of calcium carbonate and filtering hot. The calcium glycerate, which separates on cooling and concentrating, is recrystallised from hot water, suspended in water, and decomposed by treatment with the theoretical quantity of oxalic acid (determined on estimating the calcium by ignition in a sample of the salt). The clear solution filtered from calcium oxalate is evaporated as above.

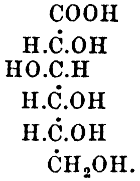
$$(OH)CH_2.CH(OH)CH_2(OH) + O_2 = (OH)CH_2CH(OH)COOH + H_2O.$$

Yield.—80% theoretical (275 gms. from 300 gms. of glycerol). Strongly acid syrup, faintly yellow colour; soluble in water, alcohol and acetone; insoluble in ether; decomposes on boiling. (A., 106, 79, 95; 120, 226; B., 9, 1902.)

Reaction CI. (*b*) **Oxidation of Aldehydes to Carboxylic Acids.** (B., 17, 1298; 24, 521; A., 227, 224.)—The aldehydes are very readily oxidised to the corresponding acids; in the oxidation of primary alcohols to acids, it is the first stage which is the more difficult to achieve. A great variety of oxidising agents may be employed—nitric acid is used for the less complex aldehydes, e.g. chloral to trichloroacetic acid; in the sugar group bromine gives very good results (see below).

$$R.CHO + O = R.COOH.$$

Preparation 192.—**Gluconic Acid** (*Pentol-hexan acid* + — + +).



$$\begin{array}{c} COOH \\ H.\dot{C}.OH \\ HO.C.H \\ H.\dot{C}.OH \\ H.\dot{C}.OH \\ \dot{C}H_2OH. \end{array}$$

$C_6H_{12}O_7$. 196.

50 gms. (1 mol.) of glucose dissolved in 400 c.cs. of water are treated in a stoppered bottle with 100 gms. (excess) of bromine. The mixture is allowed to stand, with frequent shaking, for 3 days at ordinary temperatures, and then boiled in a porcelain dish in a fume cupboard with constant stirring, until all the bromine has disappeared. The solution is cooled, diluted with water to 500 c.cs. and neutralised with lead carbonate suspended in water. The precipitate is filtered at the pump, suspended in water and saturated with hydrogen sulphide, filtered and neutralised by boiling for ½ hour with precipitated chalk. The filtrate is evaporated to about 100 c.cs., and seeded in the cold with a crystal of calcium gluconate. After 24 hours the whole is filtered at the pump and the precipitate washed with cold water, redissolved in a small quantity of hot water, and boiled with addition of animal charcoal. The latter is filtered off and the solution treated with the exact quantity of oxalic acid in aqueous solution necessary to precipitate the calcium present, a portion of the precipitate obtained above being ignited and the calcium in it estimated for the purpose. The precipitated calcium oxalate is filtered off and washed, and the washings and filtrate evaporated to a syrup on a warm water bath under reduced pressure.

$$C_5H_{11}O_5CHO + H_2O + Br_2 = C_5H_{11}O_5COOH + 2HBr.$$

Yield.—50% theoretical (30 gms.). Acid syrup; soluble in water; on standing or heating changes in part to a crystalline lactone; M.P. 130°–135°. (B., 17, 1298.)

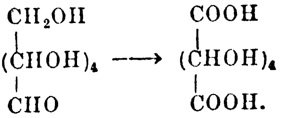
This type of preparation is important in the sugar group. It is possible to pass from one hexose to another by oxidising the first to the corresponding acid, heating of which with pyridine yields the epimeric acid; and reduction of the lactone of this yields the second hexose.

Preparation 193.—**Saccharic Acid** (*Tetrol-hexan-diacid* + — + +).

$COOH.(CHOH)_4.COOH$. $C_6H_{10}O_8$. 210.

50 gms. (1 mol.) of anhydrous glucose are heated in a dish on a water bath with 350 gms. (excess) of 25% nitric acid and, while stirred mechanically, are evaporated to a syrup, which is dissolved in a little water, and again evaporated. Should the mass begin to show the slightest sign of

charring, heating is immediately discontinued. The whole is dissolved in 200 c.cs. of water, and neutralised with a saturated solution of potassium carbonate. 25 c.cs. of 50% acetic acid are added and the liquid evaporated to about 75 c.cs. On frequent rubbing and long standing in the cold, acid potassium saccharate crystallises out, and is filtered at the pump after a further 12 hour's standing, washed with a very little cold water, and recrystallised from hot water with addition of decolorising carbon until colourless crystals are obtained. The salt is treated with excess of 10% hydrochloric acid and evaporated on a warm water bath under reduced pressure to a deliquescent mass, which is treated with absolute alcohol, filtered and the filtrate evaporated under reduced pressure till all the alcohol is removed.

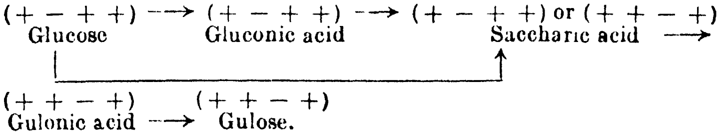


$$\begin{array}{c} CH_2OH \\ | \\ (CHOH)_4 \\ | \\ CHO \end{array} \longrightarrow \begin{array}{c} COOH \\ | \\ (CHOH)_4 \\ | \\ COOH. \end{array}$$

Yield.—20% theoretical (12 gms.). Colourless deliquescent mass; soluble in water; very soluble in alcohol; changes on standing to a crystalline lactone (M.P. 131°). (B., 24, 521.)

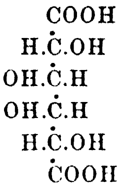
This preparation illustrates the oxidation to a carboxylic acid, both of a primary alcohol and an aldehyde. The reaction also is of importance in the sugar group, for it is possible to reduce the carboxyl group in saccharic acid, which comes from the aldehyde group, to a primary alcohol group, while the carboxyl corresponding to the primary alcohol group is reduced to an aldehyde. In this way a new sugar stereosimeric with the first may be obtained.

Following is one of the applications of the method—



The next preparation illustrates the hydrolysis of a disaccharose, and the simultaneous oxidation of the monosaccharoses so formed.

PREPARATION 194.—**Mucic Acid** (*Tetrol-hexan-diacid* + — — +).



$$\begin{array}{c} COOH \\ H.\dot{C}.OH \\ OH.\dot{C}.H \\ OH.\dot{C}.H \\ H.\dot{C}.OH \\ \dot{C}OOH \end{array}$$

$C_6H_{10}O_8$. 210.

100 gms. (1 mol.) of lactose are heated on a water bath with 1,500 gms. (excess) of 25% nitric acid, the whole being continuously stirred, until the

volume is reduced to 250 c.cs. The cooled acid mass is diluted with 750 c.cs. of water, filtered at the pump, well washed with cold water, and dissolved in just sufficient N/1 caustic soda solution (excess tends to precipitate the sodium salt. The latter solution is warmed with decolorising carbon and filtered, and the acid reprecipitated by addition of the equivalent in 5N hydrochloric acid of the N/1 caustic soda used for solution. During this addition the temperature must not rise above 15°, otherwise the lactone of the acid may be formed. The whole is kept for 12 hours in a freezing mixture, and the precipitate filtered at the pump, well washed with cold water and dried on a water bath. Saccharic acid being soluble in water remains in solution.

$$\underset{\text{Lactose.}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Glucose.}}{C_6H_{12}O_6} + \underset{\text{Galactose.}}{C_6H_{12}O_6}.$$

$$\underset{\text{Glucose.}}{C_6H_{12}O_6} \xrightarrow{O_2} \underset{\text{Saccharic acid.}}{C_6H_{10}O_8}.$$

$$\underset{\text{Galactose.}}{C_6H_{12}O_6} \xrightarrow{O_2} \underset{\text{Mucic acid.}}{C_6H_{10}O_8}.$$

Yield.—55% theoretical (32 gms.). White crystalline powder ; almost insoluble in cold water and in alcohol ; M.P. 210° (with decomposition). (A., 227, 224.)

Reaction CI. (*c*) **Action of Periodic Acid on certain Glycols** (*Malaprade*). (Bl., 1928, 683 ; C. I., 1928, 382 ; *Organic Reactions*, Adams, Vol. II, 341.)—Periodic acid, usually in aqueous solution, oxidises α-glycols quantitatively with rupture of the molecule between the contiguous C-atoms :

$$RCHOH.CHOHR_1 + HIO_4 \longrightarrow RCHO + R_1CHO + H_2O + HIO_3$$

$$RCHOH.CHNH_2R_1 + HIO_4 \longrightarrow RCHO + R_1CHO + NH_3 + HIO_3$$

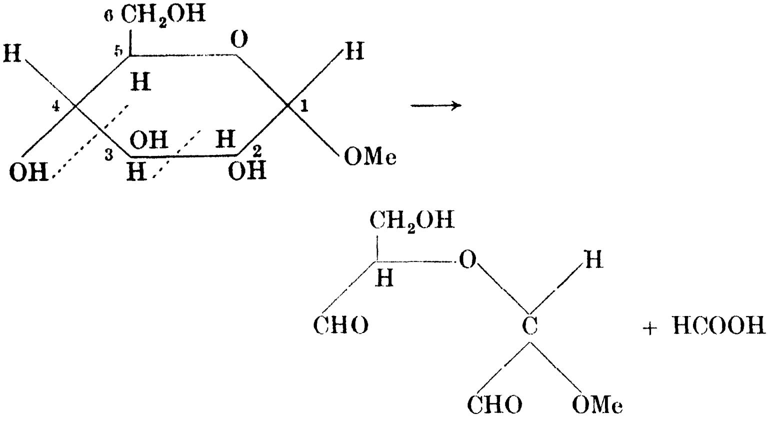
If an amino group replaces one of the hydroxyls, ammonia is liberated in place of water. The reaction can be used to ascertain the presence of contiguous hydroxyls or hydroxyl and amino groups, α-ketols, α-diketones and ketonic aldehydes each similarly yielding an aldehyde and/or an acid on rupture.

$$CH_2OHCOCH_2OH + HIO_4 \longrightarrow HCHO + CH_2OHCOOH + HIO_3.$$

$$CH_3CO.COCH_3 + HIO_4 + H_2O \longrightarrow 2CH_3COOH + HIO_3.$$

$$CH_3COCHO + HIO_4 + H_2O \longrightarrow CH_3COOH + HCOOH + HIO_3.$$

These reactions proceed at ordinary temperature, giving good yields and no side reaction thus offering many advantages over permanganate and nitric acid. The reaction products are usually stable to the reagent. It has proved extremely valuable in determining the structure of glycosides and is capable of quantitative application, e.g. methyl glucoside on oxidative degradation suffers elimination of the third C-atom as formic acid which can be estimated (Am. Soc., 1936, 378 ; 1937, 994). See Hirst, *Nature*, 156, 785.



(J. C. S., 1939, 1880 ; Am. Soc., 1940, 958, 2960 ; Bl., 1943, 245.)

Periodic Acid Reagent.—This is prepared by dissolving 1 part para-periodic acid (commercially available), in 200 parts distilled water.

$$H_5IO_6 \longrightarrow HIO_4 + 2H_2O.$$

The following illustrates the application of the reagent in the detection of above-mentioned groupings : 1 drop of ethylene glycol is shaken with 2 c.cs. of the reagent and 1–2 drops of dilute silver nitrate added. An immediate white precipitate of silver iodate is formed.

Reaction CI. (*d*) **Action of Lead Tetra-acetate on Certain Compounds.** (*Preparative Organic Chemistry*, Criegee, p. 1.)—Lead tetra-acetate, which may be prepared pure (p. 519) and which is soluble in many organic solvents, is a valuable and effective oxidising agent. Acting as an oxidising agent it loses two acetoxy groups (which can either add to a C—C bond or substitute hydrogen atoms with esterified OH groups), or by combining with two hydrogen atoms can bring about dehydrogenation. One of its most important effects is the rupture of the bond in α-glycols yielding aldehydes or ketones,

$$\rangle C(OH)\text{—}C(OH)\langle \; + Pb(OCOCH_3)_4 \longrightarrow$$
$$\rangle CO + OC\langle \; + Pb(OCOCH_3)_2 + 2CH_3COOH,$$

a behaviour (H. Acta., 1933, 959) corresponding to that of periodic acid (see p. 255).

The following illustrates its application. Three drops ethylene glycol are added to 1 gm. lead tetra-acetate dissolved in 40 c.cs. of glacial acetic acid. After 30 minutes, excess of the oxidising agent is removed by the addition of a small amount of sulphurous acid or oxalic acid. A coloration with Schiff's reagent or a precipitate with dinitrophenylhydrazine shows the presence of formaldehyde.

$$CH_2OH.CH_2OH + Pb(OCOCH_3)_4 \longrightarrow$$
$$2HCHO + Pb(OCOCH_3)_2 + 2HOCOCH_3.$$

CHAPTER XVII

OXYGEN TO CARBON

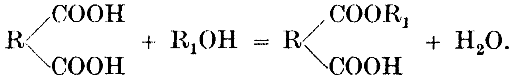
OXIDE-OXY COMPOUNDS

Esters and Acid Anhydrides

THIS section deals first with the preparation of alkyl acyl oxide compounds—esters—by the interaction of an acid or an acid derivative and an alcohol. The fact that the formation of an ester and water from a mixture of an acid and an alcohol is a reversible reaction necessitates special measures being adopted to displace the equilibrium towards the more complete formation of ester.

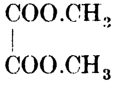
The second portion of the section discusses the preparation of di-acyl oxide compounds—acid anhydrides.

Reaction CII. Direct Action of an Acid on an Alcohol. (A. Ch., 58,44.) —Few normal esters are prepared in this way—dimethyl oxalate being an exception ; in this case the water formed is probably prevented from inducing the back reaction by the presence of anhydrous oxalic acid—but the yield is only 40%. With acid esters, however, good yields can be obtained, since only partial esterification is required.



$$R\begin{cases}COOH\\COOH\end{cases} + R_1OH = R\begin{cases}COOR_1\\COOH\end{cases} + H_2O.$$

PREPARATION 195.—**Dimethyl Oxalate** (*Dimethyl ester of ethan-diacid*).



$$\begin{array}{c}COO.CH_3\\|\\COO.CH_3\end{array}$$

$C_4H_6O_4$. 118.

In order to prevent hydrolysis of the ester as it is formed, it is necessary in this preparation to use *anhydrous* oxalic acid and to purify and dry the methyl alcohol as described on p. 216.

63 gms. (1 mol.) of oxalic acid crystals are powdered and heated on a boiling water bath till no more water is given off (1–2 hours) and are then heated in an air oven at 110°–120° until the required loss in weight (18 gms.) has taken place. During the heating, the acid should be powdered occasionally. The *anhydrous acid* is refluxed on a water bath with 50 gms. (excess) of *pure anhydrous* methyl alcohol for 2½ hours, excess alcohol removed on a water bath, and the residue distilled to 120° ; the water is run out of the condenser, and the fraction 160°–165° collected. The solid

portion is filtered off, dried on a porous plate, and recrystallised from methyl or ethyl alcohol.

$$\begin{array}{l}COOH\\ |\\ COOH\end{array} + 2CH_3.OH = \begin{array}{l}COOCH_3\\ |\\ COOCH_3\end{array} + 2H_2O.$$

Yield.—40% theoretical (25 gms.) Colourless plates; somewhat soluble in alcohol; M.P. 54°; B.P. 163°. (A. Ch., 58, 44; C. V., II, 414.)

In the next preparation the forward reaction is assisted by removal of the ester as fast as it is produced (cf. Reaction CIII.). This is only possible when a strong acid is present to act as a catalyst—the hydrogen ions cause fresh ester to be formed rapidly. It is necessary that the ester should be volatile, or in some other manner readily removed from the sphere of the reaction.

PREPARATION 196.—**Ethyl Nitrate** (*Ethyl-ester of nitric acid*).

$CH_3.CH_2.O.NO_2$. $C_2H_5O_3N$. 91.

To 20 gms. (1 mol.) of cold "boiled-out" 67% nitric acid, 2 gms. of urea in 15 gms. (excess) of absolute alcohol are added, and half of the mixture distilled off on a water bath in a tubulated retort attached to condenser and receiver. 40 gms. of similar nitric acid mixed with 30 gms. of absolute alcohol, and containing 0·5 gm. of urea, are now allowed to drop in through the tubulus from a tap funnel at the same rate as the liquid distils. Water is added to the distillate, the ester which separates is washed several times with cold water, dried over calcium chloride, and distilled from a water bath, the fraction 84°–88° being retained. Care must be taken in this experiment, as the ester is liable to explode when quickly heated. All operations should be carried out behind a safety screen.

$$C_2H_5OH + HNO_3 = C_2H_6NO_3 + H_2O.$$

Yield.—75% theoretical (22 gms.). Colourless liquid; characteristic odour; *liable to explode when quickly heated*; B.P. 86°; D. $^{15}_{4}$ 1·112.

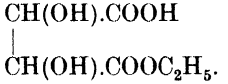
Urea is used above to decompose any nitrous acid formed, as the presence of the latter tends to cause explosion.

$$CO(NH_2)_2 + 2HNO_2 = CO_2 + 2N_2 + 3H_2O.$$

(B., 14, 421.)

The following illustrates the preparation of acid esters.

PREPARATION 197.—**Ethyl Hydrogen Tartrate** (*Monoethyl ester of* 2 : 3-*butandiol-diacid*).

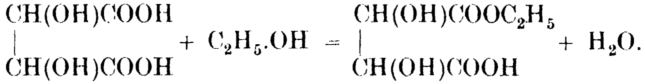


$$\begin{array}{l}CH(OH).COOH\\ |\\ CH(OH).COOC_2H_5.\end{array}$$

$C_6H_{10}O_6$. 178.

20 gms. (1 mol.) of finely-powdered tartaric acid and 30 gms. (excess) of *absolute* alcohol are heated for 6 hours at 70° on a water bath in a reflux apparatus. An equal volume of water and then an excess of powdered

barium carbonate are added, and the liquid filtered from barium tartrate and excess of barium carbonate. The filtrate is evaporated to crystallisation on a water bath, cooled, and the crystals of barium ethyl-tartrate which separate filtered off at the pump and dried on a porous plate. They are weighed and treated with the theoretical amount of 2N sulphuric acid to precipitate the barium present, barium sulphate is filtered off, and the filtrate evaporated to crystallisation point. The crystals which separate are recrystallised from a little water.



$$\begin{array}{l} CH(OH)COOH \\ | \\ CH(OH)COOH \end{array} + C_2H_5.OH = \begin{array}{l} CH(OH)COOC_2H_5 \\ | \\ CH(OH)COOH \end{array} + H_2O.$$

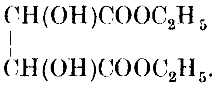
Yield.—70% theoretical (17 gms.). Colourless crystals; somewhat soluble in water; M.P. 90°. (A., 22, 248.)

By a repetition of the above process, using the alkyl hydrogen tartrate, diethyl tartrate can be obtained, but the yield is poor.

When conc. sulphuric acid acts on the alcohols, the acid esters only are formed, though sulphuric acid, by its great affinity for water, promotes almost complete esterification in other instances; for the preparation of normal sulphuric esters, see Preparation 210.

Reaction CIII. Esterification with Continuous removal of Water. (P. R. S., 25, 831; J. C. S., 87, 1657.)—In this method, which requires little elaboration, it is necessary that the acid and ester have high boiling points compared with that of water. The last is continually volatilised with the alcohol and circulated over a dehydrating agent which absorbs it—the alcohol being returned to the reaction vessel.

PREPARATION 198.—**Diethyl Tartrate** (*Diethyl ester of 2 : 3-butandiol-diacid*).



$$\begin{array}{l} CH(OH)COOC_2H_5 \\ | \\ CH(OH)COOC_2H_5. \end{array}$$

$C_8H_{14}O_6$. 206.

Method I.—The apparatus described in Preparation 1 is fitted up, a 500-c.c. flask being used, and 30 gms. (1 mol.) of finely-powdered tartaric acid, 150 gms. (excess) of absolute alcohol, and 50 gms. of crystallised benzene placed in the flask. The object of the benzene is to help to volatilise the water produced by forming with it and the alcohol the low boiling ternary system—alcohol-benzene-water. The iron tube is packed with small lumps of good quicklime, and is heated to a temperature of 90°. The mixture in the flask is boiled, a few pieces of porous porcelain being added to promote steady ebullition. Esterification proceeds almost to completion, owing to the removal by the quicklime of the water formed. After 6 hours, the liquid in the flask, which will have become quite viscid owing to the formation of the ester, is distilled on a water bath until all the benzene and excess of alcohol have been removed; the residue is fractionated from a metal bath under reduced pressure.

Yield.—90% theoretical (37 gms.). (P. R. S., 25, 831; J. C. S., 87, 1657.)

Method II.—The apparatus (Fig. 55) is fitted up, being held in position by a clamp holding the condenser C. In the flask A are placed 150 gms. of tartaric acid (or other acid to be esterified), which need not be specially dried or powdered, and which is just covered with alcohol. B contains 140 gms. (3 mols.) of the latter, and 100 gms. of fresh potassium carbonate or other suitable solid desiccating agent. The apparatus communicates with the open air only by means of the tube E. A is immersed to the neck in an oil bath which is slowly heated to 130°, and as soon as most of the alcohol in it has distilled into B, the latter is heated on a boiling water bath. The alcohol in B passes up the fractionating column D, which assists the action of the dehydrating agent, and into A, from which uncombined alcohol, and the water formed in the esterification, distil into B. After 10 hours, the excess of alcohol is distilled off from A, and the residue fractionated from a metal bath under reduced pressure.

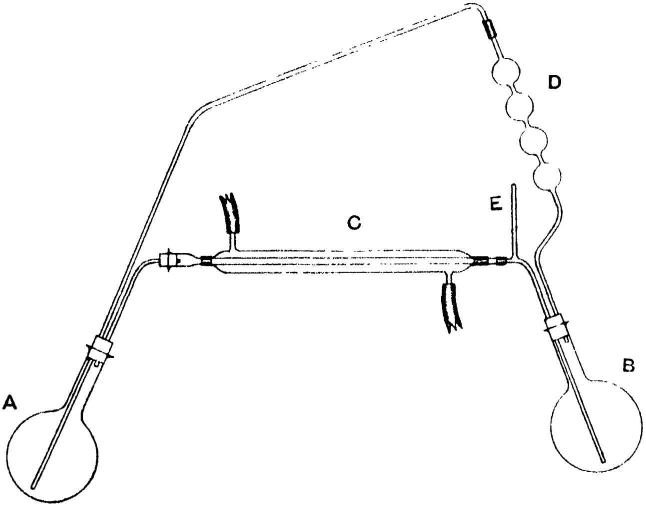


FIG. 55.

$$(CH(OH)COOH)_2 + 2C_2H_5OH = (CH(OH)COOC_2H_5)_2 + 2H_2O.$$

Yield.—80% theoretical (165 gms.). (J. C. S., 79, 517.)

Colourless crystals ; insoluble in water ; miscible with alcohol. M.P. 18·7° ; B.P. ^{11} 155° ; B.P. ^{23} 164° ; D. $^{0}_{4}$ 1·072.

For other methods of preparation and method of purification, see J. C. S., 121, 532.

Reaction CIV. Use of Concentrated Sulphuric Acid or of Hydrogen Chloride to promote Esterification. (B., 13, 1176 ; 28, 1150, 3252 ; Phil. Trans., 156, 37 ; Bl., 33, 350 ; J., (1874), 352 ; A., 204, 126.)—Conc. sulphuric acid being a dehydrating agent is frequently used to promote esterification ; it also acts as a catalyst increasing the speed of the reaction. Saturation of the alcohol with hydrogen chloride has also been employed with the same end in view, but it has been found that 4% hydrogen chloride in the alcohol gives even better results. Hence it is probable that this acid acts catalytically and not as a dehydrating agent.

A convenient method of esterification, particularly when steric hindrance tends to prevent combination, consists in dissolving the organic acid in 100% sulphuric acid (see p. 316). After a few minutes at ordinary temperature the solution is poured into excess of cold absolute alcohol. Most of the alcohol is then removed by distillation under reduced pressure and water added to the residue. Further removal of alcohol under reduced pressure is effected, the ester extracted with ether and recovered (Am. Soc., 1941, 2431).

PREPARATION 199.—**Ethyl Acetate** (*Ethyl ester of ethan acid*).

$$CH_3.COOC_2H_5. \qquad C_4H_8O_2. \qquad 88.$$

200 c.cs. of a mixture of equal volumes of glacial acetic acid (1 mol.) and absolute alcohol (1 mol.) are added, drop by drop at the same speed as the liquid distils, to a mixture of 50 c.cs. of conc. sulphuric acid and 50 c.cs. (excess) of absolute alcohol in a distilling flask attached to a condenser and receiver and heated in an oil bath kept at 140°. The distillate is shaken in an *open* tap funnel with aqueous sodium carbonate solution until the upper layer is no longer acid to moistened blue litmus paper. This layer is shaken with 50 c.cs. of a 50% aqueous solution of calcium chloride to remove alcohol, and then allowed to stand 24 hours in contact with calcium chloride. It is filtered through a dry filter paper and fractionated on a water bath, the fraction 73°–80° being redistilled.

$$CH_3COOH + C_2H_5OH = CH_3COOC_2H_5 + H_2O.$$

Yield.—85% theoretical (130 gms.). Colourless liquid; characteristic odour; somewhat soluble in water; miscible with alcohol, ether and acetic acid; B.P. 78°; D. $^{15}_{4}$ 0·9068; Phil. Trans., 156, 37; Bl., 33, 350; J. S. C. I., 43, 295.

Methyl acetate (B.P. 57°; D. [illegible] 0·904) is prepared in a similar manner from methyl alcohol.

PREPARATION 200.—**Diethyl Tartrate** (*Diethyl ester of 2 : 3-butandiol-diacid*).

$$[CH(OH)COOC_2H_5]_2. \qquad C_8H_{14}O_6. \qquad 206.$$

50 gms. (1 mol.) of finely-powdered tartaric acid are refluxed on a water bath with 150 c.cs. (excess) of absolute alcohol until dissolved, and the solution saturated with hydrogen chloride at 0°. After 12 hours it is heated under reduced pressure on a water bath to remove hydrogen chloride, excess of alcohol and water, and the residue, which consists chiefly of ethyl hydrogen tartrate, treated with a further 150 c.cs. (excess) of absolute alcohol, the mixture again saturated with hydrogen chloride at 0°, and allowed to stand for 12 hours. It is then fractionated under reduced pressure, and the fraction, B.P. ^{11} 152°–158° or B.P. $^{18-20}$ 159°–168°, refractionated under reduced pressure.

Yield.—80% theoretical (55 gms.). Colourless crystals ; M.P. 18·7° ; insoluble in water ; miscible with alcohol ; B.P. ^{11} 155° ; B.P. ^{23} 164° ; D. $^{0}_{4}$ 1·072. (B., 13, 1176 ; J. C. S., 79, 168.)

The above exemplifies the old method of saturation of the mixture with hydrogen chloride ; the Fischer-Speir modification, illustrated in the following preparation, can be employed ; the time for the preparation is shortened, and only half the above quantity of alcohol is required.

PREPARATION 201.—**Ethyl Benzoate** (*Ethyl ester of benzoic acid*).

$$C_6H_5.COOC_2H_5. \qquad C_9H_{10}O_2. \qquad 150.$$

150 gms. (excess) of absolute alcohol are cooled in ice, and dry hydrogen chloride bubbled through it until an increase in weight of 6 gms. has been obtained. 50 gms. (1 mol.) of benzoic acid are added, and the whole refluxed for 2 hours until on pouring a sample into water no benzoic acid separates. The excess of alcohol is removed on a water bath, the residue diluted with 2 volumes of water, and the whole shaken in an open vessel with solid sodium carbonate until any acid present is removed. The ester is then extracted with ether, the extract dried for 24 hours over *pure* potassium carbonate and fractionated, the fraction 204°–213° being redistilled.

$$C_6H_5.COOH + C_2H_5OH = C_6H_5COOC_2H_5 + H_2O.$$

Yield.—80% theoretical (49 gms.). Colourless oil ; sweetish odour ; insoluble in water ; miscible with alcohol and ether ; B.P. ^{750} 211° ; D. $^{15}_{4}$ 1·05. (B., 28, 1150.)

The above compound can also be made using 10 gms. of conc. sulphuric acid, 100 gms. of absolute alcohol, and 50 gms. of benzoic acid. Although less alcohol is used, the yield is 90% theoretical, being increased by the dehydrating action of the sulphuric acid. Methyl benzoate (B.P. 199°) can be prepared in a similar manner.

The following exemplifies the preparation of an ester by the above methods, using a salt of an acid from which the mineral acid present liberates the free acid. This modification is especially useful when the acid to be esterified is difficult to isolate in a free state.

PREPARATION 202.—**Diethyl Malonate** (*Diethyl ester of propan-diacid*).

$$CH_2(COOC_2H_5)_2. \qquad C_7H_{12}O_4. \qquad 160.$$

For this esterification 250 c.cs. (excess) of absolute alcohol are employed to 100 gms. of hydrated calcium malonate, which has been dried as completely as possible on a water bath, or to 95 gms. of the anhydrous salt of the acid. It is better to use the latter. 20 gms. of the dried salt are placed in a litre flask, all the absolute alcohol is poured on to it, and a stream of well-dried hydrogen chloride is passed in, so that the liquid becomes warm. The remainder of the calcium salt is added in 15-gm. lots as fast as the previous portion disappears. By this means caking of the calcium salt is prevented. The complete solution should take about 30 minutes, by which time the alcoholic liquid will be saturated with hydrogen chloride. After standing for 24 hours, the solution is evaporated to a small volume under reduced pressure, and the residual ester dissolved in ether. The ethereal solution is dried over calcium chloride, the ether removed on a water bath, and the residue fractionated, the fraction 195°–198° being retained.

$$CH_2(COO)_2Ca + 2HCl + 2C_2H_5OH = CH_2(COOC_2H_5)_2 + CaCl_2 + 2H_2O.$$

Yield.—75% theoretical (65 gms.). Colourless liquid ; B.P. (uncorr.) 195° ; B.P. (corr.) 197°–198° ; D. $^{18}_{4}$ 1·068. (A., 204, 126.)

PREPARATION 203.—**Amyl Nitrite** (*Amyl ester of nitrous acid*).

$O : N.O.C_5H_{11}$. $C_5H_{11}O_2N$. 117.

30 gms. (2 mols.) of amyl alcohol and 25 gms. (excess) of sodium nitrite are treated in a 500-c.c. round-bottomed flask cooled in ice, with 30 gms. (excess) of conc. sulphuric acid added drop by drop with constant shaking. The addition must be carried out in a fume cupboard, and care must be taken not to inhale the vapour of the amyl nitrite. When all the acid is added, the top layer of ester is separated and the residue shaken with water ; the further quantity of ester which separates is added to that first obtained, and the whole washed with water, separated, dried for 24 hours over calcium chloride and distilled, the fraction 94°–101° being redistilled.

$$2C_5H_{11}OH + 2NaNO_2 + H_2SO_4 = 2C_5H_{11}ONO + Na_2SO_4 + 2H_2O.$$

Yield.—75% theoretical (30 gms.). Greenish-yellow liquid ; characteristic odour ; insoluble in water ; miscible with ether and alcohol ; B.P. ^{760} 96° ; D. $^{0}_{4}$ 0·902. (J., 1874, 352.) See also O. S., XVI, 8.

Reaction CV. Action of Acid Anhydrides on Alcohols and Phenols. (B., 12, 2059 ; 21, 1172 ; J. C. S., 1931, 2495.)—The method is employed when the acids themselves do not react and is useful for the rapid preparation of acetates of alcohols and phenols and for the acetylation of cellulose.

$$2R_1OH + (R_{11}CO)_2O = 2R_{11}COOR_1 + H_2O.$$

Esterification is effected in the cold in presence of alkali or by heating the alcohol and anhydride together, usually in presence of a dehydrating agent—e.g. fused zinc chloride, anhydrous sodium acetate, etc.

PREPARATION 204.—**Mannitol Hexacetate.**

$(CH_2O.COCH_3)(CHO.COCH_3)_4(CH_2O.COCH_3)$. $C_{18}H_{26}O_{12}$. 434.

10 gms. of mannitol, 10 gms. of fused sodium acetate, and 40 gms. acetic anhydride are placed in a small flask provided with a reflux condenser and heated, at some distance above a wire gauze, to gentle boiling for an hour. The product is poured into water, well stirred and broken up with a glass rod. After some time it is filtered off, washed with water, and recrystallised from alcohol.

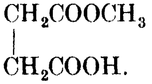
$$CH_2OH(CHOH)_4CH_2OH + 3(CH_3CO)_2O \longrightarrow C_{18}H_{26}O_{12} + 3H_2O.$$

Yield.—Almost theoretical (24 gms.). Colourless crystals ; insoluble in water ; soluble in hot alcohol ; .M.P. 119°. (B., 12 2059.)

The above represents a general method for the preparation of acetyl derivatives of hydroxy compounds for estimation of which see p. 488. Fused zinc chloride may be used in place of fused sodium acetate, but charring of the product is more likely to occur.

The next preparation illustrates the action of the anhydride of a dibasic acid.

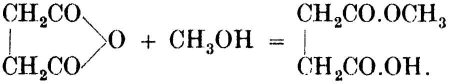
PREPARATION 205.—**Methyl Hydrogen Succinate** (*Monomethyl-ester of butan-diacid*).



$$\begin{array}{l} CH_2COOCH_3 \\ | \\ CH_2COOH. \end{array}$$

$C_5H_8O_4$. 132.

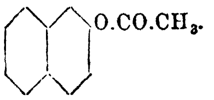
10 gms. (1 mol.) of succinic anhydride (see p. 271) are refluxed with 10 gms. (excess) of pure methyl alcohol (see p. 216) for 1 hour, excess of alcohol is removed under reduced pressure at ordinary temperature, and the residue recrystallised from hot carbon disulphide (*Caution!*).



Yield.—Almost theoretical (13 gms.). Glistening plates ; insoluble in water ; M.P. 57° ; B.P. ^{50} 151°.

Phenols and naphthols also can be readily acetylated, using acetic anhydride. The general method is shown in the next preparation.

PREPARATION 206.—**β-Naphthyl Acetate** (2-*Acetoxynaphthalene*).



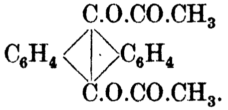
$C_{12}H_{10}O_2$. 186.

To a solution of 10 gms. of β-naphthol in 50 c.c. of 10% caustic soda solution 100 gms. of crushed ice are added, followed by 12 gms. of acetic anhydride. The product is crystallised from aqueous alcohol.

$$2C_{10}H_7OH + (CH_3CO)_2O = 2C_{10}H_7O.COCH_3 + H_2O.$$

Yield.—Theoertical (13·5 gms.). Colourless crystals ; insoluble in water ; M.P. 70°. (A., 209, 150 ; J. C. S., 1931, 2495.)

PREPARATION 207.—**9 : 10-Diacetoxyanthracene.**



$C_{28}H_{14}O_4$. 294.

10 gms. (1 mol.) of anthraquinone are refluxed and agitated for 30 minutes with 150 gms. (excess) of acetic anhydride, 10 gms. of fused sodium acetate (see p. 517) and 40 gms. (excess) of zinc dust, and the cooled mixture filtered at the pump. The product, which is the result of

reduction and acetylation, is recrystallised three times from glacial acetic acid.

$$C_6H_4(CO)_2C_6H_4 + (CH_3CO)_2O + H_2 = C_6H_4(CO.COCH_3)_2C_6H_4 + H_2O.$$

Yield.—Almost theoretical (14 gms.). Colourless needles; insoluble in water; M.P. 260°. (B., 21, 1172.)

Reaction CVI. Action of Acyl Chlorides on Alcohols. (B., 17, 2545; 19, 3218; 21, 2744; 23, 2962; A., 245, 140; 301, 102; 327, 105; J. pr., [2], 20, 263.)—Acid chlorides, especially of the aliphatic series, react with alcohols and phenols to give esters.

$$R_1.OH + R_{11}CO.Cl = R_{11}.CO.OR_1 + HCl.$$

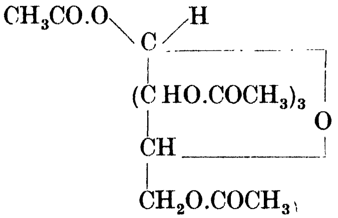
With aromatic acyl chlorides the reaction is not so rapid, but it can be greatly facilitated by the presence of caustic soda or caustic potash in dilute aqueous solution (Schotten-Baumann).

$$R_1OH + R_{11}CO.Cl + NaOH = R_{11}.CO.OR_1 + NaCl + H_2O.$$

Other alkalis can be employed—carbonates of the alkali and alkaline earth metals—pyridine, too, gives very good results, though with polyhydric alcohols the number of groups esterified may differ with organic and inorganic bases. Acetyl and similar aliphatic derivatives of hydroxy compounds cannot be prepared in this way, owing to the great instability of the acyl chlorides in presence of alkali.

The Schotten-Baumann reaction can also be applied to primary and secondary aromatic amines (see p. 310); it is much used in the identification of compounds to which it can be applied, by the preparation of their benzoyl, phenylacetyl, or benzene sulphonyl derivatives.

PREPARATION 208.—**β-Pentaacetylglucose.**



$C_{16}H_{22}O_{11}$. 390.

10 gms. powdered anhydrous glucose are ground in a mortar with 5 gms. anhydrous sodium acetate and placed in a flask with reflux air condenser attached. 50 gms. freshly-distilled acetic anhydride are added and the mixture heated on a steam bath until complete solution is effected. After 2 hours heating, the mixture is carefully poured with stirring, into 400 c.cs. ice water. The solid product is broken up after some hours and filtered and again kept for a few hours under water. Finally, it is filtered, pressed and crystallised from alcohol.

$$CH_2OH(CHOH)_4CHO \longrightarrow CH_2O(COCH_3)(CHO.COCH_3)_4CHO.$$

Yield.—70% theoretical (15 gms.). White solid; M.P. 134°.

When an acetic anhydride solution of the β-compound is heated with anhydrous zinc chloride, it is converted into α-pentacetylglucose, M.P. 112°–113°. (Am. Soc., 59, 1124 ; O. S., 22, 1.)

PREPARATION 209.—**Ethyl-3 : 5-Dinitrobenzoate.**

$(NO_2)_2C_6H_3COOC_2H_5$. $C_9H_8O_6N_2$. 240.

5 gms. of 3 : 5-dinitrobenzoic acid and 5 gms. of phosphorus pentachloride are gently warmed and the mixture allowed to cool. The solid dinitrobenzoyl chloride is separated from the phosphorus oxychloride by pressing on a porous plate. The crude chloride is then treated with 5 c.cs. of ethyl alcohol, under reflux, and warmed to about 80° for 10 minutes. The product is crystallised from 60% alcohol. M.P. 92°. (A., 202, 223.)

The above is the procedure for the preparation of dinitrobenzoates, so useful for the identification of alcohols.

PREPARATION 210.—**Dimethyl Sulphate** (*Dimethyl ester of sulphuric acid*).

$(CH_3)_2SO_4$. $C_2H_6O_4S$. 126.

(Dimethyl sulphate is *very poisonous, and great care must be taken not to inhale its vapour. Ammonia vapour neutralises the toxic effects. This preparation must be carried out in a good fume cupboard.*)

100 gms. (excess) of chlorosulphonic acid (see p. 519) are placed in a 250-c.c. distilling flask fitted with a rubber stopper, carrying a thermometer the bulb of which is immersed in the acid, and cooled to −10°; 30 gms. (excess) of pure anhydrous methyl alcohol are slowly dropped in during 2 hours by means of a dropping funnel, the stem of which is drawn out to a fine point, and then bent upwards so that the opening is just below the surface of the acid in the flask. Care must be taken that initially the stem of the funnel is full of alcohol. The side tube of the flask is connected with three wash-bottles, the first containing conc. sulphuric acid, and the third cold water to absorb the hydrogen chloride evolved ; the second is empty, and reversed to prevent the water sucking back into the sulphuric acid. During the addition, the flask is frequently shaken, and throughout, the temperature must not be allowed to rise above −10°. When all the alcohol has been added, the mixture is cautiously distilled at 20 mms. from an oil bath at 140°. The ester which comes over is washed with a little ice-water, dried over anhydrous sodium sulphate for 24 hours, and re-distilled at 20 mms. as before, collecting at 150°–160°.

$$Cl.SO_2.OH + 2CH_3.OH = SO_2(OCH_3)_2 + HCl + H_2O.$$

Methyl hydrogen sulphate, formed at an intermediate stage, yields the normal sulphate on vacuum distillation.

Yield.—90% theoretical (50 gms.). Colourless odourless liquid ; emits very poisonous vapour ; B.P. ^{760} 188°. (A., 327, 105.)

Methyl ethyl sulphate can be prepared by adding ethyl chlorosulphonate to sodium methoxide in dry ether (Am. Soc., 46, 1044), and other alkyl sulphates can be prepared by a similar method (C. r., 178, 1182.)

Preparation 211.—Dimethyl Terephthalate (*Dimethyl ester of* 1 : 4-*benzenedicarboxylic acid*).

$C_6H_4(COOCH_3)_2[1:4]$. $C_{10}H_{10}O_4$. 194.

10 gms. (1 mol.) of terephthalic acid (see p. 249) are warmed with 13 gms. (2 mols.) of phosphorus pentachloride until liquefaction occurs, 20 gms. (excess) of methyl alcohol are added, and the whole refluxed for 2 hours. On cooling, the precipitate is filtered off and recrystallised from methyl alochol.

$$C_6H_4(COOH)_2 \xrightarrow{PCl_5} C_6H_4(COCl)_2 \xrightarrow{CH_3OH} C_6H_4(COOCH_3)_2$$

Yield.—80% theoretical (9 gms.). Colourless crystals; insoluble in water; M.P. 140°. (A., 245, 140; J. pr., [2], 20, 263; D.R.P., 38973; 70483; 71446.)

Sodium terephthalate can be used alone in place of the free acid.

The following preparations exemplify the Schotten-Baumann reaction.

Preparation 212.—Methyl Benzoate (*Methyl ester of benzenemonocarboxylic acid*).

$C_6H_5COOCH_3$. $C_8H_8O_2$. 136.

20 gms. (excess) of methyl alcohol are added to 15 gms. (1 mol.) of benzoyl chloride and then 10% caustic soda solution, until the whole is alkaline. The mixture is well shaken, warmed gently, until the smell of benzoyl chloride has completely disappeared, and poured into water. The layer of ester is dissolved in ether, the solution dried over calcium chloride, and distilled, the fraction 195°–205° being redistilled.

$$C_6H_5COCl + CH_3OH + NaOH = C_6H_5COOCH_3 + NaCl + H_2O.$$

Yield.—90% theoretical (12 gms.). Colourless liquid; B.P. ^{760} 199°; D. $^{10}_{4}$ 1·1086. (B., 17, 2545; 19, 3218; 21, 2744; 23, 2962.)

Ethyl benzoate, glyceryl tri-benzoate, etc., are prepared in an exactly similar manner. The reaction can also be applied to phenols and naphthols.

Preparation 213.—Phenyl Benzoate (*Phenyl ester of benzenemonocarboxylic acid*).

$C_6H_5COOC_6H_5$. $C_{13}H_{10}O_2$. 198.

10 gms. (excess) of phenol are dissolved in 100 c.cs. of water and 10 gms. (1 mol.) of benzoyl chloride added, and then 10% aqueous caustic soda solution until the whole is alkaline. The mixture is warmed and shaken until the smell of benzoyl chloride has disappeared; the ester which separates is filtered off at the pump, washed with cold water, dried on a porous plate, and recrystallised from alcohol.

$$C_6H_5CO.Cl + C_6H_5OH + NaOH = C_6H_5COOC_6H_5 + NaCl + H_2O.$$

Yield.—Almost theoretical (21 gms.). Colourless crystals; insoluble in water; M.P. 68°. (B., 17, 2545; 19, 3218; 21, 2744; 23, 2962.)

α- and β-naphthyl benzoates (M.P. 56° and 107° respectively) are similarly prepared. Pyridine is the base used in the next preparation.

PREPARATION 214.—**Mannitol Dibenzoate** (1 : 6-*Dibenzoic ester of hexolhexan*).

$$C_6H_8(OH)_4(O.OC.C_6H_5)_2. \quad C_{20}H_{22}O_8. \quad 390.$$

To 10 gms. (1 mol.) of mannitol dissolved in 500 c.cs. of pyridine, 50 gms. (excess) of benzoyl chloride are slowly added in the warm, the whole allowed to stand overnight and poured into 1 litre of cold 10% sulphuric acid. The ester is filtered off at the pump, washed with cold water and recrystallised from alcohol.

$$\begin{array}{l} CH_2OH \\ (CHOH)_4 \\ CH_2OH \end{array} + 2C_6H_5COCl \xrightarrow{C_5H_5N} \begin{array}{l} CH_2O.OC.C_6H_5 \\ (CHOH)_4 \\ CH_2O.OC.C_6H_5 \end{array} + 2HCl.$$

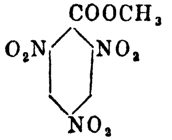
Yield.—80% theoretical (17 gms.). Colourless needles ; insoluble in water ; M.P. 178°. (A., 301, 102.)

Ethyl acetate can be prepared in a like manner.

Reaction CVII. Action of an Alkyl Iodide on the Silver Salt of an Acid. (J. C. S., 76, 600.)—This method is used when an ester is not easily obtained by the usual methods owing to steric hindrance (see also p. 262). The silver salt and alkyl iodide are heated or shaken together with or without an inert solvent, benzene, etc. The precipitated silver halide is filtered off, and the ester separated from the filtrate by distillation or some other method.

$$R_1I + RCOOAg = R.COO.R_1 + AgI.$$

PREPARATION 215.—**Methyl Trinitrobenzoate** (*Methyl ester of s-trinitrobenzoic acid*).



$C_8H_5O_8N_3$. 271.

10 gms. (1 mol.) of *s*-trinitrobenzoic acid are treated with 14 gms. (1 mol. NH_4OH of 10% (D. 0·959)) ammonium hydroxide solution, 7 gms. silver nitrate in aqueous solution added, and the precipitate filtered at the pump, washed with cold water and dried as described on p. 484. The dried silver salt and 20 gms. (excess) of methyl iodide are refluxed on a water bath for 1 hour, excess of methyl iodide is distilled off, and the residue extracted with boiling alcohol and filtered. The filtrate is concentrated to small bulk, cooled, and the precipitate recrystallised from alcohol.

$$C_6H_2(NO_2)_3(COOAg)[2:4:6:1] + CH_3I$$
$$= C_6H_2(NO_2)_3(COOCH_3)[2:4:6:1] + AgI.$$

Yield.—80% theoretical (8 gms.). Colourless crystals ; insoluble in water ; M.P. 157°. (J. C. S., 67, 600.)

Reaction CVIII. Polymerisation of an Aldehyde to an Ester (*Chem. Rev.*, 34, 362).—In presence of sodium benzylate banzaldehyde polymerises to benzyl benzoate, a reaction similar to the simultaneous oxidation and reduction of aromatic aldehydes (Cannizzaro, p. 190) and to the dismutation of acetaldehyde to ethyl acetate by aluminium ethoxide (Ann. Rep., 1925, 72).

$$\mathrm{PhCH_2ONa} \rightleftharpoons \mathrm{PhCH_2{:}\underset{..}{\ddot{O}}{:}} + \overset{+}{\mathrm{Na}} \qquad \mathrm{PhCHO} \longleftrightarrow \mathrm{PhCH{:}\underset{..}{\ddot{O}}{:}}$$

$$\mathrm{PhCH{:}\underset{..}{\ddot{O}}{:}} + \mathrm{{:}\underset{..}{\ddot{O}}{:}CH_2Ph} \longrightarrow \mathrm{PhCH({:}\underset{..}{\ddot{O}}{:})(OCH_2Ph)}.$$

$$\mathrm{PhCH({:}\underset{..}{\ddot{O}}{:})OCH_2Ph} + \mathrm{PhCH{:}\underset{..}{\ddot{O}}{:}} \longrightarrow \mathrm{PhCOOCH_2Ph} + \mathrm{PhCH_2{:}\underset{..}{\ddot{O}}{:}}.$$

See Note p. 104.

Preparation 216.—**Benzyl Benzoate** (*Benzyl ester of phenylmethan acid*).

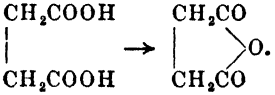
$C_6H_5CO.O.CH_2C_6H_5$. $C_{14}H_{12}O_2$. 212.

A solution of 0·75 gm. of sodium in 18 gms. of benzyl alcohol (previously dried over potassium hydroxide and redistilled) is heated on a water bath using a calcium chloride tube on the flask, and added to 75 gms. (2 mols.) of benzaldehyde (previously dried over calcium chloride and distilled in a current of carbon dioxide). The whole is heated on a water bath for 20 hours, and acidified with 5 c.cs. of glacial acetic acid. Water is added, and the oil which separates dried over calcium chloride and distilled in a high-temperature distilling flask (see p. 20). Some unchanged benzaldehyde comes over; the fraction 320°–326° is retained.

$$2C_6H_5.CHO \xrightarrow{C_6H_5CH_2ONa} C_6H_5.CH_2.O.CO.C_6H_5.$$

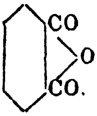
Yield.—80% theoretical (60 gms.). Colourless crystals; insoluble in water; M.P. 20°; B.P. 323°. (B., 20, 649; O. S., II, 5.)

Reaction CIX. Action of Heat on certain Dibasic Acids. (B., 10, 326.) —When acids such as phthalic, succinic or maleic, which contain carboxyl groups attached to adjacent carbons, are heated, they readily yield anhydrides.



Dibasic acids with carboxyl groups not so attached form monomeric anhydrides less readily or not at all. Some form polymeric anhydrides, e.g. adipic acid.

Preparation 217.—**Phthalic Anhydride** (*Anhydride of* 1 : 2-*benzene-dicarboxylic acid*).



$C_8H_4O_3$. 148.

20 gms. (1 mol.) of phthalic acid (Preparation 187) are sublimed over a naked flame in the apparatus described on p. 35. Long needles collect on the filter paper and funnel.

Yield.—Almost theoretical (18 gms.). Colourless needles; yields phthalic acid with water; M.P. 128°; B.P. 284°. (B., 10, 326.) For catalytic oxidation of naphthalene, see J. S. C. I., 51, 159.

Succinic anhydride (see Preparation 220) can be similarly prepared.

Phthalic anhydride with certain poly-hydroxy alcohols, e.g. glycerol, or ethylene glycol forming linear polymers—the glyptal or alkyd resins.

The following reactions, unlike the above, deal mostly with the preparation of anhydrides in which the carboxyl groups belong to different molecules:

Reaction CX. Action of an Acyl Chloride on the Sodium Salt of an Acid. (A. Ch., [3], 37, 311.)—This is a standard method of preparing acid anhydrides. By using the sodium salt of one acid with the acid chloride of another, mixed anhydrides may be obtained.

$$R_1COONa + Cl.CO.R_{11} = R_1CO.O.COR_{11} + NaCl.$$

Anhydrides can also be prepared by the action of an acid on half the quantity of phosphorus oxychloride, phosphorus trichloride, thionyl chloride, or sulphuryl chloride, necessary for its conversion to the acid chloride which is intermediately formed.

$$2CH_3COONa + POCl_3 = 2CH_3COCl + NaPO_3 + NaCl.$$
$$2CH_3COONa + 2CH_3CO.Cl = 2(CH_3CO)_2O + 2NaCl.$$
$$2R.COOH + SOCl_2 = (RCO)_2O + SO_2 + HCl.$$

This latter method is used industrially.

PREPARATION 218.—Acetic Anhydride (*Ethan acid anhydride*).

$(CH_3CO)_2O$. $C_4H_6O_3$ 102.

100 gms. (excess) of crystallised sodium acetate are heated on a metal tray or in a porcelain basin until the crystals melt in their own water of crystallisation (p. 517), solidify, and finally remelt. (*Caution!*) When the whole mass has fused (315°), it is allowed to cool and is powdered; overheating must be avoided. It is immediately introduced into a 250-c.c. retort connected by a water condenser to a receiver consisting of a distilling flask, the side tube of which is fitted with a calcium chloride tube connected with the draught pipe. The whole apparatus is fitted up in a fume cupboard. 40 gms. (1 mol.) of acetyl chloride are slowly added by means of a dropping funnel fixed in the tubulus of the retort, which is meantime cooled in water and shaken at intervals. When addition is complete, the dropping funnel is removed, the mixture stirred with a glass rod, and the tubulus closed with a glass stopper. The retort is now heated with a luminous flame, which is constantly moved about, until nothing further distils. Some fused sodium acetate is added to the distillate and the latter redistilled from the receiving flask into another distilling flask fitted with a calcium chloride tube as before Each time before begin-

ning distillation the air in the apparatus should be displaced by dry air blown into it *via* the calcium chloride tube by means of a rubber bulb attachment. This will help in the production of a colourless liquid. In the second distillation the fraction distilling at 130°–140° is collected separately.

$$CH_3COCl + NaOCOCH_3 = (CH_3CO)_2O + NaCl.$$

Yield.—80% theoretical (45 gms.). Colourless liquid; suffocating smell; B.P. 138°; D. $^{15}_{4}$ 1·08. (A. Ch., [3], 37, 311.)

Note.—If a purer product is desired, distillation over fused sodium acetate must be repeated until a drop of the distillate shaken with a little warm water (*Caution!*) gives no precipitate on addition of dilute nitric acid and silver nitrate. This test shows the complete absence of acetyl chloride. Benzoic anhydride (p. 272), etc., is obtained in similar manner.

For references to thermal " anhydrisation ", see A. C. R., 1934, 125.

Reaction CXI. Action of Dehydrating Agents on a Free Acid. (B., 34, 186, 2074; A., 226, 8.)—This is a usual method of preparing the anhydrides of acids, the chlorides of which are not readily available. Acetic anhydride is very frequently used—acetyl chloride can also be employed.

$$2R.COOH + (CH_3CO)_2O = (RCO)_2O + 2CH_3COOH.$$

Preparation 219.—**Cinnamic Anhydride** (*Anhydride of 3-phenyl-2-propen acid*).

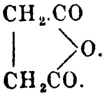
$(C_6H_5CH : CHCO)_2O.$ $C_{18}H_{14}O_3.$ 278.

50 gms. (2 mols.) of dry, finely-powdered cinnamic acid and 250 gms. (excess) of acetic anhydride are refluxed together for 8 hours, and distilled to 146°. The cold residue is extracted with ether, the extract filtered, and ether removed on a water bath. The residue is recrystallised from alcohol.

$$2C_6H_5CH : CHCOOH \xrightarrow{-H_2O} (C_6H_5CH : CHCO)_2O.$$

Yield.—Almost theoretical (46 gms.). Colourless needles; soluble in ether and in hot alcohol; M.P. 136°. (B., 34, 186, 2074.)

Preparation 220.—**Succinic Anhydride** (*Anhydride of butan-diacid*).



$C_4H_4O_3.$ 100.

18 gms. finely-powdered succinic acid and 30 gms. acetic anhydride are heated on a boiling water bath, in a flask under a reflux with calcium chloride tube, for about an hour. On cooling, at first spontaneously until crystallisation sets in, and finally in ice water until separation is complete, the crystalline anhydride is obtained. This is collected and washed with ether. It may be recrystallised from alcohol.

Yield.—80% theoretical (13 gms.). Long needles: M.P. 119·6°; (A., 226, 8; C. V., II, 560, uses phosphorus oxychloride.)

Reaction CXII. Action of certain Bases on Acyl Chlorides. (B., 34, 2070; J. pr., [2], 50, 479.)—When pyridine or quinoline act on an acid chloride, and the addition product which is formed treated with water, the acid anhydride is obtained (cf. Reaction CXI).

$$2R.CO.Cl \xrightarrow[H_2O]{C_5H_5N} (RCO)_2O + 2HCl.$$

PREPARATION 221.—**Benzoic Anhydride** (*Anhydride of benzenemonocarboxylic acid*).

$$(C_6H_5CO)_2O. \qquad C_{14}H_{10}O_3. \qquad 226.$$

25 gms. (2 mols.) of benzoyl chloride are slowly added to 20 c.cs. of pyridine and 8 gms. of anhydrous sodium carbonate; after ½ hour the whole is poured into water, the precipitate filtered and washed with cold water, and dried first on a porous plate, and then in a desiccator. It is recrystallised from petroleum ether, which is removed under reduced pressure.

Colourless needles; insoluble in water; M.P. 42°. (J. pr., [2], 50, 479; O. S., III, 21; Rec., 47, 321; E. P., 280373 (1926).)

The anhydride may also be obtained by the action of acetic anhydride on benzoic acid. (B., 57, 431; C. V., I, 91.)

Note.—The anhydrides of acetic, succinic, benzoic, and phthalic acids form derivatives with alcohols, phenols, and amines, useful for identification.

Detection of Esters, Acid Halides, and Anhydrides

Hydroxamic Acids.—The above compounds react with hydroxylamine to yield hydroxamic acids which give a violet colouration with ferric chloride.

$$RCOOR_1 \longrightarrow RCONHOH + R_1OH.$$

$$RCOX \longrightarrow RCONHOH + HCl.$$

$$(RCO)_2O \longrightarrow RCONHOH + RCOOH.$$

Example.—1 part ethyl acetate is treated with 10 parts of a 5% solution of hydroxylamine hydrochloride in methyl alcohol. A solution of aqueous alcoholic potash hydroxide is added until alkaline (litmus). This mixture is heated to boiling, cooled, and acidified with dilute hydrochloric acid and a drop of ferric chloride solution added. A violet coloration is produced.

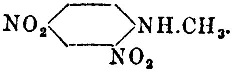
CHAPTER XVIII

THE LINKING OF NITROGEN TO CARBON

NITRO COMPOUNDS

Reaction CXIII. Action of Dilute Nitric Acid on certain Aromatic Compounds.—Dilute nitric acid, which often acts as an oxidising agent, can be used for introducing the nitro group, NO_2, under certain conditions. For example, phenol can be converted into nitrophenol by 3% nitric acid, while 4% acid converts methyl- and ethyl-acetanilide into the corresponding dinitro derivatives. The nitro group can also be substituted in the side chain by heating, say, toluene with dilute nitric acid under pressure. The reaction, however, is not generally employed, as it is necessary to boil for some hours. Sodium and potassium nitrates in dilute sulphuric acid and solutions of nitric acid in glacial acetic acid, ether, acetone, and acetic anhydride are also used.

PREPARATION 222.—**Dinitromethylaniline** (1-*Methylamino*-2 : 4-*dinitrobenzene*).



$NO_2C_6H_3(NO_2)NH.CH_3$. $C_7H_7O_4N_3$. 197.

10 gms. methyl acetanilide * are dissolved in 1 litre of dilute nitric acid (D. 1·029), and the solution heated to boiling under a reflux condenser. The liquid instantaneously assumes a brown colour, and after half an hour's heating becomes turbid and a yellow substance begins to separate out. Two hours' heating is, however, necessary to complete the reaction. On cooling, the substance separates out in yellow crystals, which are recrystallised from aqueous alcohol.

$$C_6H_5N.CH_3COCH_3 + 2HNO_3 + H_2O \longrightarrow C_6H_3(NO_2)_2NH.CH_3 + CH_3COOH + 2H_2O.$$

M.P. 175°. (B., 18, 1995.)

Reaction CXIV. Action of Concentrated Nitric Acid on Aromatic Compounds. (B., 20, 333.)—Concentrated nitric acid up to 100% is required for nitrating many aromatic compounds not oxidised by this treatment. Aliphatic nitro compounds, useful as industrial solvents, are now prepared by vapour phase nitration at 420° C. (J. Eng., 1940, 427 ; Chem. Rev., 32, 373). The reaction is represented by the equation

$$RH + HONO_2 \longrightarrow R.NO_2 + H_2O.$$

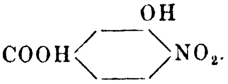
In general the temperature should be kept as low as possible to avoid oxidation. When the temperature is raised the tendency to form dinitro,

---

* Methyl acetanilide is prepared by heating mono-methylaniline with acetyl chloride. It can be purified by recrystallisation or sublimation. M.P. 101°–102°. (B., 10, 328.)

trinitro, and polynitro derivatives is much increased. The reaction is promoted, in some cases, by the presence of boron trifluoride (J. Eng., 1940, 408).

PREPARATION 223.—4-Nitro-3-hydroxybenzoic Acid.



$C_7H_5O_5N$. 183.

50 gms. *m*-hydroxybenzoic acid are dissolved in 175 c.cs. of hot nitrobenzene. The solution is cooled to 35°–40°, and 17 c.cs. fuming nitric acid dissolved in an equal amount of nitrobenzene are slowly added with stirring during 4 hours. The product is filtered, washed with carbon tetrachloride, and crystallised from dilute alcohol.

Yield.—15% theoretical (10 gms.). M.P. 227°–228°. (J. C. S., 119, 1428.)

Reaction CXV. Action of a Mixture of Concentrated Nitric Acid and Concentrated Sulphuric Acid ("Mixed" acid) on Aromatic Compounds.—This, the most important procedure for nitration, is represented:

$$R.H + HONO_2 \longrightarrow R.NO_2 + H_2O.$$

The interaction of the acids is to generate the nitronium and bisulphate ions; the former being the active nitrating agent.

$$HNO_3 + 2H_2SO_4 \longrightarrow \overset{+}{NO_2} + H_3\overset{+}{O} + 2HS\overset{-}{O_4}.$$

For studies of nitration, see J. C. S., 1934, 1357; 1946, 869, 875, 880.

(*a*) The theoretical quantity of nitric acid is added to a large excess of conc. sulphuric acid, and the mixed acid added to the compound to be nitrated. Or the compound may be dissolved in excess of conc. sulphuric acid, and the theoretical quantity of strong nitric acid then added. The quantity of sulphuric acid added must be such that its final concentration after nitration, i.e. when it contains the water formed in the reaction plus the water originally present in the nitric acid, must be above a certain minimum, depending on the compound to be nitrated. When this minimum concentration of sulphuric acid is reached nitration stops.

(*b*) In nitrating bases, the basic group must be protected from oxidation. This may be done in several ways:

1. By carrying out the nitration in presence of a large excess of conc. H_2SO_4. The amine sulphate is first formed, and then nitration takes place.
2. By introducing acyl groups previous to nitration,

$$R.NH_2 \longrightarrow R.NH.COR_1 \longrightarrow R.N(COR_1)_2,$$

where R_1 = alkyl or aryl group.

After nitration, the acyl group is split off by hydrolysis.

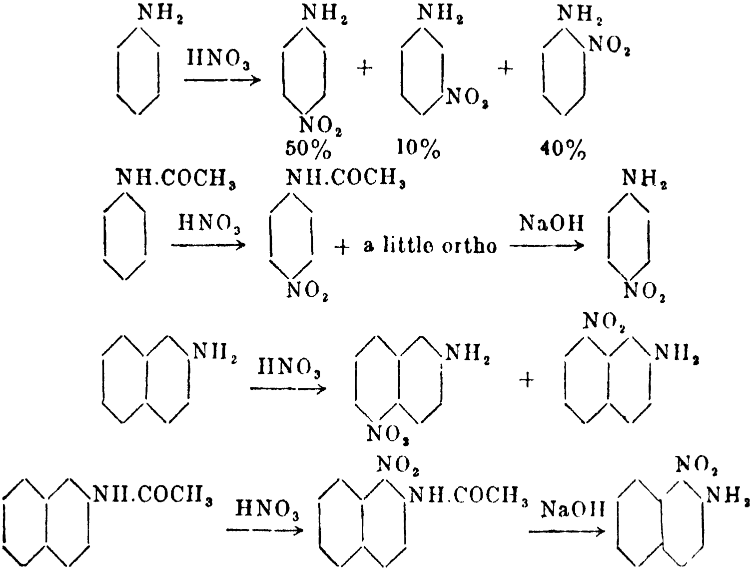
$$NO_2C_6H_4.NH.COR_1 \xrightarrow{H_2O} NO_2C_6H_4.NH_2 + R_1COOH.$$

3. By combining with benzaldehyde to form a benzylidene derivative,

$$R.NH_2 + OCH.C_6H_5 \longrightarrow R.N{=}CH.C_6H_5,$$

which can be readily nitrated, and the benzylidene group removed subsequently by hydrolysis.

By these methods usually only one isomer is formed in appreciable quantity, e.g.



(*c*) Sometimes it is necessary to protect the OH group, and the same acyl groups are introduced.

Rules of Nitration.—As a general rule, nitrations should be carried out at as low a temperature as possible, to reduce losses due to oxidation.

The number of nitro groups introduced into the nucleus is dependent on the amount and concentration of the nitric acid, temperature, and duration of nitration.

The position taken by a NO_2 group on entering the nucleus depends on the group or groups already present. In general, OH, NH_2, Cl, Br, I, CH_3, and CH_2Cl, are *o*- and *p*- directing, and their presence facilitates the introduction of the nitro group, while SO_3H, COOH, CN, CHO, CO, and NO_2 are *m*-directing, and tend to retard nitration.

The proportion of isomers formed is not altered to any great extent by temperature.

For a discussion on the different theories of substitution, see J. C. S., 1946, 968.

Analysis of a Mixed Acid.—1. *Total Acidity* (calculated as H_2SO_4).—About 5 c.cs. of mixed acid are put into a tared weighing bottle and its weight found. This is then washed into a beaker and titrated with N/1 caustic soda solution, using methyl orange as indicator.

$$\% \ H_2SO_4 = \frac{4{\cdot}9 \times \text{c.cs. of NaOH}}{\text{weight taken}}.$$

2. **H_2SO_4** (*Actual*).—About 5 c.cs. are weighed out into a tared dish, and heated on a water bath till all the HNO_3 and HCl (if any) are driven off. This is then washed into a flask and titrated , as in 1.

$$\text{Total acidity as } H_2SO_4 - \left(HNO_3 \times \frac{49}{63}\right) = \text{real } H_2SO_4.$$

It is better, however, to estimate HNO_3 as in 3.

3. **HNO_3** *by Nitrometer.*—About 5 gms. of mixed acid are weighed out and placed in the funnel of a nitrometer, and washed in with a little pure conc. H_2SO_4. The nitrometer is well shaken until all the NO is evolved. It is then allowed to stand at room temperature and the volume at N.T.P. calculated.

$$\text{This volume} \times \frac{63}{22400} = \text{weight of } HNO_3 = x.$$

$$\% \ HNO_3 = \frac{x}{\text{weight taken}} \times 100.$$

This figure includes HNO_2, which also gives NO in the nitrometer. It can be estimated as in 4. For estimation using ferrous sulphate, see J. Eng., 1915, 766.

4. **HNO_2** (*Small Amounts*).—5 c.cs. N/10 permanganate solution are diluted with distilled water to 100 c.cs. The mixed acid is then run in from a burette until the $KMnO_4$ is decolorised. The weight of mixed acid is calculated from its specific gravity.

$$HNO_3 \text{ by nitrometer} - \left(HNO_2 \times \frac{63}{47}\right) = \text{real } HNO_3$$

$$1 \text{ mol. } KMnO_4 \equiv 5 \text{ mols. } HNO_2.$$

For estimation using ceric sulphate, see J. Eng., 1948, 339.

Isolation of Nitro Compounds.—Nitro compounds in many cases separate in the liquid or solid form from the residual acid (" Waste acid "). Since these are usually somewhat soluble in waste acid a further yield can be obtained by diluting the latter with water. Liquid nitro compounds are isolated in a separating funnel, while solids are removed by filtration. Steam distillation is sometimes adopted as in Preparation 232.

" Waste acid " is often used for nitration after addition of the necessary conc. sulphuric acid or oleum, and nitric acid. (See Preparation 228.)

PREPARATION 224.—**Nitrobenzene.**

$C_6H_5.NO_2$. 123.

100 gms. of benzene are placed in a vessel, which is provided with a good efficient mechanical agitator. A mixed acid is made by taking 140 gms. nitric acid (D. 1·41) and 180 gms. conc. sulphuric acid, and

mixing well together. Considerable heat is generated in mixing these acids, and before proceeding further the mixture should be cooled. The benzene should now be agitated briskly, and the mixed acid run in slowly. The temperature rises quickly to about 45°, when the flow of acid is reduced, and, if necessary, cooling water applied to the outside of the nitrating vessel. The acid should now be added at such a speed that, when it is all in, the temperature has risen to 60°. The temperature is kept at 60°–70° until nitration is complete (2 hours).

When nitration is complete the mixture is run into a separator, diluted with water and allowed to settle. After a time the layers are separated, the nitrobenzene being washed with a little dilute sodium carbonate solution.

After settling, the nitrobenzene is run off from the bottom, and freed from water by anhydrous calcium chloride until it is clear. The water and any unchanged benzene may also be removed by distillation. The nitrobenzene is then distilled, distillation being stopped when the contents of the flask turn dark in colour, the fraction 208°–212° being collected. The residue in the flask contains dinitrobenzene.

$$C_6H_6 + HNO_3 \longrightarrow C_6H_5NO_2 + H_2O.$$

Yield.—85% theoretical (134 gms.). Pale yellow liquid with characteristic smell; M.P. 5·7°; B.P. 210°; D. $^{13}_{4}$ 1·2116; important intermediate for dyestuffs. (A., 12, 305; J. pr., 19, 375.)

Preparation 225.—*m*-**Dinitrobenzene.**

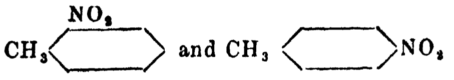
$C_6H_4(NO_2)_2$. 168.

To a mixture of 30 gms. conc. sulphuric acid and 18 gms. of fuming nitric acid, contained in a flask of about 700 c.cs. capacity, 12 gms. of nitrobenzene are gradually adding with shaking. The flask is heated on a water bath in a fume cupboard until a test sample solidifies on pouring into cold water; about 30 minutes' heating is generally required. The contents of the flask are then poured in a thin stream into a large volume of vigorously agitated ice-cold water. The crude dinitrobenzene, which contains about 3% *p*-dinitro and 1% *o*-dinitrobenzene is filtered off, washed well with water, and recrystallised from alcohol.

$$C_6H_5NO_2 + HNO_3 \longrightarrow C_6H_4(NO_2)_2 + H_2O.$$

Yield.—75–87% theoretical (12–14 gms.). Pale yellow needles; M.P. 90°. (A., 57, 214.)

Preparation 226.—*o*- **and** *p*-**Nitrotoluenes** (1-*Methyl*-2-*nitrobenzene and* 1-*methyl*-4-*nitrobenzene*).



$C_7H_7O_2N$. 137.

100 gms. toluene are placed in a nitrating vessel. A mixed acid, consisting of 150 gms. conc. sulphuric acid and 100 gms. nitric acid (D. 1·44), is cooled and run into the toluene, which is vigorously agitated. The

temperature rises to 20°–30°, and is maintained at that, cooling water being passed into the water bath if necessary. After all the acid has been added the temperature is allowed to rise to 50°. This temperature is maintained until the specific gravity of the oil (taken by hydrometer) is 1·15. The oil is then separated from the waste acid in the usual way, washed with water and sodium carbonate solution, and then dried on the water bath.

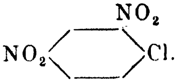
Any unnitrated toluene can be removed by distillation. The *o*-compound may be separated from the *p*-compound by fractional distillation, using a column. 40% of the mixture is distilled off, consisting chiefly of *o*-compound. The *p*-compound is obtained from the residue by cooling at 0°.

If the mixture is cooled to about −20° (see p. 12) the *p*-compound crystallises out.

The mixture consists of about 65–70% *ortho-* and about 30% *para-*, with about 4% *meta*-compound.

Yield.—Total—almost theoretical (148 gms.). (Z. e., 16, 161 ; Phil. Mag., 1876, IV, 1, 17.)

PREPARATION 227.—**2 : 4-Dinitro-chlorobenzene.**



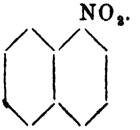
$C_6H_3O_4N_2Cl$. 202·5.

350 gms. of a mixed acid containing 50% nitric acid are placed in a cast-iron pot with good agitation. 113 gms. of chlorobenzene are then run in, the temperature being kept under 5° by external cooling. After all the mixed acid has been added the stirring is maintained for another hour at 5°–10°. The temperature is then slowly raised to 50° and kept at this for 1 hour. 350 gms. conc. sulphuric acid are then dropped in very cautiously with good stirring, and the mixture finally heated up to 115° for half an hour. After cooling, the product is poured into cold water, when it immediately solidifies. The mother liquor is poured off and the dinitrochlorobenzene washed free of acid by heating up in water beyond its melting point (51°) and stirring. The water is then poured off.

Yield.—Almost theoretical (200 gms.). Yellow crystals ; M.P. 51°.

Note.—Care should be exercised that dinitrochlorobenzene is not allowed to touch the skin, as it is liable to produce eczema and sores. (B., 27, 2457 ; U.S.P., 1220078.) Used in testing for amines.

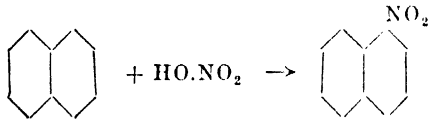
PREPARATION 228.—**α-Nitronaphthalene** (1-*Nitronaphthalene*).



$C_{10}H_7O_2N$. 173.

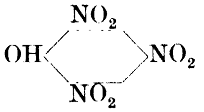
80 gms. nitric acid (D. 1·4) are mixed with 100 gms. conc. H_2SO_4 and 300 gms. waste acid from a previous nitration. (In place of waste acid

300 gms. 80% H_2SO_4 plus 1 gm. $NaNO_2$ may be used.) The temperature is raised to 40° and 100 gms. naphthalene, which has been previously melted, is run in gradually with agitation. The temperature is not allowed to rise beyond 50° until all the naphthalene has been added, when it is raised to 60°. The nitronaphthalene forms a cake on the top of the nitrating vessel as soon as agitation is stopped and cooling is applied. The nitration should be tested every hour after the temperature has reached 60° by removing part of the cake, which forms on cooling, melting and washing quickly with dilute sodium carbonate solution, removing the alkali and drying with filter paper, and taking the setting point, as described on p. 19. The temperature is maintained at 60° until a setting point 56°–58° is obtained. When nitration is complete agitation is stopped the nitrating vessel is cooled, and the cake which forms is removed from the waste acid. The cake is then boiled with water to volatilise naphthalene, and some sodium carbonate solution added to remove any adhering acid. The cake is then allowed to solidify, the wash water is run off, and the nitronaphthalene dried by heating at 120° in an air oven. It may be recrystallised from alcohol.



Yield.—90–95% theoretical (111–118 gms.). Yellow needles; M.P. 58·5°; B.P. 304°. (D.R.P., 100417; H. Acta., 15, 236.)

PREPARATION 229.—**Picric Acid** (2 : 4 : 6-*Trinitrophenol*).



$C_6H_3N_3O_7$. 187.

93 gms. phenol are heated to 100° in a sulphonating pot (Fig. 37), when 300 gms. 100% sulphuric acid is added, the temperature being kept under 110°, and maintained at this temperature for an hour until sulphonation is complete (test). It is then cooled down to 0°, agitation being maintained.

220 gms. nitric acid (D. 1·5) and 220 gms. 100% sulphuric acid are mixed together and cooled. This is added drop by drop to the sulphonic acid in the pot. It is then allowed to stand overnight at ordinary temperature, and is then very gradually heated up to 30°, and then up to 45°, but no higher.

About 50 c.cs. of the nitrating mixture is then removed from the pot and heated with stirring in a large porcelain basin on a sand bath to 110°–125°. The rest of the mixture is then removed, and is poured gradually into the preheated portion. When all has been added the temperature is kept at 110°–120° for half an hour. 700 c.cs. of water are then added at such a speed that the temperature is kept at 120°. The picric acid separates out on cooling and is filtered through cotton and washed with water.

Yield.—90% theoretical (165 gms.). Yellow powder; explosive; solubility in water at 20°, 1 in 90; M.P. 122·5°. (A., 43, 219; B., 2, 52.) Forms crystalline picrates with various types of aromatic compounds, such as hydrocarbons, ethers, amines, phenols, etc.

Note. Should normally be stored in a moist condition.

Resorcinol by similar treatment gives 2-4-6-trinitroresorcinol (styphnic acid).

PREPARATION 230.—(1) *p*-**Nitroacetanilide.**

$$NO_2C_6H_4NH.CO.CH_3. \qquad 180.$$

(2) *p*-**Nitroaniline.**

$$NO_2C_6H_4NH_2. \qquad 138.$$

(1) 20 gms. of finely-ground acetanilide are added to 80 gms. conc. sulphuric acid, which is continuously stirred. The solid slowly dissolves, and the temperature, which gradually rises, must not exceed 30°. When all is dissolved the solution is cooled in a freezing mixture to 0°, and a mixed acid, previously cooled, containing 15·5 gms. nitric acid (D. 1·38), and 15 gms. conc. sulphuric acid gradually added during the course of 5 minutes, the temperature not exceeding 3°. When all is added, the solution is allowed to stand for 2 hours or longer, until a sample on pouring into water and boiling with caustic soda gives no odour of aniline. The reaction mixture is poured on to a mixture of 50 gms. of water and 50 gms. of ice, when the nitroacetanilide is precipitated. The precipitate is filtered off and washed with water; it is then stirred with 100 c.cs. of water, sufficient sodium carbonate to render the liquid alkaline to litmus being added, and the whole boiled. By this treatment any *o*-nitroacetanilide present is hydrolysed, but the *p*-compound remains unchanged, and is filtered off at about 50° and washed with water.

Yield.—90% theoretical (23 gms.). May be recrystallised from alcohol (M.P. 207°), but is generally used in the crude form for further preparations.

(2) The product derived from the last preparation is stirred with an equal quantity of water, 20 gms. of 35% caustic soda added, and the whole boiled for 2–3 hours. At the end of this time the solution should still show a faint alkaline reaction, and the hydrolysis is complete when a sample dissolves to a clear solution in hydrochloric acid. The liquor is cooled, the *p*-nitroaniline filtered off and washed with a little cold water. It is practically pure, but may be recrystallised from water.

$$C_6H_5NH.COCH_3 + HNO_3 \longrightarrow NO_2.C_6H_4.NHCOCH_3 + H_2O.$$

$$NO_2.C_6H_4NH.CO.CH_3 + H_2O \longrightarrow NO_2.C_6H_4.NH_2 + CH_3COOH.$$

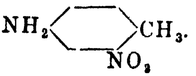
Yield.—80% theoretical (15 gms.). Yellow needles; M.P. 147°. (C. Z., 1912, 36, 1055.)

p-**Nitroaniline** (*2nd Method*).—18 gms. benzylideneaniline (Prep. 280) are added to 70 gms. of conc. sulphuric acid, the temperature being kept below 50°. The product is cooled to about 5°–10° and maintained at this temperature while a mixture of 11 gms. of nitric acid (D. 1·38) and 11 gms. of conc. sulphuric acid is run in. After standing for 20 minutes the nitration mixture is added to an equal volume of water, and the benzaldehyde removed in a current of steam. The residual liquor is cooled, diluted with water, and neutralised with caustic soda ; this causes complete separation, in a very pure form, of the *p*-nitroaniline, which is filtered off, washed with water and dried.

$$C_6H_5N{=}CH.C_6H_5 + HNO_3 \longrightarrow NO_2C_6H_4N{=}CH.C_6H_5 + H_2O.$$
$$NO_2C_6H_4N{=}CH.C_6H_5 + H_2O \longrightarrow NO_2C_6H_4NH_2 + C_6H_5CHO.$$

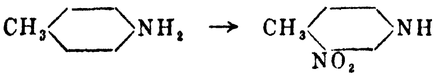
Yield.—90% theoretical (12 gms.). (D.R.P., 72173.)

PREPARATION 231.—*m*-**Nitrotoluidine** (2-*Nitro*-4-*aminotoluene*).



$C_7H_8O_2N_2$. 152.

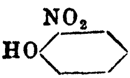
10 gms. *p*-toluidine are dissolved in 200 gms. conc. sulphuric acid. The solution is cooled by a freezing mixture to just below 0°. A mixture of 7·5 gms. nitric acid (D. 1·48) and 30 gms. conc. sulphuric acid is allowed to flow into the well-stirred solution, the temperature being maintained at 0°. When all the mixed acid has been added the mixture is allowed to stand for a short time and is then poured into 500 c.cs. of ice-cold water, the temperature being kept below 25° by the addition of more ice if necessary. The solution is now filtered from impurity and diluted to 3 times its bulk and neutralised with solid sodium carbonate, the temperature being kept as low as possible. The precipitate is then filtered off, pressed dry and finally recrystallised from alcohol.



Yield.—65–70% theoretical (10 gms.). Yellow monoclinic needles ; M.P. 77·5°. (B., 17, 263.)

Reaction CXVI. Action of Nascent Nitric Acid on Aromatic Compounds in presence of Concentrated Sulphuric Acid.—This reaction gives nitro compounds which, in many cases, are only obtained with difficulty by the action of mixed acid. Sodium or potassium nitrate is usually added to the solution of the compound in conc. sulphuric acid. It is usually necessary to keep the temperature below ordinary room temperature. See Reaction CXV.

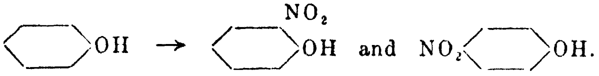
PREPARATION 232.—*o*- **and** *p*-**Nitrophenols** (1-*Hydroxy*-2- and -4-*nitrobenzenes*).



and

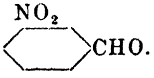
$C_6H_5O_3N$. 139.

A liquefied mixture of 20 c.cs. water and 94 gms. phenol, is allowed to drop into a solution of 150 gms. sodium nitrate in 400 c.cs. water and 250 gms. conc. sulphuric acid. The agitation must be good and during the addition the temperature must be kept at 15°–20°. The stirring is maintained for 2 hours after all has been added. A resinous mixture of nitro bodies is formed from which the supernatant liquor is poured off. The residue is then melted in 500 c.cs. of water and chalk is added with stirring until the mixture is neutral in order to free the nitro bodies from acid. The wash liquor is poured off and the nitro bodies are distilled in steam, using a wide air condenser. The ortho compound passes over. The residue in the flask is allowed to cool and is then filtered from the mother liquor. The residue which contains the para compound is then boiled up with a litre of 2% hydrochloric acid and filtered through a hot filter (see p. 12). The para compound crystallises from the hot solution in needles.



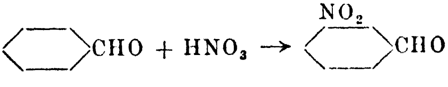
Yield.—*Ortho*, 40 gms.; *para*, 40 gms.; total nitrophenol, 60% theoretical; *ortho*, M.P. 44·3°; B.P. 214°; *para*, M.P. 114°; decomposes on boiling. (A., 103, 347; 110, 150; J. C. S., 1931, A., 212.)

PREPARATION 233.—*m*-**Nitrobenzaldehyde.**



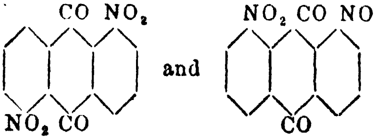
$C_7H_5O_3N$. 151.

100 gms. benzaldehyde are added to a cooled solution of 85 gms. of sodium nitrate in 200 gms. of conc. sulphuric acid. The temperature is not allowed to rise above 30°–35°. The smell of benzaldehyde disappears after the nitration is complete. The mixture is poured into ice, the oily layer separated and washed with warm water, and then with dilute caustic soda solution, and again separated. The oil is cooled (p. 12) to 10° and stirred until the *m*-nitrobenzaldehyde separates. It is then pressed to remove the *o*-compound.



Yield.—100 gms. *meta*, 25 gms. *ortho*; 90% theoretical; M.P. *o*- 46°, *m*- 58°. (B., 14, 2802; U.S.P., 1509412.)

PREPARATION 234.—**1 : 5- and 1 : 8-Dinitroanthraquinone.**



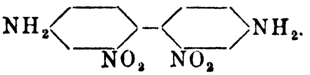
$C_{14}H_6O_6N_2$. 298.

10 gms. anthraquinone are dissolved in 100 gms. conc. sulphuric acid; 10 gms. sodium nitrate (dry) are added with agitation. The mixture is

kept at 60°–80° for 12 hours. It is then poured into water and the 1 : 5- and 1 : 8-compounds, along with any unchanged anthraquinone, separated and washed. The 1 : 5- is separated from the 1 : 8- by using alcohol or monohydrate (p. 316) as a solvent.

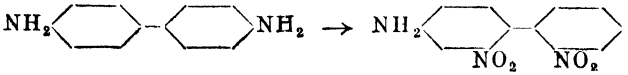
Yield.—Almost theoretical ; M.P. 1 : 5- above 330° ; 1 : 8- above 312°. (B., 16, 363 ; J. C. S., 1932, 83.)

PREPARATION 235.—2 : 2′-**Dinitrobenzidine.**



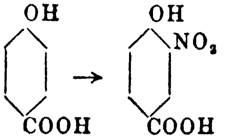
$C_{12}H_{10}O_4N_4$. 274.

To 56 gms. of pure benzidine sulphate 600 gms. of pure conc. sulphuric acid are added and the mixture well stirred. Solution is completed by heating up to 60° if necessary. The solution is cooled down to about 10°, but not lower, and 40 gms. potassium nitrate slowly added. After several hours' stirring the solution is poured into about 2 litres of cold water and the dinitrobenzidine sulphate, which is precipitated, filtered off and washed with a little water. The sulphate is then made into a cream with hot water and caustic soda solution added until an alkaline reaction is given to phenolphthalein. The free base is then filtered off, washed with water, and recrystallised from water or from alcohol.



Yellow leaflets, M.P. 214°. (B., 23, 795.)

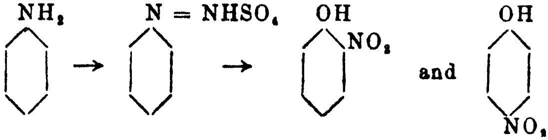
Reaction CXVII. Action of Nitrous Fumes on certain Organic Compounds.—The nitro group, NO_2, can be introduced in some cases by the action of nitrous fumes, the nitrous fumes being passed through the solution in glacial acetic acid. Sodium nitrite in acid solution may also be used, and in this reaction gives good yields with amines and phenols, the amines passing through the diazo stage into phenols, e.g.



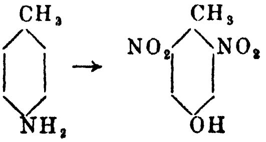
(90 % yield).

The nitrous acid in the reaction is oxidised to nitric acid, and this produces nitration.

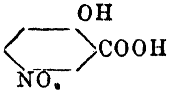
$$3HNO_2 \rightarrow HNO_3 + 2NO + H_2O.$$



When the *p*-position is occupied, the yield is almost theoretical, *e.g.*,



PREPARATION 236.—*m*-**Nitrosalicylic Acid.**

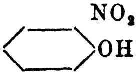


$C_7H_5O_6N$. 183.

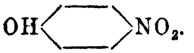
100 gms. salicylic acid and 130 gms. sodium nitrite are mixed with 150 c.cs. water and 1,200 c.cs. sulphuric acid (D. 1·52) are slowly added, the temperature being kept at 10°–15°. After 4 hours the mixture is warmed to 50° and then set aside till the evolution of nitrous fumes ceases. The mass is then warmed on the water bath. On cooling, crystals of *m*-nitrosalicylic acid separate out, and are filtered off, washed and recrystallised twice from water.

Yield.—64% theoretical (78 gms.). Needles ; M.P. 228°. (J. pr., [11], 42, 550.)

PREPARATION 237.—*o*- and *p*-**Nitrophenols.**



and



$C_6H_5O_3N$. 139.

10 gms. aniline are dissolved in 100 c.cs. of 25% sulphuric acid and the solution cooled to 15°. One-third of a solution of 300 gms. (3 mols) sodium nitrite in 100 c.cs. water is added at 15°, and the remainder without cooling. The mixture is then poured into a large evaporating basin on a water bath and boiling 50% sulphuric acid is cautiously added. When the action is over, the whole is steam distilled when the *o*-nitrophenol passes over. The *p*-compound is then extracted from the residue as in Preparation 232.

Yield.—*o*-Compound (4·7 gms.), *p*-compound (3·3 gms.), total 53% theoretical (see p. 282). (J. pr., [2] 40, 298.)

Reaction CXVIII. Action of Nitrous Acid on Aromatic Amines in presence of Cuprous Salts (Sandmeyer). B., 1887, 1495 ; J. C. S., 1947, 127.

$$R.NH_2 \longrightarrow R.NO_2.$$

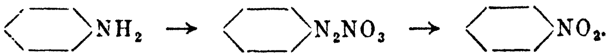
PREPARATION 238.—**Nitrobenzene.**

$C_6H_5NO_2$. 123.

9 gms. aniline are mixed with 50 c.cs. water and 20 gms. conc. nitric acid (D. 1·4). The solution is cooled to 0°–5° and 15 gms. sodium nitrite in 50 c.cs. water added. The mixture is then poured into a flask containing

the cuprous salt, prepared by dissolving 50 gms. cupric sulphate and 15 gms. grape sugar in 100 c.cs. water, and adding 20 gms. caustic soda in 60 c.cs. water to the boiling solution ; the mixture is shaken till all the copper is reduced, and is then rapidly cooled, and finally acidified by a slight excess of acetic acid.

The combined mixtures are allowed to stand for 1 hour, or until the evolution of nitrogen ceases. The nitrobenzene is then separated by steam distillation.



Yield.—50% theoretical (5 gms.). Yellow liquid ; M.P. 5·7° ; B.P. 210°. (B., 20, 1494.)

Reaction CXIX. Action of Metallic Nitrites on Organic Halogen Compounds.

Nitroparaffins and alkyl nitrites in varying quantities are produced from silver nitrite and alkyl halides.

$$RX + AgNO_2 \longrightarrow RNO_2 + RONO.$$

For an extensive review, see *Am. Soc.*, 1929, 279.

Nitromethane can also be prepared by the action of sodium or potassium nitrite on the corresponding salt of monochloracetic acid.

Preparation 239.—**Nitromethane.**

CH_3NO_2. CH_3O_2N. 61.

A 40% solution of sodium hydroxide (100–105 c.cs.) is slowly added with stirring to a mixture of 100 gms. chloroacetic acid and 100 gms. crushed ice until the mixture is just alkaline to phenolphthalein, the temperature being kept at 10°–20°. 73 gms. sodium nitrite in 100 c.cs. water are then added, and the whole heated in a 500 c.c. distilling flask attached to a downward condenser and having a thermometer immersed in the liquid. Distillation of nitromethane commences at a solution temperature of about 87° and continues as this temperature is raised to 108°–110°, at which the solution is maintained for 30 minutes. Nitromethane is separated from the aqueous layer of the distillate and the latter redistilled three times—nitromethane and aqueous layer being separated after each distillation. The total nitromethane is dried over calcium chloride and distilled, the fraction at 98°–101° being retained.

Yield.—42% theoretical (27 gms.). Heavy, inert, insoluble, colourless liquid; B.P. 101°; D. $^{4}_{4}$ 1·1580. (A., 171, 18; C.V. 1, 401; Am. Soc., 1931, 234; O. S., III, 83.) See also Reactions CXIV and CXXI (*b*).

$$ClCH_2COONa + NaNO_2 \longrightarrow NO_2CH_2COONa + NaCl$$

$$NO_2CH_2COONa + H_2O \longrightarrow NO_2CH_3 + NaHCO_3.$$

For a review of the aliphatic nitro compounds, see J. C. S., Quarterly Review, I (4), 1948.

PREPARATION 240.—**Nitroethane.**

$$C_2H_5.NO_2. \qquad C_2H_5O_2N. \qquad 75.$$

By-product.—**Ethyl Nitrite** (*Ethyl ester of nitrous acid*).

$$C_2H_5.O.NO. \qquad C_2H_5O_2N. \qquad 75.$$

42 gms. (a slight excess) of dry silver nitrite (see p. 516) are placed in a round-bottomed flask fitted with a reflux condenser. To recover the by-product (ethyl nitrite), ice-water must be used in the condenser, which should be a long one. 34 gms. (1 mol.) of ethyl iodide are added, gradually, through the condenser tube, so that the liquid boils vigorously but not too violently. The flask must not be disturbed during the process, for it is important that the silver nitrite should be gradually penetrated by the iodide. The flask is then warmed for 2 hours on a water bath, well cooled, fitted to a distillation apparatus, and the contents fractionally distilled. Ethyl nitrite distils over at 68°, and is collected in the same way as ether (see p. 21) in a flask cooled in a good freezing mixture. The temperature then rises and the second fraction, nitroethane, is collected at 110°–114° and redistilled.

$$C_2H_5I + AgNO_2 \begin{array}{l} \longrightarrow C_2H_5NO_2 + AgI. \\ \longrightarrow C_2H_5ONO_2 + AgI. \end{array}$$

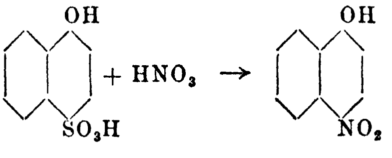
Yield.—Nitroethane : 50% theoretical (8–9 gms.). Colourless liquid ; insoluble in water ; B.P. 113°–114° ; D. $^{13}_{4}$ 1·058.

Yield.—Ethyl nitrite : 50% theoretical (8–9 gms.). Volatile liquid ; oppressive odour ; resembling that of apples when dilute ; B.P. 17° ; D. $^{15\cdot5}_{4}$ 0·947. (A., 171, 18 ; C. V., II, 204.)

Reaction CXX. Action of Concentrated Nitric Acid on certain Sulphonic Acids.

$$R.SO_3H + HNO_3 \longrightarrow R.NO_2.$$

This reaction goes easily in the anthraquinone series, but only in the naphthalene series when the SO_3H is in the α-position.



In the process of nitration with mixed acid, in many cases a sulphonic acid is formed in the first instance, the sulphonic group being ultimately replaced by the NO_2 group. (See also J. C. S., 1946, 869, 875, 880.)

Reaction CXXI. (*a*) **Action of Acyl Nitrates on certain Aromatic Compounds.**—Acetyl nitrate (acetic anhydride and 100% nitric acid) may be used for nuclear nitration (J. C. S., 81, 806 ; B., 40, 370) as also benzoyl nitrate, from silver nitrate and benzoyl chloride (B., 39, 3798). In each case nitration is usually carried out in carbon tetrachloride solution and the reaction product consists mainly of *o*-isomerides.

$$RH + Ac.ONO_2 \longrightarrow RNO_2 + AcOH.$$

Alkyl nitrates in presence of sulphuric acid, or aluminium chloride have also been used for nitration. See A., 288, 287 ; B., 1908, 726.

Reaction CXXI. (*b*) **Action of Tetranitromethane on Aromatic Bases or Phenols.**—Tetranitromethane is decomposed by weak bases in alcohol or acetone solution into nitroform and nitric acid :

$$C(NO_2)_4 + H_2O \longrightarrow HC(NO_2)_3 + HNO_3,$$

the base becoming nitrated during the process. In this way dimethyl-*p*-toluidine yields the corresponding nitroamine, and *p*-cresol can be nitrated in pyridine solutions (B., 53, 1529).

Note.—Tetranitromethane is a vigorous oxidising agent, highly toxic, and explosive. It is formed as a by-product in the nitration of aromatic hydrocarbons. (See B., 46, 2537.)

CHAPTER XIX

THE LINKING OF NITROGEN TO CARBON (*continued*)

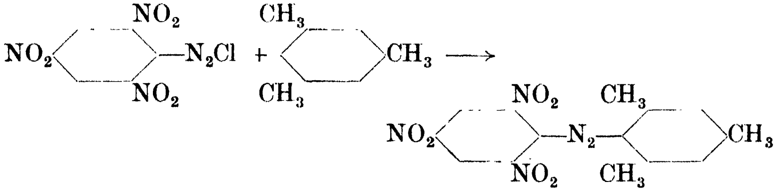
Reaction CXXII. Action of Phenols and Aromatic Amines on Diazonium Compounds.—Diazonium compounds combine with phenols and aromatic bases to form azo dyestuffs.

$$RN_2Cl + H.C_6H_4.NR_2(\text{or OH}) \longrightarrow RN_2C_6H_4NR_2(\text{or OH}).$$

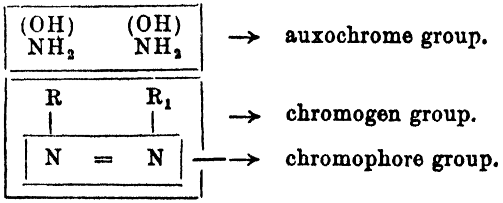
$$R\overset{+}{N}_2 + C_6H_5\overset{-}{O} \longrightarrow RN_2C_6H_5OH.$$

$$R\overset{+}{N}_2 + C_6H_5N(CH_3)_2 \longrightarrow RN_2C_6H_4N(CH_3)_2.$$

This process is known as " coupling ". In certain cases, other aromatic compounds can also couple, e.g. mesitylene with diazotised picramide in acetic acid.



The diagram shows the names given to the different groups in azo dyestuffs.



LAWS OF FORMATION OF AZO COLOURS

Amines are " coupled " in slightly acid solution, phenols in slightly alkaline solution, *p*H having an important effect on the rate of coupling.

Coupling usually takes place in the *p*-position to the NH_2 or OH group, and, if this is occupied, in the *o*-position, but never in the *m*-position.

If the NH_2 or OH group is acetylated, no coupling takes place, e.g.

$C_6H_5NH.COCH_3$ or $C_6H_5O.COCH_3$ do *not* couple.

If the NH_2 is alkylated or arylated, coupling takes place, e.g.

$C_6H_5NH.CH_3$ and $C_6H_5NH.C_6H_5$ *do* couple.

If the H in OH is replaced by any group no coupling takes place.

When both an OH and NH_2 are present in the azo compound, e.g. H-Acid (the compound which is diazotised is termed the diazo component), and coupling does take place, then the coupling can be carried out in acid or in alkaline solution, taking place in the *ortho*-position to the NH_2 in acid solution, and *ortho* to the OH in alkaline solution.

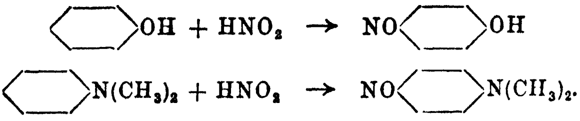
When an azo dye contains one chromophore, —N=N—, it is called a monoazo dye ; with two azo groups, disazo, and so on, e.g. sulphanilic acid → aniline gives methyl orange (monoazo), sulphanilic acid → *p*-nitroaniline (in acid solution), and the new azo compound → salicylic acid (in alkaline solution) gives anthracene acid brown (Disazo).

With compounds containing two amino groups (e.g. benzidine) tris- and poly-azo dyes can be formed, e.g. benzidine is coupled to a component containing an amino group which can be further diazotised and coupled. Salicylic acid ← benzidine → α-naphthylamine → N.W. acid (Trisazo).

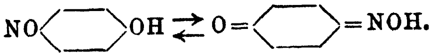
The sign → indicates " diazotised and coupled to "·

For examples, see Chapter XXVI, and *Coal Tar Dyes*, Thorpe and Linstead.

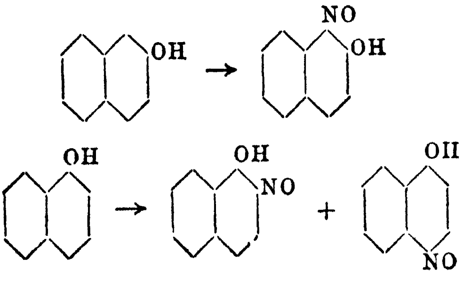
Reaction CXXIII. Action of Nitrous Acid on Phenols, and Tertiary Aromatic Amines. (A., 277, 85.)



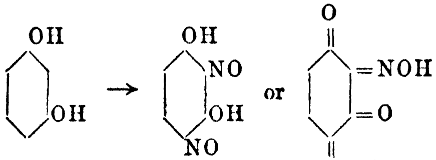
The nitrous acid is usually generated by the action of sodium nitrite in acid solution. The nitrosophenols are identical with the quinone monoximes, formed by acting on quinone with hydroxylamine.



The NO group in the benzene series is introduced in the *para*-position in both cases. In the naphthalene series the β-compound gives the 1-nitroso compound, while the α-compound gives a mixture of the 2- and 4-nitroso compounds. (J. C. S., 1930, 1969.)



Dihydroxy phenols give di-nitroso compounds.



Resorcinol Resorcin green

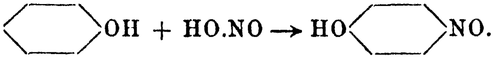
The presence of sodium nitrate in the nitrite used has a harmful effect on the stability of nitroso compounds. This action may be minimised by the addition of reducing agents, e.g. sodium metabisulphite. (J. Soc. Dyer., 41, 275.)

Phenyl dialkylamines react with nitrous acid to give nitroso compounds, the NO group entering the *p*-position, if this is free, to the basic group. These nitroso compounds, generally blue or green in colour, give yellow or red salts with mineral acids. Purely aromatic tertiary amines, e.g. triphenylamine, do not yield such nitroso compounds.

PREPARATION 241.—*p*-**Nitrosophenol.**

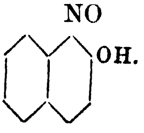
$C_6H_5O_2N$. **123.**

100 gms. of phenol are dissolved in a solution of 50 gms. of caustic soda, 100 gms. sodium nitrite and 2 litres water. 3 gms. sodium metabisulphite are also added (see above). The temperature is reduced to 7°. 200 c.cs. conc. sulphuric acid are added to 600 c.cs. water, and, when cooled, is gradually run into the solution. The nitrosophenol gradually separates out, and, after stirring for 2 hours, is filtered off and washed with ice-water.



Yield.—95% theoretical (124 gms.). Colourless crystals; soluble in hot water, alcohol, and ether; M.P. 126° (with violent decomposition). (A., 277, 85.)

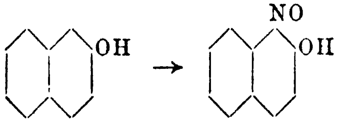
PREPARATION 242.—**Nitroso-β-naphthol** (1-*nitroso-2-hydroxynaphthalene*).



$C_{10}H_7O_2N$. **173.**

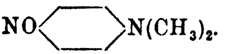
10 gms. β-naphthol are dissolved in 2·8 gms. caustic soda in 100 c.cs. water and made up to 200 c.cs. with water. 5 gms. sodium nitrite dissolved in a little water are carefully added. The mixture is cooled by the

addition of 100 gms. ice, and 140 c.cs. 10% sulphuric acid are slowly run in with constant stirring, the temperature being kept below 5°. The nitroso compound separates as a pale yellow precipitate. It is allowed to stand for 2 hours, filtered, and washed with water until the washings are only slightly acid. It is then dried and crystallised from petroleum ether.



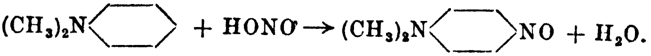
Yield.—Almost theoretical (12 gms.). Red needles; M.P. 110°; sparingly soluble in water. (B., 27, 3075; O. S., II, 61; XI, 13.)

PREPARATION 243.—***p*-Nitrosodimethylaniline.**



$C_8H_{10}ON_2$. 150.

To a solution of 8 gms. dimethylaniline in 50 c.cs. conc. hydrochloric acid and 50 gms. ice is slowly added a cold solution of sodium nitrite (4·5 gms.; 0·66 mol.) in 10 c.cs. water with stirring. The hydrochloride of *p*-nitrosodimethylaniline soon separates; after 15 minutes it is collected, washed with a little hydrochloric acid, then made into a paste with water and treated with sodium carbonate solution until alkaline. The red colour of the salt changes to the green of the free base. This latter is filtered off, washed, dried, and crystallised from benzene. The dimethylaniline is kept in excess during nitrosation in order to minimise the formation of *p*-nitrodimethylaniline (see Hodgson, J. C. S., 1941, 470).



Yield.—60% theoretical (6 gms.). Green crystals; M.P. 85°; somewhat volatile in steam; used in preparation of thiazine dyestuffs (p. 395). (B., 7, 810; 8, 616; 12, 523.)

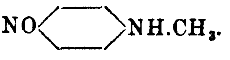
Reaction CXXIV. Action of Nitrous Acid on Secondary Amines, and subsequent Rearrangement of the Products.

$$R_2.NH + HO.NO \longrightarrow R_2N.NO.$$

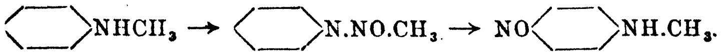
The nitrosamines are neutral oily liquids of little importance in themselves. This reaction, however, serves to separate secondary bases from mixtures of primary, secondary and tertiary. The aromatic nitrosamines undergo an interesting rearrangement when heated with alcoholic hydrochloric acid (B., 20, 1247), the nitroso group migrating to a position in the nucleus, forming *p*-nitroso compounds.

$$C_6H_5N(NO)CH_3 \longrightarrow NOC_6H_4NH.CH_3.$$

Preparation 244.—*p*-Nitrosomethylaniline.

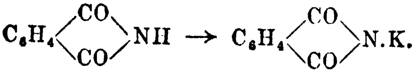
 $C_7H_8ON_2$. 136.

10 gms. methylaniline dissolved in 15 c.cs. conc. hydrochloric acid and 40 gms. ice are treated with 7 gms. sodium nitrite in 25 c.cs. water. Methyl-phenyl nitrosamine separates as a yellow oil, which solidifies on cooling (M.P. 12°–15°). 2 gms. methyl-phenyl nitrosamine are dissolved in 4 gms. ether and 8 gms. absolute alcohol which have been saturated with hydrochloric acid gas then added. After a time needles separate out which are filtered and washed with a mixture of alcohol and ether.



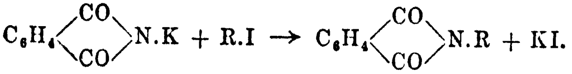
Yield.—Almost theoretical; M.P. 118°. (B., 19, 2991; O. S., XIII, 82.)

Reaction CXXV. Action of Alkyl Halides on Phthalimide (Potassium Salt).—When an alcoholic solution of phthalimide is treated with the theoretical quantity of caustic potash dissolved in alcohol, a crystalline compound—potassium phthalimide—separates out (see p. 436).



$$C_6H_4\langle{}^{CO}_{CO}\rangle NH \rightarrow C_6H_4\langle{}^{CO}_{CO}\rangle N.K.$$

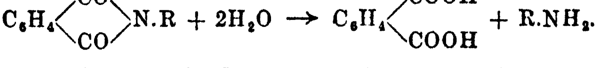
When this salt is treated with alkyl halide, a derivative of phthalimide is formed.



$$C_6H_4\langle{}^{CO}_{CO}\rangle N.K + R.I \rightarrow C_6H_4\langle{}^{CO}_{CO}\rangle N.R + KI.$$

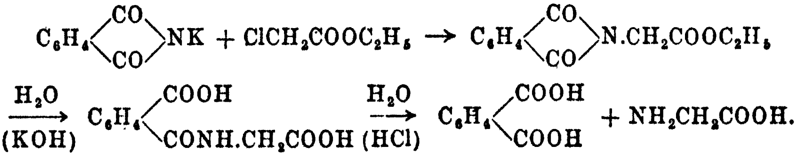
The reaction is used chiefly with alkyl halides, although when certain acidic groups are present in the nucleus in the *o*- or *p*-position to the halogen, the reaction gives satisfactory results with aryl halides.

When the phthalimide derivative is hydrolysed, primary amines are formed, so that the reaction is useful for preparing certain aliphatic amines.



$$C_6H_4\langle{}^{CO}_{CO}\rangle N.R + 2H_2O \rightarrow C_6H_4\langle{}^{COOH}_{COOH} + R.NH_2.$$

A similar reaction can also be used for the preparation of amino acids (B., 22, 426; 34, 454; 39, 534), *e.g.*,



$$C_6H_4\langle{}^{CO}_{CO}\rangle NK + ClCH_2COOC_2H_5 \rightarrow C_6H_4\langle{}^{CO}_{CO}\rangle N.CH_2COOC_2H_5$$

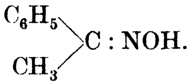
$$\xrightarrow[(KOH)]{H_2O} C_6H_4\langle{}^{COOH}_{CONH.CH_2COOH} \xrightarrow[(HCl)]{H_2O} C_6H_4\langle{}^{COOH}_{COOH} + NH_2CH_2COOH.$$

Reaction CXXVI. Action of Hydroxylamine on Aldehydes and Ketones.—The majority of aldehydes and ketones react with hydroxylamine, forming oximes.

$$RR_1CO + NH_2OH \longrightarrow RR_1C{=}NOH + H_2O.$$

Hydroxylamine hydrochloride ($NH_2OH.HCl$) is generally used; in most cases the free base is liberated by the subsequent addition of the theoretical quantity of a basic substance (caustic potash, sodium carbonate, etc.). With aldehydes it is advisable to reduce the quantity of alkali to a minimum, and possibly to warm gently. Ketones react much less readily and usually require vigorous heating for 2–3 hours. The reaction is mostly carried out in aqueous-alcoholic solution. The purification of some oximes is best effected by distillation under reduced pressure.

Preparation 245.—**Acetophenoneoxime.**



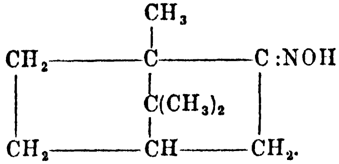
$$\begin{matrix} C_6H_5 \searrow \\ \end{matrix} \!\!\!> C : NOH. \qquad C_8H_9ON. \qquad 135.$$
$$CH_3 \nearrow$$

To 5 gms. (1 mol.) of hydroxylamine hydrochloride, dissolved in 10 c.cs. of water and contained in a flask, 3 gms. (less than 1 mol.) of potassium hydroxide dissolved in 5 c.cs. of water are added. 8 gms. (slightly less than 1 mol.) of acetophenone are then added, and the mixture heated in a reflux apparatus on a boiling water bath. Alcohol, in small quantities at a time, is added down the reflux condenser until the boiling solution just becomes clear. After an hour heating is stopped, the solution cooled, and a drop tested with litmus paper. It should be acid owing to the absorption of the hydroxylamine by the ketone. Caustic potash solution is carefully added until the solution is no longer acid. The condenser is again attached, and boiling continued for about 30 minutes, at the end of which time the solution is tested, and, if acid, is neutralised with caustic potash. After about 10 minutes further boiling the solution is once more tested with litmus, and a few drops of it mixed with ice-water. If the test sample solidifies quickly, the reaction is complete, and the contents of the flask are poured into 100 c.cs. of water containing a few lumps of ice. (If the test sample does not solidify, further heating is necessary.) The water should be vigorously stirred during the addition to cause the separation of the oxime in small lumps and flakes. The product is filtered washed with water, dried in air, and recrystallised from petroleum ether.

$$CH_3.CO.C_6H_5 \longrightarrow CH_3.C(:NOH).C_6H_5.$$

Yield.—89% theoretical (8 gms.). Colourless needles; M.P. 59°; B.P. ^{760} 246° (with decomposition); B.P. ^{20} 156°–157° (without decomposition). (B., 15, 2781; J. R. T. C., 1, 340.) *Salicylaldoxime* and *benzophenoneoxime* (C. V., II, 70) can be prepared in excellent yield by similar procedures.

PREPARATION 246.—**Camphoroxime** (*Oxime of d-camphor*).



$C_{10}H_{17}ON$. 167:

10 gms. (excess) of hydroxylamine hydrochloride, dissolved in the minimum amount of water, are added to 10 gms. (1 mol.) of camphor dissolved in 150 gms. of 90% alcohol, and the mixture treated with 15 gms. of solid caustic soda. The whole is heated on a water bath, alcohol being added if necessary to keep the camphor in solution, till after about an hour's heating no camphor is precipitated on diluting a test portion of the liquid with an excess of water. The whole liquid is then diluted with a large excess of water, filtered if necessary from a very small precipitate that may come down, and slightly acidified with acetic acid. The precipitated camphoroxime is recrystallised from dilute alcohol.

$$C_9H_{16}CO + H_2NOH = C_9H_{16}C:NOH + H_2O.$$

Yield.—75% theoretical (8 gms.). Colourless crystals; M.P. 115°. (B., 22, 605.)

PREPARATION 247.—**Benz*syn*aldoxime** (*α-Benzaldoxime*).

$$\begin{array}{l}C_6H_5C.H.\\ \quad\ \Vert\\ \quad NOH\end{array}$$

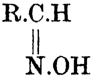
C_7H_7ON. 121.

14 gms. of caustic soda dissolved in 40 c.cs. of water and 21 gms. of benzaldehyde are mixed in a flask. 14 gms. of hydroxylamine hydrochloride are added in small portions at a time, the mixture being continually shaken. The benzaldehyde gradually disappears, and some heat is developed. On cooling, a crystalline mass separates out. Sufficient water is added to redissolve, and carbon dioxide is passed in until saturated. The oxime then separates, and is extracted with ether; the ethereal solution is dried over anhydrous sodium sulphate. The ether is removed (see p. 21), and the residue distilled under greatly diminished pressure.

$$C_6H_5.CHO + NH_2OH \longrightarrow C_6H_5CH:NOH + H_2O.$$

Yield.—50% theoretical (12 gms.). M.P. 35°; B.P. ^{14} 123°.

Reaction CXXVII. Action of Acids, Acid Chlorides, Anhydrides, *or* **Phosphorus Pentachloride on Oximes.** (B., 23, 11; J. C. S., 117, 1045.)—Aldoximes (oximes obtained from aldehydes) exist in two stereoisomeric forms depending on the relative position of the OH group.



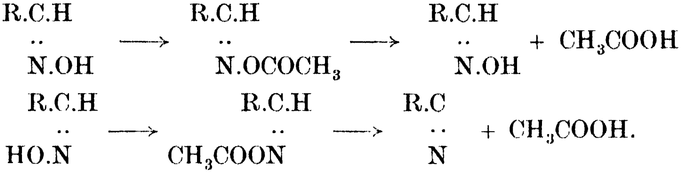
$$\begin{array}{c}R.C.H\\ \Vert\\ N.OH\end{array}$$

Syn-aldoxime (α).

$$\begin{array}{r}R.C.H\\ \Vert\\ OH.N\end{array}$$

Anti-aldoxime (β).

Both forms yield acetyl derivatives with acetic anhydride. That of the *anti*-oxime decomposes by the action of alkali yielding a nitrile which separates out; whereas that of the *syn*-oxime under the same conditions regenerates the parent form of the oxime which dissolves in the caustic soda.



$$\begin{array}{cccccc} \mathrm{R.C.H} & & \mathrm{R.C.H} & & \mathrm{R.C.H} & \\ \cdot\cdot & \longrightarrow & \cdot\cdot & \longrightarrow & \cdot\cdot & + \ \mathrm{CH_3COOH} \\ \mathrm{N.OH} & & \mathrm{N.OCOCH_3} & & \mathrm{N.OH} & \\ \mathrm{R.C.H} & & \mathrm{R.C.H} & & \mathrm{R.C} & \\ \cdot\cdot & \longrightarrow & \cdot\cdot & \longrightarrow & \cdot\cdot & + \ \mathrm{CH_3COOH.} \\ \mathrm{HO.N} & & \mathrm{CH_3COON} & & \mathrm{N} & \end{array}$$

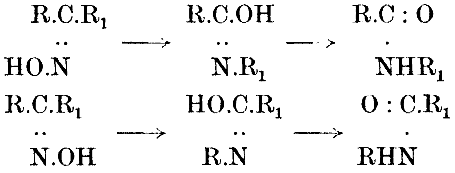
The *syn*-form is usually rearranged by hydrogen chloride in dry ether to the more symmetrical, and higher melting, *anti*-form; the reverse change is often effected by irradiation.

No isomerism is possible with oximes of symmetrical ketones, but those of mixed ketones can exist in two forms:

$$\begin{array}{lcccc} \mathrm{R.C.R} & \qquad\qquad & \mathrm{R.C.R_1} & & \mathrm{R.C.R_1} \\ \cdot\cdot & & \cdot\cdot & \text{and} & \cdot\cdot \\ \mathrm{N.OH}\ \text{(one form)} & & \mathrm{N.OH} & & \mathrm{HO.N} \end{array}$$

One ketoxime can usually be transformed into the other by heat, exposure to light, or treatment with hydrochloric acid.

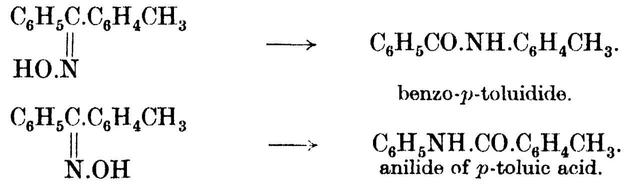
Beckmann Transformation.—When the *syn* and *anti* forms are treated with certain reagents (especially phosphorus pentachloride) a rearrangement takes place in the molecule. The hydroxyl group interchanges position with the radicle in the *trans* position, and this is followed by a transference of hydrogen from oxygen to nitrogen:



$$\begin{array}{ccccc} \mathrm{R.C.R_1} & & \mathrm{R.C.OH} & & \mathrm{R.C:O} \\ \cdot\cdot & \longrightarrow & \cdot\cdot & \longrightarrow & \cdot \\ \mathrm{HO.N} & & \mathrm{N.R_1} & & \mathrm{NHR_1} \\ \mathrm{R.C.R_1} & & \mathrm{HO.C.R_1} & & \mathrm{O:C.R_1} \\ \cdot\cdot & \longrightarrow & \cdot\cdot & \longrightarrow & \cdot \\ \mathrm{N.OH} & & \mathrm{R.N} & & \mathrm{RHN} \end{array}$$

so that substituted amides are formed.

e.g.



$$\begin{array}{ccc} \mathrm{C_6H_5C.C_6H_4CH_3} & & \\ \| & \longrightarrow & \mathrm{C_6H_5CO.NH.C_6H_4CH_3.} \\ \mathrm{HO.N} & & \\ & & \text{benzo-}p\text{-toluidide.} \\ \mathrm{C_6H_5C.C_6H_4CH_3} & & \\ \| & \longrightarrow & \mathrm{C_6H_5NH.CO.C_6H_4CH_3.} \\ \mathrm{N.OH} & & \text{anilide of } p\text{-toluic acid.} \end{array}$$

oximes of phenyl *p*-tolyl ketone

The configuration of the oxime can be determined by an examination of the transformation product. (See Ann. Rep., 1924, 111; Brit. Assoc., 1932, (Mills), and Chem. Rev., 35, 335.

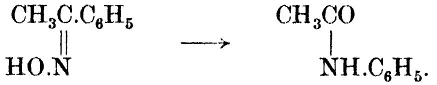
Aldoximes are quantitatively isomerised to amides by Raney nickel at 100°. (J. C. S., 1946, 599.)

$$\mathrm{RCH:NOH} \longrightarrow \mathrm{RCONH_2.}$$

Preparation 248.—**Transformation of Acetophenoneoxime** (Beckmann).

5 gms. acetophenoneoxime are dissolved in 60 c.cs. of ether, which has been dried over metallic sodium and redistilled, and to this solution is gradually added 7–8 gms. of powdered phosphorus pentachloride. The ether is then removed by distillation. To the residue after cooling are added slowly 25 c.cs. of water. The acetanilide is then filtered off and recrystallised from water.

	M.P.
Acetophenoneoxime - - - - -	59°
Acetanilide - - - - - - - -	112°



$$\underset{\mathrm{HO.N}}{\overset{\mathrm{CH_3C.C_6H_5}}{\|}} \longrightarrow \underset{\mathrm{NH.C_6H_5}}{\overset{\mathrm{CH_3CO}}{|}}.$$

Reaction CXXVIII. Action of Phenylhydrazine, etc., on Aldehydes and Ketones.—Phenylhydrazones of aldehydes and ketones are generally formed by warming these substances in aqueous-alcoholic solution with phenylhydrazine, phenylhydrazine acetate or phenylhydrazine hydrochloride in presence of excess sodium acetate. Derivatives of phenylhydrazine (e.g. *p*-nitro-, bromo-, dinitro-phenylhydrazine) react similarly.

α-Hydroxy-aldehydes and α-hydroxy-ketones can react with 3 mols. of phenylhydrazine in the following manner :

$$\mathrm{—CHOH.CHO} + \mathrm{H_2N.NHC_6H_5} \longrightarrow \mathrm{—CHOH.CH{=}N.NHC_6H_5} \longrightarrow$$

$$\mathrm{—CO.CH_2NH.NHC_6H_5} \xrightarrow{\mathrm{H_2N.NHC_6H_5}} \mathrm{—C({=}N.NHC_6H_5)CH_2NH.NHC_6H_5}.$$

$$\longrightarrow \mathrm{—C(NH.NHC_6H_5){=}CHNH.NHC_6H_5} \xrightarrow{-\mathrm{H_2NC_6H_5}}$$

$$\mathrm{—C({=}NH)CH{=}N.NHC_6H_5} \xrightarrow{\mathrm{H_2N.NHPh}}$$

$$\mathrm{—C({=}N.NHC_6H_5)CH{=}N.NHC_6H_5} + \mathrm{NH_3}.$$

Many of the simpler sugars react after this manner, forming osazones, which have characteristic appearances under the microscope, and are of special value for identification purposes. (J. C. S., 125, 222.)

Preparation 249.—**Glucosazone.**

$C_4H_5(OH)_4.C(:NNH.C_6H_5).CH.N.NHC_6H_5$. $C_{18}H_{22}N_4O_4$. 358.

2 gms. of glucose are dissolved in 10 c.cs. water and a solution of 4 gms. phenylhydrazine in 4 gms. glacial acetic acid and 10 c.cs. water is added. The mixture is heated on the water bath for 90 minutes, when the yellow osazone separates out. It is filtered, washed with water, and recrystallised from alcohol.

Yield.—2 gms. golden-yellow needles ; M.P. 204°. (B., 17, 579 ; 20, 21.)

Preparation 250.—Acetonephenylhydrazone (*Propanon-phenylhydrazone*).

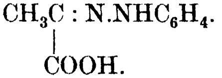
$(CH_3)_2C{=}N.NHC_6H_5$. $C_9H_{12}N_2$. 148.

1 volume of glacial acetic acid is added to phenylhydrazine (1 mol.). The solution is diluted with 2 volumes of water, and acetone (1 mol.) is added. The acetonephenylhydrazone which separates is extracted with ether. The extract is separated, dried over anhydrous potassium carbonate, distilled under reduced pressure, and the fraction 163–168° at 91 mms. retained. The oil still contains traces of ammonia, but this may be removed by allowing to stand in a vacuum desiccator over sulphuric acid for a short time.

$$(CH_3)_2CO + H_2N.NH.C_6H_5 \longrightarrow (CH_3)_2C{=}N.NH.C_6H_5 + H_2O.$$

Yield.—Theoretical. Colourless, somewhat unstable oil; B.P. ^{91} 165°. (B., 16, 662.)

Preparation 251.—Phenylhydrazone of Pyruvic Acid (*Propanon-acid-phenylhydrazone*).



$$\begin{matrix}CH_3C : N.NHC_6H_4.\\ |\\ COOH.\end{matrix}$$

$C_9H_{10}O_2N_2$. 178.

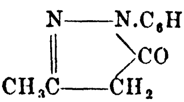
5 gms. (2 mols.) of phenylhydrazine are dissolved in 5 gms. (excess) of glacial acetic acid and 5 c.cs. of water added. 2 gms. (1 mol.) of pyruvic acid are added, and the mixture shaken. The precipitate, after filtration, is washed with dilute acetic acid. It may be recrystallised from alcohol.

$$CH_3.CO.COOH + H_2N.NH.C_6H_5 = CH_3.C : (N.NHC_6H_5)COOH + H_2O.$$

Yield.—Theoretical (4 gms.). Yellow needles; M.P. 192° (the substance must be heated quickly as it decomposes somewhat below its melting point). (J. pr., [2], 52, 39; B., 16, 2241.)

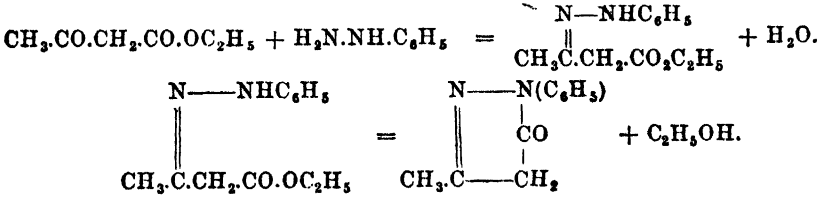
The following modification of the reaction is of interest:

Preparation 252.—1-Phenyl-3-methylpyrazolone.



$C_{10}H_{10}ON_2$ 174.

13·5 gms. of ethyl acetoacetate are added to 10 gms. of phenylhydrazine and vigorously shaken. The oil thus obtained is removed and heated on the water bath for about 2 hours until a test portion solidifies when treated with ether. A little ether is poured into the warm liquid, the white crystals which separate being washed with ether and dried at 100°. The product is recrystallised from hot water or alcohol.



$$CH_3.CO.CH_2.CO.OC_2H_5 + H_2N.NH.C_6H_5 = \begin{matrix}N{-}NHC_6H_5\\ \|\\ CH_3C.CH_2.CO_2C_2H_5\end{matrix} + H_2O.$$

Yield.—Theoretical (16 gms.). White crystals; almost insoluble in cold water, ether and ligroin; fairly soluble in hot water; easily soluble in alcohol; M.P. 127°. (B., 16, 2597.)

Reaction CXXIX. Action of Semicarbazide on Aldehydes and Ketones.—This gives rise to semicarbazones which are useful for identification purposes since they crystallise well and melt sharply.

$$R.CHO + NH_2.NH.CO.NH_2 \longrightarrow R.CH : N.NH.CO.NH_2 + H_2O.$$

The most convenient general procedure consists in dissolving semicarbazide hydrochloride in a small quantity of water and adding this to a solution of the aldehyde or ketone in pyridine, which also serves to combine with the hydrochloric acid liberated (J. R. T. C., 1929, 52). Alternatively, the semicarbazide hydrochloride (1 mol.) may be dissolved in water along with sodium acetate (rather more than 1 mol.) and this mixture treated with an alcoholic solution of the aldehyde or ketone. When the last-mentioned is soluble in water (e.g. acetone) it is not necessary to use alcohol as solvent.

A few compounds, e.g. benzaldehyde, react with semicarbazide hydrochloride in aqueous solution.

The semicarbazide may be prepared from hydrazine sulphate by the actions of sodium carbonate and potassium cyanate according to the scheme:

$$(NH_2NH_2)_2.H_2SO_4 + 2KCNO \longrightarrow 2NH_2CO.NHNH_2 + K_2SO_4.$$

PREPARATION 253.—**Acetophenonesemicarbazone.**

$$C_6H_5C(CH_3) : N.NH.CO.NH_2. \qquad C_9H_{11}ON_3. \qquad 177.$$

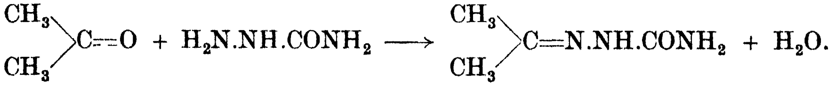
A solution of 5 gms. of semicarbazide hydrochloride in 5 c.cs. of water is added to 20 c.cs. of cold pyridine containing 5 gms. of acetophenone. The semicarbazone separates almost immediately in a high state of purity. A second crop may be obtained by diluting the mother liquor with water. The product is easily crystallised from aqueous alcohol.

Yield.—Almost theoretical. Soluble in alcohol, acetic acid or hot benzene. Sparingly soluble in water. M.P. 198°.

PREPARATION 254.—**Acetonesemicarbazone.**

$$(CH_3)_2C{=}N.NH.CONH_2. \qquad C_4H_9ON_3. \qquad 115.$$

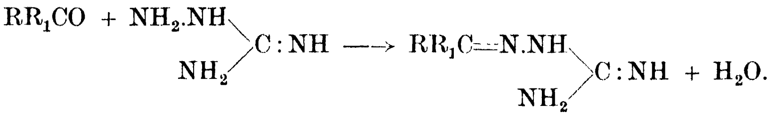
25 gms. of semicarbazide hydrochloride are dissolved in a small quantity of water; to this a solution of 21·8 gms. of potassium acetate in a small quantity of alcohol is added. The mixed solution is well shaken and cooled in ice in order to precipitate as much of the potassium chloride as possible, and then filtered. To the filtrate 12·9 gms. of acetone are added and the solution allowed to stand overnight. The precipitated acetone semicarbazone is filtered off. If more acetone is added to the filtrate further precipitation occurs. It is then recrystallised from hot alcohol.



$$\begin{matrix}CH_3\\ CH_3\end{matrix}\!\!>C{=}O + H_2N.NH.CONH_2 \longrightarrow \begin{matrix}CH_3\\ CH_3\end{matrix}\!\!>C{=}N.NH.CONH_2 + H_2O.$$

Yield.—95% theoretical (24 gms.). M.P. 188°–189° with decomposition. (A., 283, 19.)

Reaction CXXX. Formation of Substituted Hydrazine Derivatives.—(*a*) Amino guanidine combines with aldehydes and ketones in the presence of a mineral acid.



$$RR_1CO + \begin{array}{l} NH_2.NH\diagdown \\ NH_2\diagup \end{array}\!\!C:NH \longrightarrow RR_1C{=}\begin{array}{l} N.NH\diagdown \\ \quad NH_2\diagup \end{array}\!\!C:NH + H_2O.$$

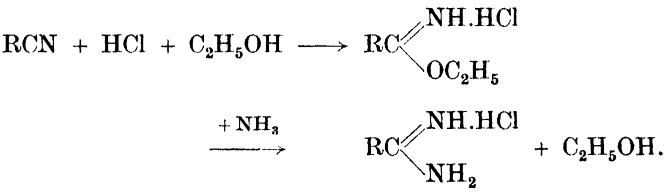
Many of the resulting compounds form crystalline picrates, and are isolated as such. The compounds with aromatic aldehydes are isolated as difficultly soluble nitrates.

(*b*) Semioxamazide, $NH_2.CO.CO.NH.NH_2$, possesses similar properties to semicarbazide, and reacts well with aldehydes, but with ketones the reaction does not seem to be generally applicable.

$$R.CHO + H_2N.NH.CO.CO.HN_2 \longrightarrow R.CH:N.NH.CO.CO.NH_2 + H_2O.$$

The aldehydes or ketones and the semioxamazide are weighed in molecular proportions, and when the former are insoluble in water it is best to dissolve them in a small quantity of alcohol. The semioxamazide, dissolved in the minimum quantity of water, is then added and the mixture thoroughly shaken for some time, when a precipitate of the semioxamazone separates. The semioxamazones are usually white powders of definite melting point, sparingly soluble in the usual organic solvents and insoluble in water. (See also J. C. S., 123, 394.)

Reaction CXXXI. Formation of Amidines. (B., 10, 1889; C. V., I, 5.)—Aliphatic or aromatic nitriles, dissolved in an inert solvent, such as ether, two or three mols. of alcohol added, and the solution saturated with hydrogen chlorides, yield iminoether hydrochlorides. If these products are added to alcoholic ammonia, amidines are obtained.



$$RCN + HCl + C_2H_5OH \longrightarrow RC\begin{array}{l} \diagup\!\!\diagup NH.HCl \\ \diagdown OC_2H_5 \end{array}$$

$$\xrightarrow{+NH_3} RC\begin{array}{l} \diagup\!\!\diagup NH.HCl \\ \diagdown NH_2 \end{array} + C_2H_5OH.$$

Iminoether hydrochlorides are sensitive to moisture which must be rigorously excluded during the preparation. The salts can also react with alcohol, hence a large excess (ten times) of ammonia for the ammonolysis is necessary.

Amidines are strong monoacid bases and form well-defined salts with mineral acids, of which the nitrate is often sparingly soluble in water.

For extensive review, see Chem. Rev., 35, 351.

PREPARATION 255.—**Phenylacetamidine Nitrate.**

$C_6H_5CH_2C(:NH)NH_2.HNO_3$. $C_8H_{11}O_3N_3$. 197.

To 24 gms. distilled phenylacetonitrile (0·2 mol.) (p. 158) dissolved in 30 c.cs. of sodium-dried ether in a 250-c.c. flask are added 25 c.cs. (0·34 mol. of ethyl alcohol previously dried over a little sodium or calcium (p. 217), and the mixture cooled in ice-salt. Hydrogen chloride gas, dried by passage through conc. sulphuric acid, is led into the nitrile solution, the exit from the absorption vessel being protected by a calcium chloride tube. When the solution has been saturated, the vessel is sealed and allowed to stand for two days at room temperature; the red colour which may develop is due to impurities in the alcohol. The phenylacetiminoethyl ether hydrochloride usually crystallises, and is isolated by evaporation of the solvent at 40° C. under reduced pressure. The residue, a slightly-coloured crystalline powder, is not purified, but immediately added to a solution prepared by saturating 300 c.cs. of absolute alcohol at 0° C. with dry ammonia. The mixture is heated in a pressure bottle (a heavy-walled screw-top bottle is suitable) for twelve hours in a water-bath at 40° C. and the solution then evaporated at 40° under reduced pressure. (*Caution!* the pressure bottle should be cooled in ice before opening.) The residue of amidine hydrochloride, is dissolved in water at 40°, treated with decolourising carbon, filtered and cooled, and 50% aqueous ammonium nitrate added dropwise; phenylacetamidine nitrate separates as white plates, is filtered, washed with ice-water, and dried in a vacuum desiccator.

Yield.—70% theoretical (24 gms.). White plates; M.P. 170° C. (C. V., I, 6.)

Reaction CXXXII. Action of Alkyl Halides on Ammonia or Amines (Hofmann).—Primary, secondary, tertiary, and quarternary compounds may be formed:

$$RI + NH_2 \longrightarrow RNH_2 \xrightarrow{RI} R_2NH \xrightarrow{RI} R_3N \xrightarrow{RI} (R_4\overset{+}{N})I^-.$$

In this way secondary and tertiary amines can be obtained from primary. The reaction takes place usually in alcoholic, or aqueous solution, and heat is often necessary. R may be aliphatic or aromatic, and the iodide is the most reactive halide. Aryl halides react only with difficulty.

PREPARATION 256.—**Trimethyl-β-naphthylammonium iodide** (*Methiodide of dimethyl-β-naphthylamine*).

$C_{10}H_7N(CH_3)_3I$. $C_{13}H_{16}NI$. 313.

5 gms. (1 mol.) of β-naphthylamine, 20 gms. (excess) of methyl iodide, and 20 c.cs. water are placed in a flask and boiled under reflux until the amine completely dissolves (about 3 hours). The quaternary compound formed separates out on cooling. It is filtered off, washed sparingly with water, and dried on porous plate.

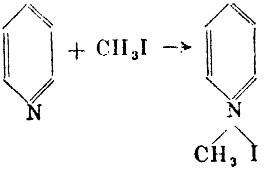
$$C_{10}H_7NH_2 + 3CH_3I \longrightarrow C_{10}H_7N(CH_3)_3I + 2HI.$$

Yield.—Theoretical (12 gms.). Colourless needles; decompose when heated or exposed to air. (B., 11, 638; 13, 2054.)

PREPARATION 257.—**Pyridine Methiodide.**

$C_5H_5NCH_3.I.$ $C_6H_8NI.$ 221.

1 c.c. of pyridine and 1 c.c. of methyl iodide are mixed with a glass rod in a small test tube. A vigorous reaction sets in and product becomes very hot. After a few minutes, 5 c.cs. absolute alcohol are added, and gently warmed to dissolve. On cooling, the product crystallises out in flat needles, which are filtered off and washed with a little alcohol.



M.P. 117°. (B., 3438.)

The following are developments and modifications of the present reaction :

PREPARATION 258.—**Methylaniline** (*Phenylmethylamine*).

$C_6H_5NH.(CH_3).$ $C_7H_9N.$ 107.

20 gms. (1 mol.) of acetanilide (see p. 310), 5 gms. (excess) of sodium wire, and 100 gms. of pure xylene (dried over sodium) are refluxed for 2–3 hours in an oil bath at 130°. After cooling, 15 gms. (rather more than theoretical) of methyl iodide are added, and the mixture digested for a short time until no more methyl iodide condenses in the condenser tube. The xylene is then distilled off.

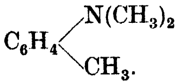
The methylacetanilide is boiled with concentrated alcoholic potash solution for about 24 hours in a reflux apparatus. The alcohol is distilled off, and the residue neutralised by addition of hydrochloric acid. The residual xylene is then distilled off in steam, the solution made alkaline, over anhydrous sodium sulphate or potassium hydroxide and fractionated.

$$C_6H_5NH.COCH_3 + CH_3I \longrightarrow C_6H_5N.(CH_3)CO.CH_3 \longrightarrow C_6H_5NH.CH_3.$$

Yield.—Theoretical (15 gms.). Yellowish oil ; B.P. 192° ; D. $^{15}_{4}$ 0·976.

In certain cases addition of sodium bicarbonate as condensing agent is effective, e.g. benzylaniline (C. V., I, 102).

PREPARATION 259.—**Dimethyl-*o*-toluidine.**

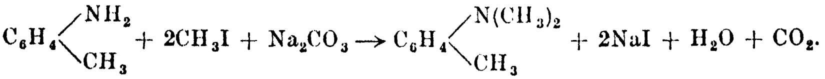


$$C_6H_4\begin{cases}N(CH_3)_2\\CH_3.\end{cases}$$

$C_9H_{13}N.$ 135.

15 gms. *o*-toluidine, 42 gms. methyl iodide and 16 gms. sodium carbonate dissolved in 250 c.cs. water are heated in a reflux apparatus on a water bath for about 2 hours until methyl iodide no longer condenses in the condenser tube. The liquid is then made strongly alkaline with caustic

soda solution ; the amine is extracted with ether, the extract dried over solid potash and distilled. The amine comes over at 175°–185°.

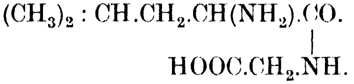


$$C_6H_4\left\langle\begin{matrix}NH_2\\CH_3\end{matrix}\right. + 2CH_3I + Na_2CO_3 \rightarrow C_6H_4\left\langle\begin{matrix}N(CH_3)_2\\CH_3\end{matrix}\right. + 2NaI + H_2O + CO_2.$$

Yield.—80% theoretical (15 gms.). Pale yellow liquid ; B.P. 183°. (B., 24, 563.)

The following preparation is of interest in connection with Fischer's researches on the proteins :

PREPARATION 260.—**Leucylglycine.**



$$\begin{array}{r}(CH_3)_2 : CH.CH_2.CH(NH_2).CO.\\ |\\ HOOC.CH_2.NH.\end{array}$$

$C_8H_{16}O_3N_2$. 188.

10 gms. (1 mol.) of glycine (Prep. 488) are dissolved in 133 c.cs. (1 mol.) of N caustic soda, and while cooled with ice and vigorously shaken the solution is treated alternately with 170 c.cs. (excess) of cold N caustic soda, and 37 gms. (1 mol.) of α-bromoisocaproyl bromide (C., 1910, I, 1345) in four portions, each new addition being made only when the smell of the acid bromide has disappeared. The whole operation lasts about 20 minutes. The liquid is filtered from the small amount of oil it contains, and then treated with 35 c.cs. (excess) of 5N hydrochloric acid. The oil which is precipitated is extracted with ether, and the condensation product precipitated from the ethereal solution after the latter has been concentrated by the addition of a large quantity of petroleum ether. The product α-bromoisocaproylglycine soon crystallises. It is filtered at the pump, washed with petroleum ether, and recrystallised from hot water, or from chloroform.

$$(CH_3)_2 : CHCH_2CHBrCOBr + NH_2CH_2COOH$$
$$= (CH_3)_2 : CHCH_2CHBr.CO.NH.CH_2COOH + HBr.$$

Yield.—75% theoretical (26 gms.). Colourless crystals ; M.P. 133°.

The chief fraction of the raw product can also be obtained in crystalline form at once if the alkaline solution is first made slightly acid, treated with a few crystals previously prepared, and then continually stirred while the rest of the hydrochloric acid is slowly poured into it.

The α-bromoisocaproylglycine is converted into leucylglycine by dissolving it in 5 times its weight (excess) of 25% ammonia (D. 0·910), and allowing the solution to stand for 4 days at room temperature. The crystalline paste of ammonium bromide and dipeptide, which is produced when the solution is concentrated on a water bath, is treated with absolute alcohol and again evaporated. The residue is boiled with alcohol, and when cold the leucylglycine, which is insoluble in alcohol, is filtered off at the pump and washed with alcohol until a sample of it dissolved in water gives no further precipitate with silver nitrate. The dipeptide is purified by dissolving it in 15 times its weight of hot water. On cooling, about half the product separates out in crystalline form. By concentrating the mother liquor and precipitating with alcohol, the rest may be obtained. The product should be free from bromine.

$$(CH_3)_2 : CH.CH_2CHBr.CO.NH.CH_2.COOH + 2NH_3$$
$$= (CH_3)_2 : CH.CH_2CH(NH_2).CO.NH.CH_2.COOH + NH_4Br.$$

Yield.—80% theoretical (6 gms. for each 10 gms. of the α-bromoisocaproylglycine taken). Colourless crystals; soluble in water; insoluble in alcohol; M.P. (decomposition) 243°. (B., 42, 3398; C., 1909, II, 1546.)

Reaction CXXXIII. Action of Aromatic Halogen Compounds on Ammonia or Amino Compounds.—Aliphatic halides readily react with ammonia and amines according to Reaction CXXXII. Aromatic halides are less reactive, unless negative groups are also present. The addition of copper powder or cuprous halide greatly accelerates the elimination of halogen hydride.

In the technical preparations various reagents, e.g. lime and calcium chloride are added to the catalyst to eliminate corrosion at the high temperatures and pressures required. (E.P., 402063; U.S.P., 1840760.)

PREPARATION 261.—Diphenylamine (*Phenylamine*).

$C_6H_5NHC_6H_5$. $C_{12}H_{11}N$. 169.

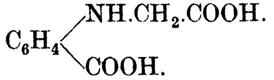
10 gms. (1 mol.) acetanilide, 5 gms. dry potassium carbonate, 20 gms. (excess) of bromobenzene, and 1·5 gms. cuprous iodide in 60 c.cs. nitrobenzene solution are refluxed for 15 hours. The dark brown liquid is then steam distilled until no more nitrobenzene passes over. The residue in the distillation flask, consisting of the acetyl derivative of diphenylamine, is a thick brown oil. It is dissolved in ether, filtered, dried over anhydrous sodium sulphate, and the ether removed on a water bath. The residue is crystallised from alcohol from which it separates as white plates, melting at 102°.

The crystals are dissolved in 30 c.cs. of alcohol, and hydrolysed by boiling with 30 c.cs. of conc. hydrochloric acid for 2–3 hours. The product is distilled in steam, a yellow oil passing over, which solidifies in the condenser.

$$C_6H_5NHCOCH_3 + C_6H_5Br \rightarrow (C_6H_5)_2N.COCH_3 \rightarrow (C_6H_5)_2NH + CH_3COOH.$$

Yield.—60% theoretical (7·5 gms.). Yellow plates; soluble in hot alcohol; M.P. 53°; B.P. 310°. (B., 40, 4543.)

PREPARATION 262.—Phenylglycine-*o*-carboxylic Acid.



$$C_6H_4\begin{cases} NH.CH_2.COOH. \\ COOH. \end{cases}$$

$C_9H_9O_4N$. 195.

20 gms. potassium-*o*-chlorobenzoate (prepared from the free acid and caustic potash), 5·5 gms. solid caustic potash, 7 gms. potassium carbonate, 7·5 gms. glycocoll, 15 c.cs. water, and a small quantity of copper powder are placed in a flask provided with a reflux condenser. The mixture is heated to boiling in an oil bath for an hour, the contents finally becoming yellow in colour. The product is cooled somewhat, and boiling water added to redissolve the crystals which have separated. The solution is

filtered and the filtrate, while hot, treated with excess of hydrochloric acid; phenylglycine-*o*-carboxylic acid separates, and after some time is filtered off and recrystallised from water.

Yield.—Practically theoretical (19 gms.). M.P. 200° (with decomposition). (D.R.P., 142507.) Used in preparation of indigo (p. 397).

Reaction CXXXIV. Action of Silver Cyanide on Alkyl Halides.

$$RX + AgNC \longrightarrow RNC + AgX.$$

Isocyanides (isonitriles or carbylamines) are formed in this reaction.

PREPARATION 263.—**Ethyl*iso*cyanide** (*Ethylcarbylamine*).

$C_2H_6.NC.$ $C_3H_5N.$ 55.

20 gms. (1 mol.) of ethyl iodide are gently refluxed *in a fume cupboard* under a long condenser with 30 gms. (excess) of dry silver cyanide until the liquid ceases to drip back, and the mass is pasty (about 1 hour). A soluble crystalline compound ethyl argento-cyanide, $C_2H_5Ag(NC)_2$, is now contained in the flask. Ethyl isocyanide is formed from it either by heating it to 180°, or better, by heating to 100° with concentrated potassium cyanide solution. A solution of 10 gms. (1 mol.) powdered 98% potassium cyanide in 25 c.cs. of water is added, and the contents of the flask distilled from a water bath in a fume cupboard, the distillate being collected in a flask with an outlet to a good draught pipe. It is redistilled with the same precautions, the fraction 75°–78° being separately collected.

$$C_2H_5I + 2AgNC = C_2H_5Ag(NC)_2 + AgI.$$
$$C_2H_6Ag(NC)_2 + KNC = KAg(NC)_2 + C_2H_5NC.$$

Volatile liquid; very offensive odour; B.P. 78°. (J. pr., [1], 30, 319.)

Reaction CXXXV. Action of Chloroform and Alcoholic Potash on Aliphatic and Aromatic Primary Amines.

$$R.NH_2 + CHCl_3 + 3KOH \longrightarrow R.NC + 3KCl + 3H_2O.$$

The isonitriles formed have a characteristic poisonous odour. When used as a test for primary amines they should be destroyed (hydrolysed) by pouring into conc. hydrochloric acid—using a fume cupboard for the entire operation.

Reaction CXXXVI. Action of the Hydrochloride of a Primary Aromatic Base on the Base.

$$R.NH_2 + HCl.NH_2R \longrightarrow R.NH.R + NH_4Cl.$$

The reaction takes place at a high temperature and usually under high pressure in an autoclave, secondary amines being formed.

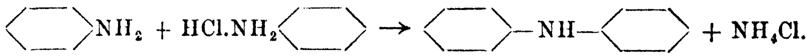
PREPARATION 264.—**Diphenylamine.**

$C_{12}H_{11}N.$ 169.

93 gms. aniline and 93 gms. aniline hydrochloride are heated for 20 hours at 230° in an enamelled autoclave, the pressure reaching about 6 atms. Iron should not be in contact with the reaction products; it

reduces the yield. After 2 hours, the water present is cautiously blown off through the valve, this process being repeated three times during an hour. The presence of water has a very marked influence on the reaction. Some aniline and ammonia also escape. The reaction is complete after about 20 hours. The contents of the autoclave are then placed in a porcelain basin with a litre of water, and heated to 80°. 70 c.cs. strong hydrochloric acid are added until the reaction is just acid to Congo Red. It is then allowed to cool. After several hours the crude diphenylamine separates as a solid cake, which can easily be removed from the mother liquor. It is then melted under a little water, and any unchanged aniline extracted with a little hydrochloric acid, and washed with dilute sodium carbonate. The diphenylamine is then purified by distillation with superheated steam (see p. 29), the temperature of the oil bath being 250°, and that of the superheated steam 300°. The diphenylamine is obtained as an almost colourless liquid, which solidifies to a pale yellow cake.

Aniline can be recovered from the acid mother liquors.



Yield.—60% theoretical (100 gms.). Colourless crystals; peculiar smell; M.P. 53°; B.P. 310°; important intermediate for dyestuffs. (B., 40, 4541.)

Reaction CXXXVII. Action of Bromine (or Chlorine) and Alkali on certain Amides and Imides (Hofmann).—This method is applicable for the preparation of both aliphatic and aromatic amines. (*Organic Reactions*, Adams, Vol. III, 268.)

$$R.CO.NH_2 + Br_2 \longrightarrow R.CO.NHBr + HBr.$$

$$R.CO.NHBr \longrightarrow R.N:CO + HBr.$$

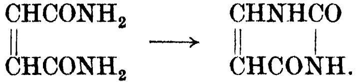
$$RNCO + H_2O \longrightarrow R.NH_2 + CO_2.$$

The reaction proceeds in stages, a bromamide being first formed; this loses a molecule of hydrogen bromide on further action with caustic soda, yielding probably an isocyanate, which, being unstable in presence of excess of alkali, is hydrolysed to an amine and carbon dioxide. Sodium hypochlorite (or hypobromite) and sodium hydroxide are the reagents used. The reaction finds industrial application in the preparation of anthranilic acid for the synthesis of indigo. (See also Reaction CLXIV.)

The reaction may take a different course. For example, with excess of amide derivatives of urea may be formed:

$$2CH_3CONH_2 + KOBr \longrightarrow CH_3NHCONHCH_3.$$

In certain instances, intramolecular changes may also take place resulting in ring closure:

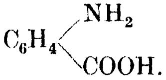


$$\begin{array}{c} CHCONH_2 \\ \| \\ CHCONH_2 \end{array} \longrightarrow \begin{array}{c} CHNHCO \\ \|\quad\quad | \\ CHCONH. \end{array}$$

maleamide uracil

The reaction has also been applied to the synthesis of Xanthine derivatives (J. C. S., 1939, 916; 1947, 378).

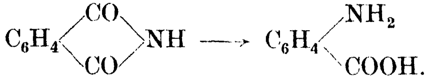
Preparation 265.—Anthranilic Acid (*o-Aminobenzoic acid*).



$$C_6H_4{<}\begin{matrix}NH_2\\COOH.\end{matrix}$$

$C_7H_7O_2N$. 137.

40 gms. of finely-powdered phthalimide and 80 gms. of caustic soda are dissolved together in 180 c.cs. of water, the solution being cooled during the operation. The solution is agitated, and 400 gms. of a 5% solution of sodium hypochlorite run in. When all is added, the solution is warmed for a few minutes at 80° to complete the reaction ; it is then cooled and neutralised exactly with hydrochloric or sulphuric acid. An excess of strong acetic acid is added to precipitate the anthranilic acid, which is filtered off and washed with water. Any anthranilic acid remaining in the filtrate is precipitated as copper anthranilate by the addition of a saturated solution of copper acetate. After standing for some time the precipitate is filtered off and suspended in a small quantity of warm water, while a current of sulphuretted hydrogen is passed into the suspension. The copper sulphide formed is filtered off, and anthranilic acid recovered from the filtrate by concentration on a water bath. It may be recrystallised from hot water.



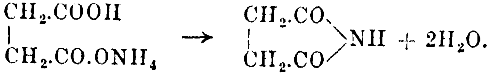
$$C_6H_4{<}\begin{matrix}CO\\CO\end{matrix}{>}NH \longrightarrow C_6H_4{<}\begin{matrix}NH_2\\COOH.\end{matrix}$$

Total Yield.—85% theoretical (31·5 gms.). M.P. 145°. (D.R.P., 55988 ; J. Soc. Dyers, 1901, 17, 139.)

Reaction CXXXVIII. Action of Heat on Ammonium Salts.—Ammonium salts of monobasic acids yield amides,

$$R.COONH_4 \longrightarrow R.CO.NH_2 + H_2O.$$

while those of dibasic acids yield imides.



$$\begin{matrix}CH_2.COOH\\ |\\ CH_2.CO.ONH_4\end{matrix} \longrightarrow \begin{matrix}CH_2.CO\\ |\\ CH_2.CO\end{matrix}{>}NH + 2H_2O.$$

Preparation 266.—Acetamide.

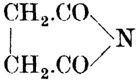
$CH_3CO.NH_2$. C_2H_5ON. 59.

20 gms. ammonium acetate (as dry as possible), and 25 gms. glacial acetic acid are placed in a small round-bottomed flask provided with a reflux condenser, and heated to gentle boiling over a wire gauze for 3 hours. The flask is then connected by means of a cork and delivery tube with a sloping water condenser and slow distillation begun. The distillate up to 160° is discarded. Above 160° the water is run out of the condenser and the distillate collected in a small distilling flask. This portion is redistilled and the fraction 210°–225° separately collected ; it solidifies on cooling to a mass of white crystals. These may be recrystallised from ether as long needles.

$$CH_3.COONH_4 \longrightarrow CH_3.CONH_2 + H_2O.$$

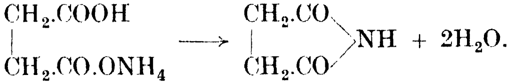
Yield.—80% theoretical (12 gms.). M.P. 82° ; B.P. 222°. (B., 15, 980.) For modification of above, see Am. Soc., 33, 974, and O. S., IX, 90.

Preparation 267.—Succinimide (*Imide of butan-diacid*).



$$\begin{array}{l} CH_2.CO \\ | \qquad\qquad \rangle NH. \\ CH_2.CO \end{array} \qquad C_4H_5O_2N. \qquad 99.$$

20 gms. of succinic acid are dissolved in a small quantity of water in a basin, and the solution neutralised with ammonia. The solution is boiled to expel excess of ammonia, after which a further 20 gms. of succinic acid dissolved in water are added. The solution is evaporated to complete dryness on a water bath ; the dry residue is transferred to a retort and heated quickly with a large luminous flame. The sublimate of succinimide is recrystallised from pure acetone.



$$\begin{array}{l} CH_2.COOH \\ | \\ CH_2.CO.ONH_4 \end{array} \longrightarrow \begin{array}{l} CH_2.CO \\ | \qquad\qquad \rangle NH \\ CH_2.CO \end{array} + 2H_2O.$$

Yield.—70% theoretical (11 gms.). Colourless rhombic plates ; M.P. 126° ; B.P. 288°. (A., 49, 198 ; C. V., 11, 562.)

A variation of the foregoing procedure consists in heating a mixture of an acid (monobasic or dibasic) with urea (J. S. C. I., 1947, 345) as in the following preparation.

Preparation 268.—Adipamide.

$$NH_2CO(CH_2)_4CONH_2. \qquad C_6H_{12}O_2N_2. \qquad 144.$$

A mixture of 36 gms. (1 mol.) adipic acid and 15 gms. (1 mol.) urea in a large boiling tube (immersed in an oil or fusible metal bath) is heated at 180° for 6 hours. After cooling somewhat, the residue is crystallised from aqueous alcohol (1 : 1) from which it separates as a colourless, crystalline mass.

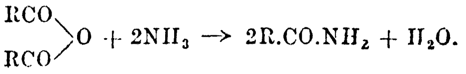
$$HOOC(CH_2)_4COOH + NH_2CONH_2 \longrightarrow (CH_2)_4(CONH_2)_2 + CO_2 + H_2O.$$

Yield.—85% theoretical (30 gms.). M.P. 223°–224°.

Reaction CXXXIX. Action of Ammonia on Esters, Acid Chlorides or Anhydrides. Amide formation takes place :

(1) $$R.COOR_1 + NH_3 \rightarrow R.CO.NH_2 + R_1OH.$$

(2) $$R.COCl + NH_3 \rightarrow R.CO.NH_2 + HCl.$$

(3) 

$$\begin{array}{l} RCO \\ \qquad\quad \rangle O \\ RCO \end{array} + 2NH_3 \rightarrow 2R.CO.NH_2 + H_2O.$$

(1) Is restricted mostly to esters of aliphatic acids (ammonolysis). (2) Is employed for the preparation of aromatic amides. If the anhydride of a dibasic acid, e.g. phthalic, is employed, an imide results.

Preparation 269.—Acetamide.

15 gms. ethyl acetate are treated in a small flask with an equal weight of conc. ammonia solution. The flask is loosely corked and left in a warm place (say, near a steam bath) until the two layers originally present give place to one uniform solution. This solution is then distilled, water,

alcohol and ammonia passing over up to 100°; the fraction 210°–225° is separately collected, and if it does not solidify on cooling it is redistilled. The final product is recrystallised from ether.

$$CH_3.CO.OC_2H_5 + NH_3 \longrightarrow CH_3.CONH_2 + C_2H_5.OH.)$$

Yield.—80% theoretical (8·5 gms.). M.P. 82°. (B., 15, 981.)

Oxamide is obtained as a white amorphous precipitate when equal weights of dimethyl (or diethyl) oxalate and conc. ammonia are mixed. The precipitate is filtered off and recrystallised from alcohol.

$$CH_3.O.OC.CO.OCH_3 + 2NH_3 \longrightarrow NH_2OC.CONH_2 + 2CH_3OH.$$

PREPARATION 270.—**Benzamide.**

$C_6H_5.CONH_2$. C_7H_7ON. 121.

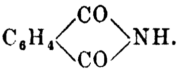
10 gms. finely-powdered dry ammonium bicarbonate are placed in a mortar in a fume cupboard. 5 gms. benzoyl chloride are added and the whole well mixed with a pestle during 10 minutes. If the odour of benzoyl chloride persists at the end of this time, a few drops of conc. ammonia are added. The product is diluted with a little water, the benzamide filtered off and recrystallised from boiling water.

$$C_6H_5COCl + 2NH_4HCO_3 \longrightarrow C_6H_5CONH_2 + NH_4Cl + 2CO_2 + 2H_2O.$$

Yield.—93% theoretical (4 gms.). Glistening plates; M.P. 130°. (A., 3, 268; B., 10, 1785; J. C. S., 1930, 2788.)

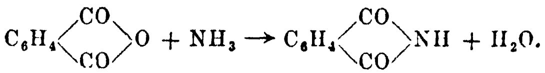
Benzamide may also be prepared by adding 5 gms. benzoyl chloride drop by drop to 20 c.cs. conc. ammonia solution.

PREPARATION 271.—**Phthalimide.**



$C_6H_4\langle{}^{CO}_{CO}\rangle NH$. $C_8H_5O_2N$. 147.

A mixture of 25 gms. phthalic anhydride and 25 gms. ammonium carbonate is powdered and heated in a long-necked flask until the whole liquefies at 300°. After cooling the mass is crystallised from water.



$$C_6H_4\langle{}^{CO}_{CO}\rangle O + NH_3 \rightarrow C_6H_4\langle{}^{CO}_{CO}\rangle NH + H_2O.$$

Yield.—90% theoretical (22 gms.). White needles; M.P. 232°. (A., 247, 294; B., 10, 579; Am. Soc., 1920, 1282; O. S., II, 75.)

Reaction CXL. Action of Ammonia on Phenols and Sulphonic Acids.

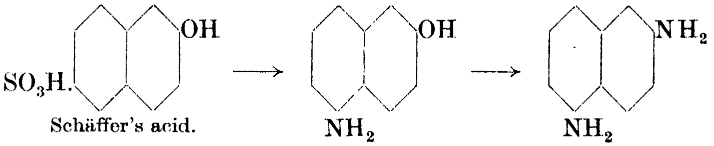
(1) $R.OH + NH_3 \longrightarrow R.NH_2 + H_2O.$

(2) $R.SO_3H + NH_3 \longrightarrow R.NH_2 + H_2SO_3.$

(1) Takes place readily with polyhydric phenols and naphthols, also if negative groups are present in the molecule, e.g. nitrophenols (*Organic Reactions*, Adams, Vol. I, 105; J. C. S., 1946, 1036.)

The reaction is usually carried out under pressure, and the yield is improved by the presence of sodium or ammonium sulphite (Bucherer's method), the sulphurous esters of phenols reacting more readily than phenols. Concentrated ammonia is used, or its addition compound with zinc chloride. Reaction (2) is carried out similarly to (1) and takes place readily in the anthraquinone series, but not in the naphthalene series, where sodamide is sometimes used. (B., 1906, 3009.) For use of barium amide, see Am. Soc., 1934, 1748.

An interesting case of group migration may be mentioned here.

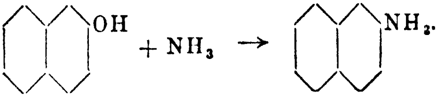


For preparation of primary, etc., amines from alcohols, see E. P., 410500.

PREPARATION 272.—**β-Naphthylamine** (*2-Aminonaphthalene*).

$C_{10}H_9N$. 143.

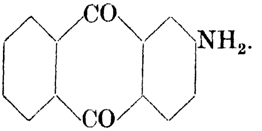
Method I.—144 gms. β-naphthol and 600 gms. ammonium sulphite are placed in an autoclave with stirrer and immersed in an oil bath (see p. 50). 125 gms. 20% ammonia are also added, and the mixture is heated for 8 hours at an internal temperature of 150°, and a pressure of 6 atms. (*Note.*—Brass gauges should not be used.) The contents are allowed to cool and the cake of β-naphthylamine is broken up and thoroughly washed with water on a filter. Thereafter it is dissolved in 1½ litres water and 110 gms. conc. hydrochloric acid (which should be free from sulphuric acid) and filtered. To the filtrate are added about 400 gms. saturated sodium sulphate solution until precipitation of the naphthylamine sulphate is complete (test). It is then filtered and washed with water. The free base is obtained by stirring a thin paste of the sulphate and water at 80° and adding caustic soda solution until the liquid gives an alkaline reaction to phenolphthalein. It is then filtered, washed and dried at 80°.



Yield.—85°–95% theoretical (120–135 gms.). White plates; M.P. 112°; B.P. 294°; the sulphate is less soluble than that of α-naphthylamine; important intermediate for dyestuffs. (E.P., 1387, 1900; F.P., 297464, 394820.)

Method II.—50 gms. β-naphthol and 200 gms. powdered zinc-ammonium chloride (p. 514) are mixed and heated in an oil bath in a vessel with a reflux condenser for 2 hours at 200°. The product, after cooling, is treated with 25% caustic soda solution until the zinc oxide redissolves, and the solution boiled for a few minutes. On cooling, β-naphthylamine separates. It may be removed and purified, as described in Method I. It may also be separated by extraction with ether, or by distillation in a current of superheated steam. (B., 13, 1300.)

PREPARATION 273.—2-Aminoanthraquinone.



$C_{14}H_9O_3N$. 223.

20 gms. sodium anthraquinone sulphonate (" silver salt ") and 200 c.cs. of conc. aqueous ammonia (D. 0·88) are heated in an autoclave of 500 c.cs. capacity to 180°, and maintained at this temperature for 6 hours. The autoclave is left to cool overnight, then opened, and the aminoanthraquinone filtered off and dried.

Red crystals ; M.P. 302°. (B., 12, 1567 ; E.P., 358852.)

Reaction CXLI. Action of Acids, Acid Anhydrides and Chlorides on Primary and Secondary Amines.—Substituted carboxyamides are usually prepared by treating amines with organic acids, acyl chlorides or anhydrides. When the acid is used a salt is first formed from which a molecule of water is eliminated on further heating.

$$RCOOH + R_1NH_2 \longrightarrow R.COONH_3R_1 \longrightarrow R.CONHR_1 + H_2O.$$

$$RCOCl + R_1NH_2 \longrightarrow R.CONHR_1 + HCl.$$

$$(RCO)_2O + 2R_1NH_2 \longrightarrow 2RCONHR_1 + H_2O.$$

When benzoyl chloride is used it is necessary to have present, or to add subsequently, an excess of caustic soda or some other basic substance (Schotten-Baumann Reaction).

When an acid anhydride is used the reaction is usually carried out by the application of heat, and may be hastened by the addition of dehydrating agents, e.g. fused sodium acetate or fused zinc chloride.

Hinsberg Separation. (B., 23, 2963 ; 38, 906).—Primary, secondary and tertiary amines may be distinguished by shaking the mixture with benzene -or *p*-toluene-sulphonyl chloride in presence of a large volume of dilute alkali. The tertiary amine is unaffected and can be removed by extraction or steam distillation ; the secondary amine forms an insoluble sulphonamide which can be filtered off, the primary forms a soluble sulphonamide which can be precipitated by the addition of mineral acid to the filtrate. For the purification of diethylaniline, see Prep. 279.

$$C_6H_5NH_2 + ClSO_2C_6H_5 \longrightarrow C_6H_5NHSO_2C_6H_5.$$

$$C_6H_5NHC_2H_5 + ClSO_2C_6H_5 \longrightarrow C_6H_5N(C_2H_5)SO_2C_6H_5.$$

PREPARATION 274.—Acetanilide (*Phenyl-amide of ethan acid*).

$CH_3CONHC_6H_5$. C_8H_9ON. 135.

25 gms. (1 mol.) of redistilled aniline, 10 gms. fused sodium acetate and 30 gms. (excess) of glacial acetic acid are boiled in a flask with an air condenser ground into the neck, until no aniline separates on treating a sample with a cold caustic soda solution (8 hours). The hot liquid is poured into 500 c.cs. cold water, the precipitate filtered, and washed with cold water. The crude acetanilide is boiled with a litre of water, a little

alcohol being added until it all goes into solution. It is filtered through a hot water filter (see p. 12), and the solution allowed to crystallise. If the product is dark coloured, it is redissolved as before, boiled with 5 gms. of decolourising carbon for ½ hour, filtered, and allowed to crystallise.

Yield.—85% theoretical (30 gms.). Rhombic plates; sparingly soluble in hot water; M.P. 112°; B.P. 295°. (Am. Soc., 1946, 2123.)

PREPARATION 275.—**Benzanilide** (*Phenylamide of benzenecarboxylic acid*).

$C_6H_5NH.CO.C_6H_5$. $C_{13}H_{11}ON$. 97.

Method I.—12 gms. of aniline are placed in a dish in a fume cupboard, and 10 gms. of benzoyl chloride are gradually added. Much heat is developed. When cold the product is extracted first with dilute hydrochloric acid to remove aniline, then with dilute caustic soda to remove benzoic acid, and finally with water. After pressing it is crystallised from alcohol.

$$C_6H_5.CO.Cl + 2C_6H_5NH_2 \longrightarrow C_6H_5.CO.NH.C_6H_6 + C_6H_5NH_2.HCl.$$

Yield.—Almost theoretical (20 gms.). (A., 60, 311.)

In the above process only one-half of the amine is transformed into its benzoyl derivative. By working in presence of dilute caustic soda or other alkali (Schotten-Baumann Reaction, see benzoyl-*p*-toluidide), the amine is completely converted into its benzoyl derivative.

Method II.—A mixture of 15 gms. (1 mol.) of aniline and 20 gms. (1 mol.) of benzoic acid is heated in a retort at 180°, and the temperature raised gradually to 225°; a further 10 gms. of aniline are added, and heating continued. The hot mass is then poured into an evaporating dish and allowed to solidify. It is powdered, washed with dilute hydrochloric acid to remove unchanged base, then with water to remove the benzoate, then with dilute caustic soda to remove free acid, and finally with water. It is dried and crystallised from alcohol.

$$C_6H_5NH_2 + C_6H_5COOH \longrightarrow C_6H_5NH_2.C_6H_5COOH \longrightarrow C_6H_5NHCOC_6H_5 + H_2O.$$

Yield.—80% theoretical (26 gms.). Colourless plates; insoluble in water; M.P. 162°. (Bl., [3], 11, 8933; O. S., VII, 6.)

PREPARATION 276.—**Benzoyl-*p*-toluidide** (*p-Toluoyl-amide of benzene carboxylic acid*).

$C_6H_5CONH.C_6H_4CH_3[1:4]$. $C_{14}H_{13}ON$. 211.

2 gms. (1 mol.) of finely-divided *p*-toluidine are mixed with 10 c.cs. of a 10% aqueous solution of sodium hydroxide, and 2 c.cs. benzoyl chloride (excess) are added gradually to the warm mixture in a corked flask, which is mechanically shaken. Thorough shaking is essential. If any excess of benzoyl chloride remains, it is destroyed by warming with a further quantity of sodium hydroxide solution. The mixture is then poured into water, and the precipitate filtered, dried, and recrystallised from alcohol.

$$CH_3C_6H_4NH_2 + C_6H_5COCl + NaOH = C_6H_5CONHC_6H_4CH_3 + NaCl + H_2O.$$

Yield.—Almost theoretical (4 gms.). Colourless crystals; insoluble in water; M.P. 158°. (B., 19, 3219.)

PREPARATION 277.—**Diaceto-*o*-toluidide.**

$CH_3.C_6H_4N(CO.CH_3)_2[1:2]$. $C_{11}H_{13}O_2N$. 191.

10 gms. of *o*-toluidine, 38 gms. of acetic anhydride and 5 gms. fused sodium acetate are heated to boiling for 1 hour in a flask provided with an air condenser and calcium chloride tube. After this time the product is distilled from a distilling flask at a pressure of 20 mms. Acetic acid and acetic anhydride pass over first; then diacetyl derivative distils at 152°–153°, and sodium acetate and some mono-acetyl derivative remain in the flask.

$$CH_3.C_6H_4NH_2 + (CH_3CO)_2O \longrightarrow CH_3.C_6H_4N(COCH_3)_2 + H_2O.$$

Yield.—80% theoretical (14 gms.). Colourless crystals; somewhat unstable; M.P. 18°. (B., 26, 2855.)

Reaction CXLII. Action of Primary Aromatic Amines on Alcohols.—The reaction is generally carried out by heating under pressure, and in presence of a mineral acid. Secondary and tertiary amines are formed.

$$RNH_2 + R_1OH \longrightarrow RNHR_1 + H_2O.$$
$$R.NHR_1 + R_1OH \longrightarrow RN(R_1)_2 + H_2O.$$

PREPARATION 278.—**Dimethylaniline.**

$C_6H_5N(CH_3)_2$. $C_8H_{11}N$. 121.

93 gms. pure aniline, 105 gms. pure methyl alcohol and 9·4 gms. conc. sulphuric acid are heated in an enamelled autoclave to 200°. The pressure rises to about 30 atms., and the contents are left for 6 hours at 215°. They are allowed to cool, and then 25 gms. 30% caustic soda solution added. The product is now heated to 170° in the autoclave for a further 5 hours. This second heating is necessary to decompose the sulphoammonium bases formed, and which are decomposed into sulphuric acid, alcohol, and tertiary amine. The contents of the autoclave, after cooling, are distilled in steam. The dimethylaniline is salted out of the distillate with common salt. It is then separated and distilled.

$$C_6H_5N\boxed{H_2 \;+\; \begin{matrix}HO\\HO\end{matrix}}\begin{matrix}CH_3\\CH_3\end{matrix} \rightarrow C_6H_5N.(CH_3)_2.$$

Yield.—95% theoretical (117 gms.). Colourless liquid when pure; turns brown on standing; B.P. 195°; D. 0·96; important intermediate for dyestuffs and for the explosive tetryl (trinitrophenylmethylnitramine).

Purification.—Aniline and monomethyl aniline may be removed by refluxing for three hours two volumes of impure dimethylaniline with one volume of acetic anhydride and distilling.

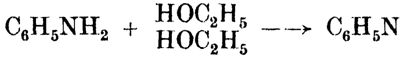
PREPARATION 279.—**Diethylaniline.**

$C_6H_5N(C_2H_5)_2$. $C_{10}H_{15}N$. 149.

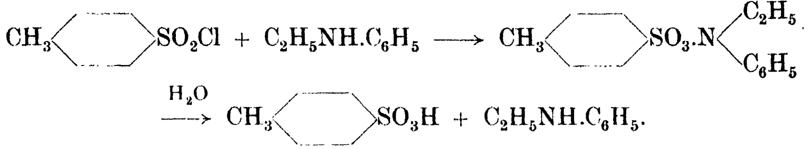
130 gms. dried aniline hydrochloride and 140 gms. 95% alcohol are heated in an enamelled autoclave at 180° for 8 hours. After cooling, the

contents of the autoclave are placed in a round-bottomed flask and the alcohol and ethyl ether distilled off. The residual mixture of mono- and diethylaniline is treated with 100 gms. 30% caustic soda solution. The product is stirred up at ordinary temperature with 40 gms. of *p*-toluene sulphonic chloride, which forms a non-volatile derivative with the monoethylaniline. The diethylaniline is then distilled from the mixture in steam, and separated as in Preparation 278.

The monoethylaniline can be obtained by hydrolysing the toluene sulphonic derivative with conc. sulphuric acid.



$$C_6H_5NH_2 + \begin{matrix} HOC_2H_5 \\ HOC_2H_5 \end{matrix} \longrightarrow C_6H_5N(C_2H_5)_3.$$



Yield.—80% theoretical (120 gms.). Colourless liquid when pure; B.P. 216·5; D. 0·939; important intermediate for dyestuffs. (A., 74, 128; D.R.P., 250236.)

Reaction CXLIII. Condensation of Aromatic Aldehydes with Primary Aromatic Amines.—Formation of anils (Schiff's bases) takes place readily on heating (Chem. Rev., 26, 324).

$$R.CHO + NH_2R_1 \longrightarrow RCH{=}NR_1 + H_2O.$$

Substituted aldehydes and substituted amines also react: for example, the sodium salt of α-naphthylamine 4-sulphonic acid when dissolved in water and shaken with an alcoholic solution of benzaldehyde yields sodium benzylidine naphthionate.

With aliphatic aldehydes the reaction takes the following course:

$$CH_3.CHO + 2NH_2.C_6H_5 \longrightarrow CH_3CH(NH.C_6H_5)_2 + H_2O.$$

Formaldehyde reacts like the aromatic aldehydes, yielding dehydroformaldehyde-aniline (or methylene) compounds.

$$C_6H_5NH_2 + OCH_2 \longrightarrow C_6H_5N{=}CH_2 + H_2O.$$

PREPARATION 280.—**Benzylideneaniline** (*Benzalaniline*).

$C_6H_5N{=}CH.C_6H_5$. $C_{13}H_{11}N$. 181.

9·3 gms. of aniline (1 mol.) and 10·6 gms. of benzaldehyde (1 mol.) are placed in a porcelain dish on an oil bath and heated for 5 hours at 125°. The product, while still warm, is poured into ice-water with stirring. Benzylideneaniline solidifies, is filtered and washed. The product can be used directly for the preparation of *p*-nitroaniline. It is insoluble in water, but can be recrystallised from alcohol.

$$C_6H_5NH_2 + OCH.C_6H_5 \longrightarrow C_6H_5N{=}CH.C_6H_5 + H_2O.$$

Yield.—85% theoretical (15 gms.). M.P. 54°. (J., 1850, 488; O. S., VIII, 22.)

Reaction CXLIV. Action of Ammonia on Aldehydes.—The simplest case is the formation of an aldehyde ammonia by the action of dry ammonia gas on the aldehyde in dry ethereal solution. Acetaldehyde and several of the aliphatic aldehydes react after this fashion. (See Preparation 440.)

$$R.CHO + NH_3 \longrightarrow R.CHOH.NH_2.$$

Formaldehyde and most of the aromatic aldehydes do not react in this way with ammonia, but form complex condensation products (Prep. 281.) Glucose and other monosaccharides condense with ammonia and amines to give glucamines ; e.g. hydrogen and ethylamine at 90°–100° and 100 atms. in presence of nicklel-keiselgühr (p. 178) give ethylglucamines, $C_2H_5NH.CH_2.(CHOH)_4CH_2OH$. (E.P., 426062.)

PREPARATION 281.—**Hexamethylenetetramine** (*Hexamine*).

$$(CH_2)_6N_4. \qquad C_6H_{12}N_4. \qquad 140.$$

50 c.cs. of " formalin " containing 40% formaldehyde and 30 c.cs. of conc. ammonium hydroxide solution (D. 0·88) are mixed in a round-bottomed flask. The flask is connected to a suction pump and the contents evaporated on a water bath under diminished pressure to a thick paste. A second equal quantity of ammonium hydroxide is then added and evaporated as before. The residue is treated with sufficient boiling absolute alcohol to dissolve, filtered hot, and the filtrate set aside to cool. Colourless crystals separate, which are filtered off and washed with a little absolute alcohol.

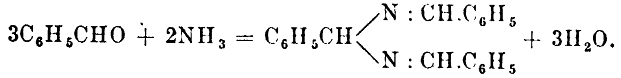
$$6CH_2O + 4NH_4OH \longrightarrow (CH_2)_6N_4 + 10H_2O.$$

Yield.—80% theoretical (12·5 gms.). Sublimes about 260° ; very soluble in water. (B., 19, 1842.)

PREPARATION 282.—**Hydrobenzamide.**

$$(C_6H_5CH)_3N_2. \qquad C_{21}H_{18}N_2. \qquad 298.$$

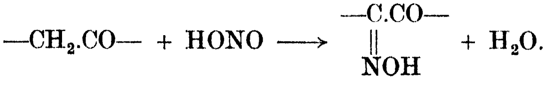
5 c.cs. of benzaldehyde and 25 c.cs. conc. ammonium hydroxide solution are placed in a stoppered flask and allowed to stand for 2 days. Crystals of hydrobenzamide separate, which are filtered off, washed with water, and recrystallised from alcohol.



$$3C_6H_5CHO + 2NH_3 = C_6H_5CH\begin{cases} N : CH.C_6H_5 \\ N : CH.C_6H_5 \end{cases} + 3H_2O.$$

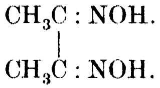
Yield.—90% theoretical (4·2 gms.). M.P. 110° ; insoluble in water, easily soluble in alcohol. (A., 21, 130.)

Reaction CXLV. Action of Nitrous Acid on certain Ketones.—Isonitroso compounds are formed by the action of nitrous acid on ketones which contain the $CH_2.CO$— group.



$$—CH_2.CO— + HONO \longrightarrow \begin{array}{c} —C.CO— \\ \| \\ NOH \end{array} + H_2O.$$

Preparation 283.—Dimethylglyoxime (*Diacetyldioxime*).



$$\begin{array}{l} CH_3C:NOH. \\ \quad | \\ CH_3C:NOH. \end{array}$$

$C_4H_8O_2N_2$. 116.

In a fume cupboard is placed a three-necked flask containing 62 gms. of *dry* methylethyl ketone and 4 c.cs. conc. hydrochloric acid. A condenser and thermometer are attached along with a delivery tube for ethyl nitrite, the flask being immersed in a water bath. The temperature is raised to 40° and 30 gms. ethyl nitrite (see Prep. 240) added over about one hour, the temperature being allowed to rise to 55°. The alcohol is then removed with the condenser by heating the mixture to 90°.

A solution of sodium hydroxylamine mono-sulphonate is made by adding to 500 gms. in 60 gms. sodium nitrate and 20 gms. sodium bisulphite, 15 c.cs. glacial acetic acid and 55 c.cs. conc. hydrochloric acid being added with stirring beneath the surface. The temperature is kept below 0°. The monoxime as prepared above is added to this solution, and the temperature raised to 70° where it is kept for several hours. Crystals of dimethylglyoxime which separate on cooling, are filtered, and washed with water until free of sulphate.

$$CH_3CH_2COCH_3 + C_2H_5ONO \longrightarrow CH_3C(NOH)COCH_3 + C_2H_5OH.$$

$$CH_3C(NOH)COCH_3 + SO_3Na.NHOH \longrightarrow$$
$$CH_3C(NOH)C(NOH)CH_3 + NaHSO_4.$$

Yield.—55% theoretical (55 gms.). White crystals; M.P. 238°–240°. Important analytical reagent for estimating nickel. (C. V., II, 204.)

CHAPTER XX

THE LINKING OF SULPHUR TO CARBON

SULPHONIC ACIDS

Reaction CXLVI. Action of Concentrated Sulphuric Acid on Hydrocarbons or Substituted Hydrocarbons.—When conc. sulphuric acid acts on an aromatic hydrocarbon or substituted hydrocarbon, one or more of the H atoms in the nucleus is replaced by the sulphonic group ($SO_2.OH$).

$$R.H + H_2SO_4 \longrightarrow R.SO_2OH + H_2O.$$

It is necessary to use a large excess of conc. H_2SO_4. In this way the concentration of the acid is little affected by the amount of water formed in the reaction. Sulphonation does not go to completion, however, unless sulphuric acid is above a certain minimum concentration characteristic of the compound being sulphonated (e.g. 78% in the case of benzene).

Some sulphonic acids, e.g. benzene and toluene sulphonic acids, may be formed at ordinary temperatures, while others require a considerably higher temperature. In some cases 100% H_2SO_4 (monohydrate—$SO_3.H_2O$) is necessary. The influence of temperature (see table below), concentration of acid, time of reaction, and the presence of other substituents is very marked, and different isomers are formed under different conditions.

Effect of Temperature on Sulphonation of Toluene :

Temp.	*ortho*	*meta*	*para*
0°	42·7	3·8	53·5%
35°	31·9	6·1	62·0%
100°	13·3	8·0	78·7%

The reaction may be assisted mechanically by mixing with kieselgühr, or other finely-divided material, and catalytically by the addition of iodine, alkali metavanadate (U.S.P., 1915925) in the case of benzene, or boron trifluoride in the case of benzene, toluene, and naphthalene (J. Eng., 1940, 408), and of boric acid, mercury and mercury salts in the case of anthraquinone.

The sulphonic group is strongly acidic, and will decompose carbonates with the formation of stable salts, a property which is used in their separation. The presence of a basic group in the nucleus is not sufficient to neutralise its acidity, thus sulphanilic acid is distinctly acid.

Isolation of Sulphonic Acids.—Sulphonic acids are usually isolated in the form of their salts in order to get rid of the excess of sulphuric acid used in the reaction. The calcium or barium salts are formed where these are soluble by adding lime or barium carbonate, and the excess sulphuric acid precipitated as $CaSO_4$ or $BaSO_4$, and removed by filtration. The filtrate containing the salt in solution may then be concentrated till the salt crystallises out or it may be evaporated to dryness. The sodium salt may be obtained from the sulphonation mixture by diluting and adding a saturated solution of common salt, and allowing to crystallise. Isomers may be separated by the fractional crystallisation of their salts; it is often best, however, to form the sulphonyl chlorides by treatment with PCl_5, and then the sulphonamides by the action of ammonia (see Prep. 291); after fractional crystallisation of the amides the acids are set free by heating under pressure with hydrochloric acid. The sulphonyl chlorides, and the sulphonamides which generally crystallise well and have definite melting points, are used for the identification of sulphonic acids. See p. 310.

Tests for Complete Sulphonation.—The sulphonation is tested by the solubility of the product in water or dilute alkali. Complete solubility is seldom obtained owing to the formation of a sulphone by condensation.

$$R.SO_3H + H.R \longrightarrow R.SO_2.R + H_2O.$$

The sulphones are insoluble in water, but may be distinguished, say, from unchanged naphthalene by extracting and taking the melting point. The following factors influence the formation of sulphones; concentration of acid (H_2SO_4 or SO_3), temperature of sulphonation, duration of sulphonation. Conditions have to be chosen so that the quantity of sulphone is reduced to a minimum.

Apparatus used in Sulphonation.—The most convenient type of apparatus for this process is a cast-iron pot with a good mechanical agitator, a thermometer pocket, and an opening for reflux condenser (see Fig. 37). It is of the utmost importance that the agitation should be as efficient as possible. Fig. 38 shows a convenient apparatus in glass, when the cast-iron pot is not procurable.

PREPARATION 284.—Benzenesulphonic Acid.

$C_6H_5.SO_3H$. $C_6H_6O_3S$. 158.

Method I.—300 gms. of conc. sulphuric acid (96%) and 60 gms. of benzene are placed in the sulphonating vessel and the temperature raised to the boiling point of benzene, 80°, the agitation being maintained from the commencement of the heating. The benzene vapour is condensed and returned by the reflux. The heating is continued for 8–10 hours, when the sulphonation should be complete (test). Milk of lime is made up in a basin by adding 1 part quicklime to 5 parts hot water, and stirring. The sulphonation is cooled and poured into 300 c.cs. of water.

Isolation of Calcium Salt.—The milk of lime is now carefully added with stirring until the solution is just neutral (test with phenolphthalein paper). It is then boiled, and after cooling to 60° the $CaSO_4$ is filtered off on a Buchner funnel, and washed with a little hot water.

Isolation of Free Acid.—To the filtrate which contains the Ca salt in solution, dilute sulphuric acid is added until all the Ca is precipitated (test), and this is filtered off and washed with a little hot water. The filtrate is then evaporated until the free acid crystallises out.

Isolation of Sodium Salt.—The sodium salt is isolated when fusion with caustic soda is anticipated. To the filtrate containing the Ca salt in solution, sodium carbonate is added until no more $CaCO_3$ is precipitated (test). The $CaCO_3$ is filtered off and washed, and the filtrate evaporated, yielding the Na salt.

If the sulphonation mixture is treated with lime so as to give a neutral reaction to litmus, the completion of the conversion to the sodium salt can then be conveniently judged when an alkaline reaction to phenolphthalein is obtained during the addition of sodium carbonate.

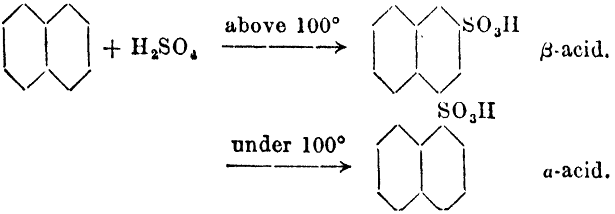
$$C_6H_6 + H_2SO_4 \longrightarrow C_6H_5.SO_3H + H_2O.$$

Yield.—75–80% theoretical. Na and Ca salts, white powders, soluble in water; used in preparation of phenol, see p. 214.

PREPARATION 285.—**Naphthalene-β-sulphonic Acid (Na salt).**

$C_{10}H_7SO_3H$. $C_{10}H_8SO_3$. 208.

120 gms. of conc. sulphuric acid are heated to 160° and 100 gms. of melted naphthalene poured in from a basin, good agitation being maintained. When all the naphthalene is added, the temperature is raised to 170° for 3 hours, and then to 180° for 1 hour, until sulphonation is complete (test). The excess sulphuric acid is removed as $CaSO_4$, as in Preparation 284. The filtrate containing the calcium salt of the β-acid as well as some calcium salt of the α-acid is concentrated until a sample, on cooling, sets to a thick mass. It is allowed to crystallise overnight, and filtered. The calcium salt of the α-acid remains in the filtrate. The sodium salt is isolated as above.



Yield.—75% theoretical (130 gms.). White powder; soluble in water; used in preparation of β-naphthol. (Rec., 36, 20, 197.)

PREPARATION 286.—***d*-Camphorsulphonic Acid** (*Reychler's Acid*).

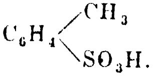
$C_{10}H_{15}O.SO_3H$. $C_{10}H_{16}O_4S$. 232.

45 gms. (1 mol.) of camphor are finely-powdered and added to a well-stirred mixture containing 30 gms. (1 mol.) of conc. sulphuric acid, and 60 gms. of acetic anhydride. The camphor dissolves readily, and the solution is allowed to stand for 2–3 days until no more *d*-camphor sulphonic acid crystallises out. The crystals are then filtered through asbestos or glass wool, washed with acetic acid until colourless, and recrystallised from acetic acid or ethyl acetate.

$$C_{10}H_{16}O + H_2SO_4 \longrightarrow C_{10}H_{15}O.SO_2OH + H_2O.$$

Yield.—50% theoretical (35 gms.). Large prisms; decompose at 193°; $[\alpha]_D = +21°$. (B., 3, 120; J. C. S., 81, 1442.)

PREPARATION 287.—*o*- and *p*-**Toluenesulphonic Acids.**



$C_6H_4\left\langle\begin{array}{l}CH_3\\SO_3H.\end{array}\right.$ $C_7H_8O_3S$. 172.

130 gms. pure toluene are heated with 450 gms. conc. sulphuric acid in a cast-iron pot fitted with a suitable agitator (see Fig. 37). A crystal of iodine is added, and the temperature allowed to rise to 100°. The sulphonation is complete in about 6 hours, when the reaction mixture is transferred to a large basin, diluted with water, and milk of lime added gradually to neutralise the excess acid. The calcium sulphate and any ferric hydroxide present are removed by filtration and washed with hot water. Sodium carbonate is added to the filtrate until just alkaline to phenolphthalein, and the calcium carbonate filtered off. The filtrate is then evaporated almost to dryness, when the sodium salts of *o*- and *p*-sulphonic acids separate out.

Yield.—95% theoretical (340 gms.) (total *o* and *p*).

o- Crystallises with $2H_2O$; plates. (Am. Soc., 8, 176 ; B., 12, 1851.)

p- Crystallises with $4H_2O$; plates or prisms ; M.P. 92°. (Am Soc., 10, 140.)

Separation of *o*- and *p*-Toluenesulphonic Acids.—The mixture prepared above is treated gradually with an equal weight of finely-pulverised phosphorus pentachloride. When the reaction is complete, cold water is added, the whole being surrounded by a freezing mixture. The *p*-sulphonyl chloride separates as a solid (M.P. 69°) recrystallisable from alcohol. The *o*-sulphonyl chloride is an oily liquid (M.P. 10°), and is separated from the filtrate by means of a funnel.

$$C_6H_4CH_3SO_3Na + PCl_5 \longrightarrow C_6H_4CH_3SO_2Cl + POCl_3 + NaCl.$$

These sulphonyl chlorides form derivatives with primary and secondary amines useful for identification purposes.

Reaction CXLVII. Action of Fuming Sulphuric Acid (oleum) on Hydrocarbons or Substituted Hydrocarbons.—It is sometimes difficult to introduce a sulphonic group by means of conc. sulphuric acid. and it is then necessary to use fuming acid (i.e. acid containing up to 70% free SO_3). The same factors as before have an important influence on the reaction. Usually a high temperature is necessary where more than one SO_3H has to be introduced. In some cases oleum is used in preference to sulphuric acid, in order to reduce the time and the temperature of sulphonation.

Estimation of SO_3 in Oleum.—The oleum is melted, if necessary, by placing the bottle in warm oil (*caution!*), and a quantity is dropped into the bottom of a clean, dry, tared test tube to a depth of about 1½ inches (8–10 gms.). The whole is weighed, and the weight of oleum obtained by difference. The test tube is now heated and drawn out near its open end and sealed. This is then carefully placed in a graduated litre flask containing about 500 c.cs. of water. The flask is securely stoppered, and the test tube broken by shaking. Shaking is continued till all the white fumes disappear. The flask is then allowed to cool, and its contents made up to 1 litre. 250 c.cs. are then removed and titrated with normal caustic soda solution, using methyl orange as an indicator.

If W = weight of oleum, n = c.cs. N.NaOH to neutralise W,

then $$\%SO_3 = \frac{4{\cdot}9n - 100W}{{\cdot}225W}.$$

The percentage of SO_3 can also be obtained by estimating the total H_2SO_4 by titration given by the oleum, reckoned as H_2SO_4. The % excess of H_2SO_4 over 100, when multiplied by 4·44 gives the percentage of SO_3, e.g. if total $H_2SO_4 = 105\%$ of the oleum, then $\%SO_3 = 5 \times 4{\cdot}44 = 22{\cdot}2$.

The results obtained are a little high, as oleum contains a small percentage of SO_2. This may be estimated by titrating 250 c.cs. with N/10 iodine solution, using starch as indicator. By subtracting this result from the total obtained by titration with NaOH, the true percentage of SO_3 can be calculated.

For estimation of oleum by titration with water, see J. C. S., 1946, 585.

Preparation of Oleum of a given Strength.

1. From two oleums of different strength.

oleum $= a\%SO_3$ oleum $= c\%SO_3$

oleum $= b\%SO_3$ required,

then $$x = \frac{100(a-b)}{b-c}$$

where x = quantity of c to be added to 100 gms. of a to give b.

2. From oleum and conc. sulphuric acid.

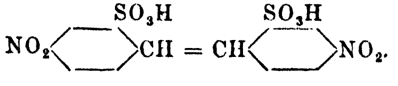
oleum $= a\%SO_3$ oleum $= b\%$ required,

conc. sulphuric acid $= c\%H_2SO_4$

then $$x = \frac{100(a-b)}{444 - 4{\cdot}44c + b}$$

where x = quantity of conc. H_2SO_4 to be added to 100 gms. of a to give b.

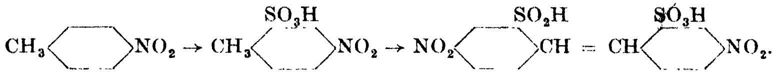
PREPARATION 288.—**4 : 4′-Dinitrostilbine-2 : 2′-disulphonic Acid (Na Salt).**



$C_{14}H_{10}O_{10}N_2S_2$. 430.

300 gms. 25% oleum are heated to 70°, 100 gms. *p*-nitrotoluene are carefully added and the temperature allowed to rise to 100° with cooling, if necessary. When all is added the temperature is held at 110° until sulphonation is complete (see p. 317), The Na-salt is separated as in Prep. 284, dissolved in 500 c.cs. water at 60°, and 50 gms. sodium carbonate added. The solution is filtered from iron oxide and made up to 2 litres at 50°. 160 gms. at 35% caustic soda solution are added during ½ hour. No sodium salt should separate out. A mixture of 1,700 gms. sodium hypochlorite solution, containing about 5% NaOCl and 300 gms. of 35% caustic soda solution, is allowed to drop in during 10 hours. The temperature must not exceed 56°, otherwise yellow dyestuffs are formed. The mixture is allowed to stand at 55° for 24 hours. Free chlorine should be present during the whole period (test with starch-potassium iodide paper). It is then cooled to ordinary temperature and 400 gms. salt added. After

standing for a day the yellow crystalline sodium salt of the acid is precipitated, and is filtered off and washed with brine.



Yield.—About 40% theoretical (60 gms.). Used for preparation of diamido-stilbene-disulphonic acid and stilbene dyestuffs. (B., 30, 3100.)

PREPARATION 289.—**Benzene Sulphonic Acid (Na Salt).**

$C_6H_5SO_3Na$. $C_6H_5O_3SNa$. 180.

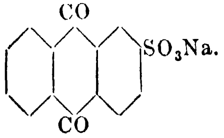
20 gms. benzene are added, a few c.cs. at a time, to 45 c.cs. fuming sulphuric acid (6–8 per cent.)in a 200-c.c. round-bottomed flask (*caution!*). The mixture is shaken until the first instalments dissolve when the next few c.cs. are added with shaking, the temperature being kept between 35° and 50°. When all the benzene has dissolved the solution is poured slowly (*caution!*) into 200 c.cs. water and filtered to remove sulphone (see p. 310). To the filtrate are added carefully 25 gms. solid sodium bicarbonate, then 50 gms. sodium chloride and heat applied until all dissolves. The hot solution is filtered and rapidly cooled while stirred. The sodium benzene sulphonate which separates is filtered, pressed, washed with 40 c.cs. saturated sodium chloride, then with a little alcohol, and dried in air or oven. It may be crystallised from alcohol.

$$C_6H_6 + SO_3 \longrightarrow C_6H_5SO_3H.$$

Yield.—45% theoretical (20 gms.). See p. 318.

This procedure is used in the sulphonation of *p*-nitrochlorobenzene, *p*-nitrotoluene, *o*-nitrochlorobenzene, chlorobenzenes, etc.

PREPARATION 290.—**Anthraquinone-β-Sodium Sulphonate ("Silver Salt").**



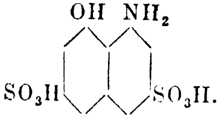
$C_{14}H_7O_5SNa$. 310.

100 gms. dry, finely-divided anthraquinone are added cautiously to 150 gms. oleum containing 25% SO_3, with continuous stirring, the temperature being kept at 25°–30°. The temperature is then raised to 120° during 4 hours, and then to 140° during a further 2 hours, using an oil bath. The vessel must be kept closed to prevent loss of SO_3. After cooling, the mixture is poured into 3 litres of water (*caution!*) and the unchanged anthraquinone filtered off (25–40 gms.). Chalk is added to the filtrate until completely neutralised, and the calcium sulphate filtered off. The calcium in solution is then precipitated as carbonate by adding dilute sodium carbonate (test). The filtrate is evaporated to about 400 c.cs., allowed to cool when the sodium salt separates (2 days), is filtered, washed with water, and dried.

Yield.—40–60% theoretical (60–90 gms.). Silvery glistening plates; soluble in water; crystallises with $1H_2O$; used for making alizarin (see p. 399). (A., 160, 131; Z. a., 44, 912.)

The α-sulphonic acid is formed in presence of mercury (C. V., II, 539.).

PREPARATION 291.—1 : 8-Aminonaphthol-3 : 6-Disulphonic Acid (*H. acid*)—Mono-sodium Salt.



$C_{10}H_9O_7NS_2$. 319.

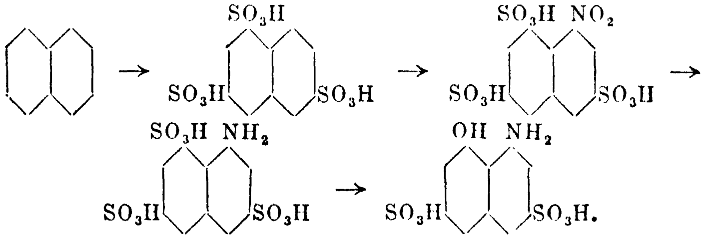
Sulphonation.—1,024 gms. of 24% fuming sulphuric acid (fuming acid of higher strength than this may be diluted with 100% sulphuric acid), or the equivalent of fuming acid of strength 22–24%, are weighed and introduced into a sulphonation pot. The acid is stirred and heat applied until the temperature reaches 100°; 128 gms. of naphthalene are added quickly in portions at a time, and this causes a considerable rise in temperature. When the naphthalene is all in, the temperature is raised to 165°, at which it is maintained for 8 hours, with slow stirring. During this process naphthalene 3.6.8-trisulphonic acid is the chief product formed. After the above time the pot is allowed to cool to room temperature.

Nitration.—At room temperature the sulphonation mixture should be capable of being stirred, but if not conc. sulphuric acid must be added until the contents can be stirred. .The pot is then placed in a bath, which can be filled with cold water, the agitator is set in motion, and conc. nitric acid slowly run from a dropping funnel to effect nitration. The temperature should be maintained at about 20° during nitration. The theoretical quantity of nitric acid, calculated from the naphthalene used, is necessary, and acid of about 60% is preferable, the strength being ascertained by use of a hydrometer (p. 522).

After the nitric acid has been added, the mixture is allowed to stand at 25° for an hour, and then the temperature is raised to 50° in the course of the next hour. After this time it is poured into 1,500 c.cs. water; volumes of nitrous fumes are given off, and the temperature rises considerably. During this process 1-nitro-3 : 6 : 8-naphthalene-trisulphonic acid is the chief product formed.

Reduction.—256 gms. of iron borings are weighed and about 10 gms. of these added to the solution of nitro-sulphonic acid at about 50°; this causes the evolution of nitrous fumes. The remaining iron is added in portions at such a rate that the reduction proceeds briskly; the agitation should be vigorous enough to keep the iron swirling round. After all the iron has been added, agitation is continued for an hour; the temperature is then raised to 50°, 150 gms. of common salt added, and the agitation continued for an hour while the mixture cools. The acid sodium salt of naphthylamine-trisulphonic acid is by this means precipitated; along with any unattacked iron this is filtered off and washed with 10% brine. The contents of the funnel are placed in a vessel and boiled up with water until all the naphthylamine-sulphonic acid dissolves; while still almost boiling the solution is again filtered to separate the iron residue. The filtrate, while still warm, is treated with 15 gms. common salt for each 100 c.cs. volume and agitated while the salt dissolves ; before this is complete, separation of the sulphonic acid begins. The mixture is afterwards cooled to 15°, and the purified aminosulphonic acid (Na salt) filtered off. The precipitate is washed on the funnel with 100 c.cs. of 10% brine, pressed in a screw press (p. 37) and dried at 100°. When dry, it is ground up, and a sample estimated with standard nitrite (see p. 499) ; it is generally of 75–80% purity.

Caustic Fusion.—This operation is performed in a small autoclave: for manipulation of which see p. 50, 85 gms. caustic soda and 134 c.cs. water are placed in the vessel and heat applied until solution takes place ; 128 gms. of naphthylamine-trisulphonic acid (70–80%) are then added, and the lid of the autoclave bolted on. The mixture is gradually heated up to 180° and maintained at this point for 5 hours, the pressure being about 100 lbs. After cooling, the autoclave is opened, allowing any residual pressure to escape gradually—a certain amount of ammonia is always present. The reaction product is introduced into a large beaker or stoneware jar, diluted with 750 c.cs. water, and acidified with conc. hydrochloric, or 50% sulphuric acid ; volumes of sulphur dioxide from the decomposition of the sodium sulphite are given off. When testing for acidity, a small sample should be withdrawn and boiled to expel sulphur dioxide, prior to testing with Congo paper. The aminonaphthol-disulphonic acid, which is formed in this reaction, being only very sparingly soluble in solutions of sodium chloride or sulphate, is practically all precipitated as the mono-sodium salt on acidification. After acidification the mixture is cooled to room temperature and allowed to stand for 1 hour. The precipitate is then filtered off, washed with 100 c.cs. of 10% brine, pressed, and dried at 100°.



Yield.—50 gms. of 80–85% purity (see estimation, p. 503). Monosodium salt is soluble in water and crystallises with $1\frac{1}{2}H_2O$; fine needles. (B., 27, 2148 ; D.R.P., 69722.)

Reaction CXLVIII. Action of Chlorosulphonic Acid ($Cl.SO_3H$) on Hydrocarbons or Substituted Hydrocarbons. (B., 42, 2057, 2274).—Chlorosulphonic acid (see p. 519) is used for sulphonating in special cases. See J. C. S., 1932, 715.

$$R.H + Cl.SO_3H \longrightarrow R.SO_3H + HCl.$$

The chief advantage in the use of this acid is its selective property, whereby certain sulphonic acids are formed, which are not formed by direct sulphonation with sulphuric acid or oleum, or which may be formed only in presence of other isomers, the separation of which might be difficult. For example, naphthalene sulphonated with oleum at the ordinary temperature gives a mixture of 1 : 5- and 1 : 6-disulphonic acids, while chlorosulphonic acid yields only the 1 : 5-acid. Similarly, with toluene, chiefly the ortho acid is formed. With excess of chlorosulphonic acid a sulphonyl chloride is formed (chlorosulphonation), except in the case of phenols or naphthols, which give the free sulphonic acid.

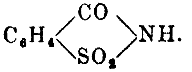
$$R.H \longrightarrow R.SO_2OH \longrightarrow R.SO_2Cl.$$

When chlorosulphonic acid reacts with amides, acid chlorides are formed, while amines yield sulphamic acids.

$$SO_3HCl + 3C_6H_5NH_2 \longrightarrow C_6H_5NH.SO_3H.C_6H_5NH_2 + C_6H_5NH_2.HCl.$$

When the sulphonic acid produced by the interaction of chlorosulphonic acid has to be nitrated afterwards, it must be isolated previous to nitration, otherwise the chlorine liberated may form chloro-derivatives.

PREPARATION 292.—"**Saccharin**" (*o-Benzoicsulphinide*).



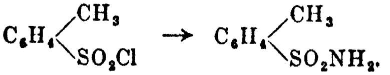
$$C_6H_4\left\langle\begin{matrix}CO\\SO_2\end{matrix}\right\rangle NH. \quad C_7H_5O_3NS. \quad 183.$$

1. *Toluene-o- and p-sulphonyl-chloride.*—In a fume cupboard 100 gms. pure toluene are slowly run into 400 gms. well-stirred chloro-sulphonic acid cooled to 0°, the temperature during the addition being kept at 0°–5°, stirring being continued for about 5 hours at the same temperature. The mass is poured on to 1,000 gms. ice, the oil decanted, washed well with water, chilled to −20° (p. 12) and the product filtered to separate the *o*- and *p*-isomers. The almost pure *p*-toluene sulphonylchloride may be crystallised from light petroleum, M.P. 69°; the liquid *o*-isomer, B.P. 126°/10mms. may be fractionated under reduced pressure, but is pure enough for next stage.

$$C_6H_5CH_3 \longrightarrow CH_3C_6H_4SO_2Cl.$$

Yield.—Ortho 85% theoretical (110 gms.). Para 15% theoretical (30 gms.). (E.P., 25273, 1894.)

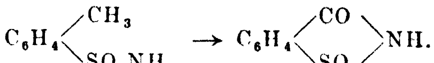
2. *Toluene-o-sulphonamide.*—The *o*-sulphonyl chloride is gradually added to an equal quantity of 20% ammonia solution, which is cooled in a freezing mixture. When all has been added, the reaction is completed by removing the freezing mixture and gently heating. The sulphonamide is then filtered off and dissolved in N caustic soda solution, filtered, and reprecipitated by adding sufficient hydrochloric or sulphuric acid to precipitate 75% of the amide in solution. The precipitate is redissolved by heating, and almost pure *o*-sulphonamide crystallises out on cooling (M.P. 133°–134°).



$$C_6H_4\left\langle\begin{matrix}CH_3\\SO_2Cl\end{matrix}\right. \rightarrow C_6H_4\left\langle\begin{matrix}CH_3\\SO_2NH_2.\end{matrix}\right.$$

3. *Saccharin.*—One equivalent of the *o*-sulphonamide (171 gms.) is dissolved in one equivalent of caustic soda (40 gms.) and 2,565 gms. of water.

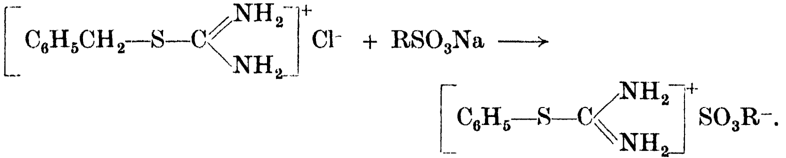
This is heated to 40°–50°, and 256 gms. of solid potassium permanganate are slowly added with stirring. When all the permanganate has been added and the colour has almost disappeared, a little NaHS is added to decolourise, and the precipitated manganese compound filtered off and washed with water until acid added to the filtrate gives no precipitate of saccharin. The combined filtrate and washings are then cooled down to ordinary temperature and neutralised with hydrochloric acid, using methyl orange as indicator. This treatment precipitates unchanged *o*-sulphonamide, which is filtered off. Hydrochloric acid is added to the filtrate, and the precipitate filtered, washed with water, and dried at 40°.



$$C_6H_4\begin{cases}CH_3\\SO_2NH_2\end{cases} \rightarrow C_6H_4\begin{cases}CO\\SO_2\end{cases}NH.$$

White crystalline powder; M.P. 220°; soluble in hot water and in alcohol, and in alkalis or alkali carbonates with formation of salts. About 500 times sweeter than cane sugar. (E.P., 3563, 1903.)

Identification of Sulphonic Acids.—The formation of sulphonyl chlorides and sulphonamides, as shown above, can be used to identify sulphonic acids. Likewise S-benzyl-*iso*-thiouronium chloride reacts with alkali sulphonates giving salts of definite melting point (p. 452):

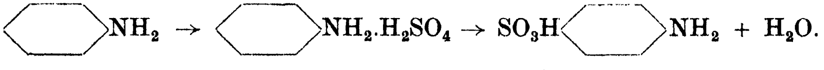


$$\left[C_6H_5CH_2—S—C\begin{cases}NH_2\\NH_2\end{cases}\right]^+Cl^- + RSO_3Na \longrightarrow \left[C_6H_5—S—C\begin{cases}NH_2\\NH_2\end{cases}\right]^+SO_3R^-.$$

e.g. *p*-toluene sulphonic acid:

Sulphonyl chloride	71°.
Sulphonamide	137°.
S-benzyl thiouronate	183°.

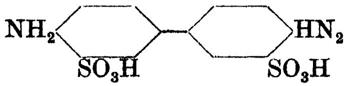
Reaction CXLIX. Intramolecular Rearrangement of Aromatic Amine Sulphates.—When sulphuric acid is added to an amine a sulphate is usually formed. If the sulphate is heated either alone (baking process) or with excess of conc. sulphuric acid, a rearrangement takes place, the sulphonic group entering the *p*-position to the basic group.



Sulphonic acids of amines can with advantage be made by the baking process. See Prep. 293.

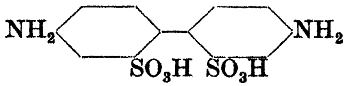
Benzidine gives:

By ordinary process ⟶



(*a*)

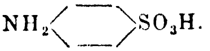
By baking process ⟶



(*b*)

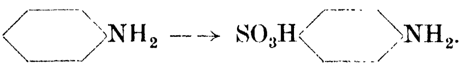
(*a*) yields cotton dyestuffs, while (*b*) yields wool dyestuffs.
In the baking process much less sulphuric acid is required.

PREPARATION 293.—**Sulphanilic Acid** (1-*Amino*-4-*benzenesulphonic Acid*).



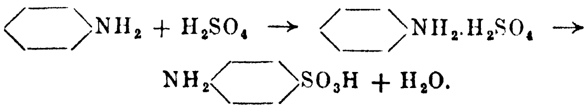
$C_6H_7O_3NS$. 173.

Method II.—20 gms. of aniline are gradually added to 65 gms. of conc. sulphuric acid placed in a round-bottomed flask. Much heat is developed, and the contents of the flask should be cooled when the aniline is being added. The flask which contains aniline sulphate and excess conc. sulphuric acid is now heated on an oil or paraffin bath to 185° for about 5 hours. When a test portion, treated with dilute caustic soda solution, liberates no free aniline, the sulphonation is complete. The contents of the flask, after cooling, are poured into cold water, when the sulphanilic acid separates, usually as discoloured crystals. These are filtered off and recrystallised from water, adding a little decolourising carbon, if necessary, A further crop can be obtained from the mother liquor.



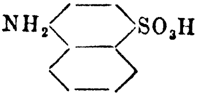
Yield.—55% theoretical (20 gms.).

Method II (baking process).—93 gms. of aniline are placed in a basin and 105 gms. of conc. sulphuric acid gradually added in a stream with good agitation. The hot paste is then spread on a lead tray and placed in an air oven at 190°–200° for 8 hours. The cake is now ground up and boiled for some time with water to which some caustic soda has been added till alkaline, to remove the unchanged aniline present (about 3%). It is then filtered through a cotton filter, and the acid is obtained by adding sulphuric acid to the filtrate until acid to Congo paper. If the acid is discoloured it is boiled up with decolourising carbon, filtered, and allowed to crystallise.



Yield.—90% theoretical (155 gms.). Rhombic crystals; does not melt; forms two hydrates; $+2H_2O$ when crystallised below 20°; $+1H_2O$ when crystallised between 20°–44°; important intermediate for dyestuffs. (A., 100, 163; Z. a., 9, 685.)

PREPARATION 294.—**Naphthionic Acid** (1-*Naphthylamine*-4-*sulphonic acid*).

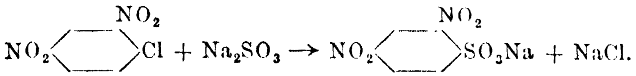


$C_{10}H_9O_3NS$. 223.

The process is similar to that used for sulphanilic acid. 70 gms. of α-naphthylamine and 50 gms. of conc. sulphuric acid are used. Before the paste is spread on the tray it is mixed with about 3 gms. of oxalic acid. It is then placed in the oven and heated, as before. When the mass has been cooled and powdered, it is boiled up with water and neutralised with milk of lime (test) and filtered. The acid is obtained by acidifying the filtrate with hydrochloric acid.

Yield.—80–85% theoretical (88–94 gms.). Crystallises with $\frac{1}{2}H_2O$; used largely in preparation of azo dyestuffs. (B., 13, 1948; 19, 578; Z. a., 9, 685.)

Reaction CL. Action of Sulphites and Bisulphites on Substituted Hydrocarbons.—(*a*) Metallic sulphites and bisulphites are used in certain cases for introducing the SO_3H group, and especially to replace halogens where the halogen is in the nucleus, and *ortho* to a NO_2, SO_3H or CHO group.



(*b*) In some cases reduction takes place simultaneously with sulphonation, e.g. *m*-dinitrobenzene gives *m*-nitroaniline sulphonic acid and nitrobenzene diazonium chloride gives *p*-nitrophenylhydrazine sulphonic acid.

(*c*) The same reagents are used for the formation of alkyl sulphonic acids by interaction with alkyl halides.

$$C_2H_5I + Na_2SO_3 \longrightarrow C_2H_5SO_3Na + NaI.$$

Halogens in the side chain of aromatic compounds also undergo this reaction.

(*d*) With certain olefinic compounds, additive compounds are formed.

$$R.CH{=}CH.COOH + K_2SO_3 \longrightarrow R.CH_2CH(COOH)SO_3K.$$

PREPARATION 295.—***p*-Aminobenzenesulphonamide** (*Sulphanilamide*).

$NH_2C_6H_4SO_2NH_2$. $C_6H_8O_2N_2S$. 172.

***p*-Acetylaminobenzenesulphonyl chloride** (This preparation should be conducted in a good fume cupboard).—36 gms. chlorosulphonic acid (*caution!* p. 519) in a dry flask are cooled below 15°, but not below 10°, in an ice-bath, and 7 gms. finely-powdered, dry, acetanilide added in small portions with good mixing, the temperature being kept under, but near, 20°. When all but a few particles of the acetanilide has dissolved the flask, covered with a watch glass, is placed in a hot water bath at 60°–70° for 1 hour. The mixture is carefully poured (*caution!*) in a thin stream into 150 gms. crushed ice and stirred with the addition of some water to facilitate mixing. The whitish mass is broken up, filtered and washed with cold water.

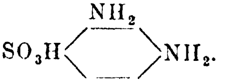
***p*-Acetylaminobenzenesulphonamide.**—25 c.cs. conc. ammonia are added to the above product, the mixture rubbed to a paste with a glass rod and heated to 70° for half an hour. The mixture, cooled in an ice-bath, is acidified with dil. sulphuric acid (test with Congo Red), and after further cooling the product is filtered, washed with ice-water, and dried in a steam oven.

Aminobenzenesulphonamide.—The product (above) is weighed, and treated with 2 c.cs. dil. hydrochloric acid (1 vol. conc. acid to 2 vols. water) per gm. This mixture is boiled under reflux for one hour on a sand bath, care being taken in the initial stages to avoid charring. The solution mixed with an equal volume of water and a little decolourising carbon is heated to boiling and filtered. To the filtrate is added solid sodium carbonate in small portions until just alkaline to litmus. The amide separates and, after cooling in ice, is filtered, washed with cold water and dried.

$$C_6H_5NHCOCH_3 \longrightarrow ClSO_2C_6H_4NHCOCH_3 \longrightarrow NH_2SO_2C_6H_4NHCOCH_3 \longrightarrow NH_2SO_2C_6H_5NH_2.$$

Yield.—45% theoretical on acetanilide (4 gms.). Colourless needles from water ; soluble in dil. acids and alkalis ; M.P. 163°.

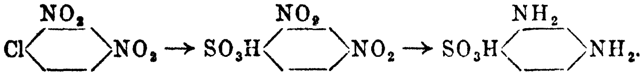
PREPARATION 296.—*m*-Phenylenediamine-4-sulphonic Acid.



$C_6H_8O_3N_2S$. 188.

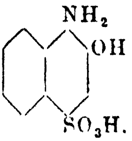
101 gms. dinitrochlorobenzene are dissolved in 250 c.cs. of methylated spirits. To this is added 40 gms. SO_2, in the form of a conc. solution of sodium sulphite—about 160 gms. $NaHSO_3$, containing 25% SO_2 mixed with 50 gms. 40% NaOH until alkaline to phenolphthalein. The sulphite may separate out, even when the mixture is hot, but this is of no consequence. The mixture is heated on the water bath to boiling for 5 hours with good stirring. The product is then cooled, and the sodium salt of the dinitrobenzene sulphonic acid separates in glistening, yellow leaflets. The sodium salt is then reduced, as in the preparation of *m*-phenylene diamine (see p. 367).

The solution of the diamine sulphonic acid is evaporated to about 200 c.cs. and 50 gms. common salt added. It is then just acidified with HCl (Congo paper should be turned only faint violet), and the free acid crystallises out. It is filtered and washed with very little water.



Yield.—65% theoretical (61 gms.). Dimorphous ; α-form, monoclinic plates ; β-form, triclinic prisms ; calcium and barium salts easily soluble in water. (A., 205, 104.)

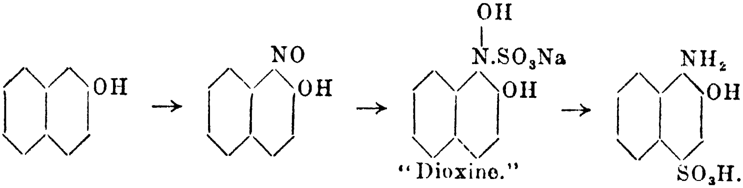
PREPARATION 297.—1 : 2 : 4-Aminonaphtholsulphonic Acid.



$C_{10}H_9O_4NS$. 239.

100 gms. of β-naphthol are converted into the corresponding nitroso-naphthol (see preparation, p. 290). The moist nitroso-naphthol is stirred

up with a little water and cooled to 5° with ice. To the paste 260 gms. sodium bisulphite solution, containing 25% SO_2, are quickly added. The nitroso-naphthol goes into solution after a few minutes; a small quantity of dilute caustic soda can be cautiously added, if necessary. The solution is filtered to remove resinous matter. The filtered solution is treated at 25° with 100 gms. conc. sulphuric acid, which has been diluted with 200 gms. of water. The solution should then give a strongly acid reaction. It is allowed to stand for 1 hour, and it is then warmed to 50° and left overnight—it solidifies to a solid cake. It is filtered off and washed well with water.



Yield.—90% theoretical (149 gms.). Almost insoluble in cold water, sparingly soluble in hot; sodium salt sparingly soluble in hot water (B., 27, 23). See also O. S., XI, 12.

PREPARATION 298.—**Phenylsulphopropionic Acid** (*2-Sulphonic acid of 3-phenylpropan acid*) (**K salt**).

$C_6H_5.CH_2CH.(COOH)(SO_3K)$. $C_9H_9O_5SK$. 268.

15 gms. (1 mol.) of cinnamic acid and 13 gms. (1 mol.) of normal potassium sulphite are refluxed with 280 c.cs. of water for 12 hours, then allowed to cool, and acidified with acetic acid. A crystalline precipitate of phenylsulphopropionic acid separates, which is filtered off and recrystallised from water. A further yield may be obtained by evaporating the filtrate to dryness, extracting the potassium acetate with hot alcohol, and crystallising the residue of phenylsulphopropionic acid from water.

$$C_6H_5CH : CH.COOH + K_2SO_3 + CH_3.COOH \longrightarrow$$
$$C_6H_5CH_2.CH(COOH)(SO_3K) + CH_3COOK.$$

Needles; melts and decomposes on heating; soluble in hot water. (A., 154, 63.)

PREPARATION 299.—**Ethylsulphonic Acid (Ba salt).**

$CH_3.CH_2.SO_3H$. $C_2H_6O_3S$. 110.

20 gms. (2 mols.) of ethyl iodide are boiled under reflux with a solution of 20 gms. (excess) of crystallised ammonium sulphite in 40 c.cs. of water until all goes into solution (6 hours). 100 c.cs. of water are added, and the solution boiled with 30 gms. (excess) of lead oxide until all ammonia is expelled. The lead salt of ethylsulphonic acid and lead iodide are formed; the latter is removed by filtration after the solution cools.

Sulphuretted hydrogen is passed into the filtrate until no more lead sulphide—from the decomposition of the lead salt of ethylsulphonic acid—is formed. Lead sulphide is filtered off, and the filtrate neutralised by the addition of excess (20 gms.) of barium carbonate. After filtration, the filtrate containing barium ethylsulphonate is evaporated.

$$2C_2H_5I + 2(NH_4)_2SO_3 + 2H_2O \rightarrow 2C_2H_5SO_2OH + 2NH_4OH + 2NH_4I.$$

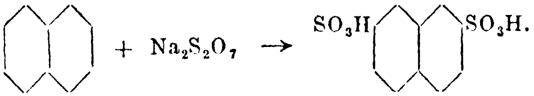
$$2C_2H_5SO_2OH \xrightarrow{PbO} (C_2H_5SO_2O)_2Pb \xrightarrow{H_2S} 2C_2H_5SO_2OH \rightarrow (C_2H_5SO_2O)_2Ba.$$

Yield.—90% theoretical (22 gms.). (A., 168, 146.)

The free acid is stable and forms a deliquescent crystalline mass (B., 15, 445).

Reaction CLI. Action of Polysulphates on certain Hydrocarbons.—The SO_3H group may be introduced in certain cases by the use of a mixture of potassium hydrogen sulphate and conc. sulphuric acid or of sodium pyrosulphate, $Na_2S_2O_7$.

$$C_6H_6 + KH_3(SO_4)_2 \rightarrow C_6H_5SO_3H + KHSO_4 + H_2O.$$



Reactions of the Sulphonic Group.

1. $R.SO_3H + NaOH \longrightarrow R.OH.$

2. $R.SO_3H + H_2O \xrightarrow{H_2SO_4} R.H.$ (C. V., II, 97.)

3. (*a*) $R.SO_3H + NH_3 \xrightarrow[\text{pressure}]{NaHSO_3} R.NH_2.$

(*b*) $R.SO_3H + NaNH_2 \longrightarrow R.NH_2.$

4. $R.SO_3H + HNO_3 \longrightarrow R.NO_2.$

5. (*a*) $R.SO_3H + Cl \longrightarrow R.Cl$ (goes readily if SO_3H in α-position). (C. V., II, 128.

(*b*) $R.SO_3H + PCl_5 \longrightarrow R.Cl.$

6. (*a*) $R.SO_3H + PCl_5 \longrightarrow R.SO_2Cl.$

(*b*) $R.SO_3H + ClSO_3H \longrightarrow R.SO_2Cl$ (p. 324).

7. $R.SO_3Na + NaCN \longrightarrow R.CN.$

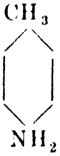
8. $R.SO_3Na + NaCOOH \longrightarrow R.COOH.$

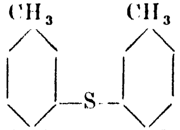
CHAPTER XXI

THE LINKING OF SULPHUR TO CARBON (*continued*)

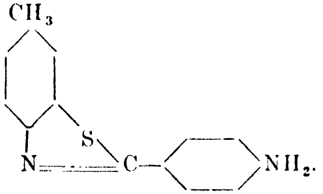
Reaction CLII. Action of Sulphur and Sodium Sulphide on Aromatic Bases.—Aromatic amines usually react with sulphur when heated in presence of sodium sulphide to give compounds of complex structure, two or more nuclei joining together through the S-atom. Several compounds or more are usually formed in the reaction, e.g. *p*-toluidine gives four different products when fused with sulphur. The final products are dyestuffs, some of unknown constitution, and are known as sulphur or sulphide dyestuffs.

The formulae show the compounds obtained from *p*-toluidine.

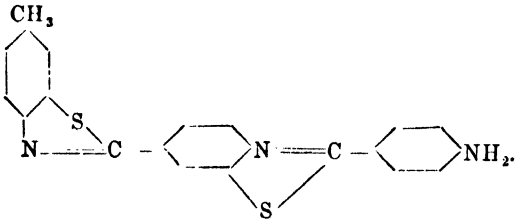




Thio-*p*-toluidine.



Dehydrothio-*p*-toluidine.



*Bis*dehydrothio-*p*-toluidine or Primuline base.

The dyestuffs produced are of various shades; generally speaking, diphenylamines give blue and black dyes, toluidines yellow and brown, and diamines red dyes.

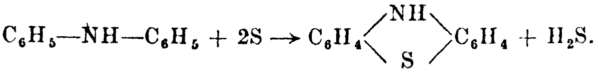
For dyestuff preparations, see Chapter XXVI.

PREPARATION 300.—**Phenothiazine** (*Thiodiphenylamine*).

$$C_6H_4\langle{}^{NH}_{S}\rangle C_6H_4. \qquad C_{12}H_9NS. \qquad 199.$$

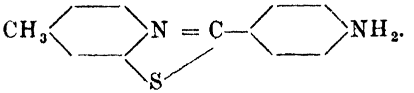
22 gms. of diphenylamine, 8·2 gms. of sulphur, and 3·2 gms. of anhydrous aluminium chloride are melted together. The reaction sets in at 140°–150° with rapid evolution of sulphuretted hydrogen; by lowering the temperature a few degrees the reaction can be slackened. When it has

moderated, the temperature is raised to 160° for a time. The melt, when cool, is ground up and extracted, first with water and then with dilute alcohol. The residue consists of almost pure thiodiphenylamine. It can be recrystallised from alcohol.



Yield.—93% theoretical (23·5 gms.). Yellowish leaflets; M.P. 190°. (D.R.P., 237771.)

PREPARATION 301.—**Dehydrothio-*p*-toluidine** 2(*4′-aminophenyl*)-6-*methyl-benzthiazole*).



$C_{14}H_{12}N_2S$. 240.

An intimate mixture of 100 gms. *p*-toluidine and 50 gms. sulphur is heated for 4 hours at 220°. It is then poured on to a tray, cooled, ground and extracted with 45% sulphuric acid in instalments until no further base is extracted (test extract with alkali). The total extract is filtered and the filtrate diluted with water to precipitate the base, which is collected and re-extracted with 30% sulphuric acid. The filtered solution is made alkaline with conc. sodium hydroxide solution which precipitates the crude base. This, when dry, is distilled in an all-glass apparatus and subsequently crystallised from alcohol, from which it separates in glistening plates.

Yield.—36% theoretical (40 gms.). M.P. 195°; see primuline (see p. 397). (B., 22, 333; 22, 424; 25, 1084; J.S.C.I., 1948, 400).

Reaction CLIII. Action of Sulphur Dioxide on Aromatic Hydrocarbons in presence of Aluminium Chloride or Mercuric Chloride. (A. Ch., [6], 14, 443.)

$$C_6H_6 + SO_2 \xrightarrow{AlCl_3} C_6H_5SO_2H.$$

Sulphinates may also be formed by:

1. Action of SO_2 on zinc alkyls.

$$(C_2H_5)_2Zn + 2SO_2 \longrightarrow (C_2H_5SO_2)_2Zn.$$

2. Action of zinc on sulphonyl chlorides.

$$2C_2H_5SO_2Cl + 2Zn \longrightarrow (C_2H_5SO_2)_2Zn + ZnCl_2.$$

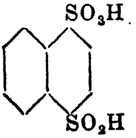
Reaction CLIV. Action of Sulphur Dioxide on a Diazonium Compound in presence of finely-divided Copper. (Gattermann, B., 32, 1136.)

Sulphinic acids are formed in good yield.

$$2R.N_2Cl + 2SO_2 + 2Cu \longrightarrow 2R.SO_2H + 2N_2 + Cu_2Cl_2.$$

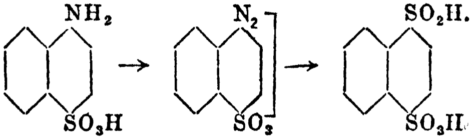
Sulphinic acids are unstable liquids passing readily into sulphonic acids on oxidation with alkaline permanganate. Where a mixture of isomeric sulphonic acids is formed by direct sulphonation the individual sulphonic acids may be prepared by this method from the corresponding amines. For example, *o*-toluenesulphonic acid may be prepared from *o*-toluidine.

PREPARATION 302.—Naphthalene-1 : 4-Sulphosulphinic Acid.



$C_{10}H_8O_5S_2$. 272.

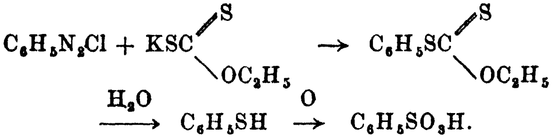
50 gms. sodium naphthionate (see p. 326) are diazotised in the usual way (see p. 380). The diazo-anhydride compound separates. Sulphur dioxide is then passed in until the solution is saturated, the temperature being kept below 0°. Copper powder (see p. 515) is then added very gradually until the evolution of nitrogen ceases, a slow stream of SO_2 being passed through during the addition. The whole is then filtered, and common salt is added to saturate the filtrate, when the sodium salt of 1 : 4-sulphosulphinic acid separates, and after filtration is recrystallised from water. The free acid may be isolated by passing hydrochloric acid gas into the solution in water of the sodium salt.



Yield.—Almost theoretical (62 gms.). (J. C. S., 95, 342.)

Reaction CLV. Action of Potassium Xanthate on Diazonium Compounds with Subsequent Hydrolysis and Oxidation. (E.P., 11865, 1892.)

Sulphonic acids are formed :



$$C_6H_5N_2Cl + KSC\begin{matrix}\diagup\!\!\diagup S\\ \diagdown OC_2H_5\end{matrix} \rightarrow C_6H_5SC\begin{matrix}\diagup\!\!\diagup S\\ \diagdown OC_2H_5\end{matrix}$$

$$\xrightarrow{H_2O} C_6H_5SH \xrightarrow{O} C_6H_5SO_3H.$$

Reaction CLVI. Action of Hydrogen Sulphide on Diazonium Compounds. (B., 29, 272.)

In neutral solution at 0° diazo sulphides are formed, e.g.

$$NO_2C_6H_4N_2Cl \longrightarrow (NO_2C_6H_4N_2)_2S.$$

In hydrochloric acid solution, the disulphide is ultimately formed :

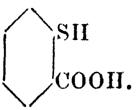
$$(NO_2C_6H_4N_2)_2S_2.$$

On heating a diazonium solution in presence of hydrogen sulphide, nitrogen is evolved, and a mercaptan is formed :

$$R.N_2Cl + H_2S \longrightarrow R.SH.$$

For a warning regarding the explosive reaction of certain diazonium compounds with sulphides, see C. & I., 1945, 362 ; 1946, 9.

Preparation 303.—**Sulphosalicylic Acid** (*Thiophenol-o-carboxylic acid.*)



$C_7H_6O_2S$. 154.

10 gms. anthranilic acid (see p. 251) are dissolved in 150 c.cs. water and 5 gms. of hydrochloric acid. 20 gms. of ice are added and the whole diazotised in the usual way. H_2S is passed through the diazonium solution until the yellow precipitate becomes red. $C_6H_4(COOH)N_2SH$ is formed, and after filtration the moist precipitate is dissolved in sodium carbonate solution, and heat is applied until a test portion gives a white precipitate with hydrochloric acid. The solution is acidified with hydrochloric acid and the sulphosalicylic acid filtered off and washed with cold water.

Insoluble in water; M.P. 163°–164°; salts amorphous. (D.R.P., 69073; B., 22, 2206; 31, 1666.)

Reaction CLVII. Action of Hydrosulphides on Alkyl Halides or Sulphates, or on certain Aromatic Halogen Derivatives.

$$R.Cl + KSH \longrightarrow R.SH + KCl.$$

$$R.HSO_4 + KSH \longrightarrow R.SH + KHSO_4.$$

The mercaptans are colourless liquids, mostly insoluble in water, possessing a characteristic and disagreeable odour.

Other methods by which mercaptans can be formed are:

1. Action of KSCN on diazonium salts and subsequent hydrolysis (B., 23, 738).

$$R.N_2Cl \longrightarrow R.SCN \longrightarrow R.SH.$$

2. Action of KSH on diazonium salts (B., 20, 349).

$$R.N_2Cl \longrightarrow R.SH.$$

3. See Reaction CLVI.

Preparation 304.—**Sulphosalicylic Acid** (*Thiosalicylic Acid*).

50 gms. *o*-chloro-benzoic acid are dissolved in 38·5 gms. caustic soda solution containing 13·5 gms. caustic soda. 100 gms. of sodium hydrosulphide and 0·5 gm. copper sulphate are then added, and the whole heated with stirring to about 200° until the mass becomes dark red and melts. The temperature is raised to 250° at which it gradually solidifies. The melt is dissolved in a litre of water and boiled with decolourising carbon, if necessary, and the thiosalicylic acid precipitated from the filtrate by adding hydrochloric acid. (See Preparation 304.)

Yield.—Almost theoretical (48 gms.). See O. S., XII, 76.

Preparation 305.—**Ethyl Mercaptan** (*Ethanthiol*).

C_2H_5SH. C_2H_6S. 62.

50 c.cs. conc. sulphuric acid and 50 c.cs. 20% oleum are added to 100 c.cs. 99% alcohol. the temperature being kept below 70°. The mix-

ture is allowed to stand overnight in a freezing mixture, and then poured on to a mixture of ice and 8% sodium carbonate solution, with stirring. The neutral solution is concentrated until a crust of salt forms on the surface. Sodium sulphate separates out on cooling and is filtered off. A 40% solution of caustic potash in water is saturated with H_2S, the volume of the solution being 1½ times the volume of the filtrate. This solution of potassium sulphide is then added to the filtrate and the whole gently distilled, when the ethyl mercaptan passes over. It is shaken up with conc. caustic soda solution to separate ethyl sulphide. The ethyl mercaptan, after removing the oil, is precipitated by adding acid to the alkaline solution.

$$C_2H_5OH \longrightarrow C_2H_5.HSO_4 \longrightarrow C_2H_5.SH.$$

Colourless liquid ; almost insoluble in water ; offensive odour. B.P. 36°. (A., 34, 25.)

Reaction CLVIII. Action of Phosphorus Pentasulphide on Acids or Alcohols.

$$5C_2H_5OH + P_2S_5 \longrightarrow C_2H_5SH + P_2O_5.$$

$$5CH_3COOH + P_2S_5 \longrightarrow CH_3COSH + P_2O_5.$$

The oxygen is replaced by sulphur with the formation of mercaptans and thio-acids.

Dithio ethers are formed from mercaptans by oxidation with sodium plumbite (p. 515) and sulphonic acids by oxidation with hypochlorite.

$$2RSH \longrightarrow R.S.S.R.$$

$$RSH \longrightarrow RSO_3H.$$

These reactions are employed to remove mercaptans from motor spirit, etc.

PREPARATION 306.—**Thioacetic Acid.**

CH_3COSH. C_2H_4OS. 76.

150 gms. of phosphorus pentasulphide are ground up and mixed with an equal weight of glacial acetic acid and 50 gms. of glass beads. The whole is placed in a distilling tank of at least 1 litre capacity, fitted with a condenser and a thermometer, and continuously warmed with a naked flame Heating is stopped as soon as the reaction begins, which is allowed to proceed spontaneously, heating being applied when it moderates. Much frothing may take place. The reaction is stopped when the thermometer reaches 103° and the product fractionated.

Yield.—25% theoretical (47·5 gms.). Offensive-smelling liquid, decomposed by water ; B.P. 93°. (B., 28, 1205.)

Reaction CLIX. Action of Sulphonyl Chlorides on Hydrocarbons in presence of Aluminium Chloride. (B., 26, 2940.)

$$R.SO_2Cl + C_6H_6 \xrightarrow{AlCl_3} R.SO_2.C_6H_5 + HCl.$$

The compounds formed are termed sulphones ; they are also formed by the action of conc. and fuming sulphuric acid on hydrocarbons (see

p. 320), and by heating aromatic sulphonic acids with an aromatic hydrocarbon in presence of a dehydrating agent, such as P_2O_5.

$$R.SO_2OH + C_6H_6 \xrightarrow{P_2O_5} R.SO_2.C_6H_5.$$

The interaction of halogen compounds and the salts of sulphinic acids yields the same products.

$$R.SO_2Na + BrC_6H_5 \longrightarrow R.SO_2C_6H_5 + NaBr.$$

The sulphones are inert compounds, of little importance.

Reaction CLX. Action of Phosphorus Pentasulphide on Ethers. (B., 27, 1239.)

Thio-ethers are obtained according to the equation :

$$5(C_2H_5)_2O + P_2S_5 \longrightarrow 5(C_2H_5)_2S + P_2O_5.$$

The thio-ethers are neutral volatile compounds of little importance.

Reaction CLXI. Action of Sodium or Potassium Sulphide on Alkyl Halides or Alkyl Sulphates. (B., 27, 1239.)

Thio-ethers are obtained.

$$2C_2H_5I + K_2S \longrightarrow (C_2H_5)_2S + 2KI.$$

$$2C_2H_5.SO_4K + K_2S \longrightarrow (C_2H_5)_2S + 2K_2SO_4.$$

CHAPTER XXII

THE LINKING OF HALOGEN TO CARBON

Reaction CLXII. Replacement of Oxygen and Hydroxyl by Halogens.—The oxygen of ketone and aldehyde groups is readily replaced by halogen under the influence of phosphorus trichloride or pentachloride ; the reaction may be carried out with or without a solvent ; solvents commonly employed are chloroform, benzene, petroleum ether, acetyl chloride and phosphorus oxychloride.

Alcoholic hydroxyl may be replaced by halogen :

(*a*) With halogen acids.

The action is slow with hydrochloric acid, heating under pressure or the use of a dehydrating agent being usually necessary. Hydrobromic acid reacts more easily and hydriodic still more easily. Instead of the acids, bromine and iodine may be allowed to act on the alcohols in presence of phosphorus. For summary, see A. C. R., 1934, 119.

(*b*) With phosphorus oxychloride, phosphorus pentachloride phosphorus trichloride or tribromide, or sulphur monochloride.

The pentachloride, trichloride and tribromide of phosphorus are also used for replacing hydroxyl by halogen in phenols, carboxylic acids and sulphonic acids. The use of phosphorus trichloride is to be preferred in the preparation of many acid chlorides, since three molecules of acid chloride are then formed per molecule of phosphorus halide, as against one molecule of acid chloride when the pentachloride is used :

$$3R.COOH + PCl_3 \longrightarrow 3R.CO.Cl + H_3PO_3$$

$$R.COOH + PCl_5 \longrightarrow R.CO.Cl + POCl_3 + HCl$$

and further, no volatile compound of phosphorus is formed. Phosphorus tribromide, and not the pentabromide, is generally used for the preparation of acid bromides. Thionyl chloride does not react with aldehydic and ketonic groups, but reacts readily with carboxyl groups, and sometimes with alcoholic hydroxyl groups (J. S. C. I., 45, 36, 55 ; Am. Soc., 50, 145 ; O. S., XIII, 32).

$$2R.COOH + SOCl_2 \longrightarrow 2RCOCl + SO_2 + H_2O.$$

Excess of the reagent ($SOCl_2$), without solvent, is generally employed, and the excess removed by distillation or by treatment with formic acid.

Other compounds used for replacing hydroxyl by halogen are carbonyl chloride, benzenesulphonyl chloride and sulphuryl chloride.

PREPARATION 307.—**Benzophenone Chloride** (*Diphenyldichloromethane*).

$(C_6H_5)_2CCl_2$. $C_{13}H_{10}Cl_2$. 237.

24 gms. (1 mol.) of benzophenone are refluxed with 40 gms. (excess) of phosphorus pentachloride on an oil bath at 220°–240° for 4 hours. The

mixture is fractionally distilled under reduced pressure, the fraction boiling at 193° at 30 mms. being retained. It is redistilled under reduced pressure.

$$(C_6H_5)_2CO + 2PCl_5 = (C_6H_5)_2CCl_2 + POCl_3.$$

Colourless oil; B.P. ^{30} 193°; B.P. ^{760} 305°, with decomposition; D. $^{18\cdot5}_{4}$ 1·235. (B., 3, 752; 29, 2944.)

PREPARATION 308.—**Hippuryl Chloride.**

$C_6H_5.CONH.CH_2.COCl$. $C_9H_8O_2NCl$. 197·5.

In this preparation moisture must be excluded as far as possible.

5 gms. (1 mol.) of hippuric acid are finely ground and passed through a fine sieve. The powder is added to a solution of 6·5 gms. (excess) phosphorus pentachloride in 50 gms. of acetyl chloride contained in a strong glass bottle. The bottle is fitted with a good stopper and agitated in a shaking machine for 2 hours. The crystals formed are filtered off, washed with petroleum ether, and dried in a vacuum desiccator containing sulphuric acid. The product may be recrystallised from warm acetyl chloride (i.e. heated on a water bath); a higher temperature, or very prolonged heating, brings about some decomposition.

$$C_6H_5.CO.NH.CH_2.COOH + PCl_5 \rightarrow C_6H_5CO.NH.CH_2.COCl + POCl_3 + HCl.$$

Yield.—80% theoretical (4·5 gms.). Colourless needles; becomes yellow at 125°, then dark red, and melts at a higher temperature; with alcohol or water yields hippuric acid. (B., 38, 605.)

PREPARATION 309.—**Benzoyl Chloride** (*Acyl chloride of benzoic acid*).

C_6H_5COCl. C_7H_5OCl. 140·5.

50 gms. (1 mol.) of phosphorus pentachloride are weighed by difference in a fume cupboard into a 250-c.c. distilling flask. 28 gms. (1 mol.) of benzoic acid are added. Dense clouds of hydrogen chloride are evolved during the reaction, and when this is over the contents of the distilling flask are fractionally distilled, the phosphorus oxychloride which passes over about 107° being rejected, and the fraction 190°–200° collected separately.

$$C_6H_5COOH + PCl_5 = C_6H_5COCl + POCl_3 + HCl.$$

Yield.—75% theoretical (25 gms.). Colourless liquid; pungent smell; fumes in moist air; B.P. 198·5°; D. $^{19}_{4}$ 1·214. (A., 3, 262; 60, 255.)

PREPARATION 310.—**Acetyl Chloride** (*Ethanoyl Chloride*).

CH_3COCl. C_2H_3OCl. 78·5.

50 gms. of glacial acetic acid are placed in a 250-c.c. distilling flask connected by a water condenser with another distilling flask the side of which is fitted with a calcium chloride tube. 40 gms. of phosphorus trichloride are slowly added through a dropping funnel, the distilling flask being cooled in a cold water bath. The bath is then heated at 45°

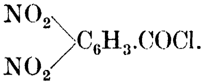
(*caution!*) until the evolution of hydrogen chloride diminishes, after which it is heated to boiling till nothing further distils. The acetyl chloride contains some phosphorus trichloride, so it is redistilled from the collecting flask over fused sodium acetate (about 3 gms.), the fraction 53°–56° being separately collected in the same way as before.

$$3CH_3COOH + PCl_3 = 3CH_3COCl + H_3PO_3.$$

Yield.—55% theoretical (35 gms.), calculated on acetic acid taken. Colourless, pungent smelling liquid; fumes in moist air; B.P. 55°; $D.\ ^{20}_{4}$ 1·105. (A. Ch., [3], 37, 285; C. r., 40, 944; 42, 224.)

The presence of phosphorus trichloride in the first distillate may be proved by adding a few drops of water to a drop of the distillate (*caution!*), oxidising the phosphorus acid formed to phosphoric acid by boiling with nitric acid, and the testing with ammonium molybdate. The acetylphosphorus acid remaining in the residue from the second distillation can be proved to be present by evaporating with water on a water bath till the smell of acetic acid disappears, and then testing for phosphoric acid after treatment with nitric acid.

PREPARATION 311.—**3 : 5-Dinitrobenzoyl chloride.**



$$\begin{matrix} NO_2 \\ NO_2 \end{matrix}\!\!>C_6H_3.COCl.$$

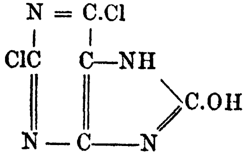
$C_7H_3O_5N_2Cl$. 230·5.

1 gm. 3 : 5-dinitrobenzoic acid and 2 gms. phosphorus pentachloride are warmed over very small flame in a dry test-tube until reaction commences. When this subsides the mixture is boiled for about 2 minutes until solution is complete, then poured on to a watch glass. After solidification the solid is pressed on filter paper or porous tile; as thus obtained the product is used for preparation of esters.

$$(NO_2)_2C_6H_3COOH \longrightarrow (NO_2)_2C_6H_3COCl.$$

Yield.—90% theoretical (1 gm.). Faint yellow needles; M.P. 74°. Important reagent for identification of alcohols.

PREPARATION 312.—**2 : 6-Dichlorouric Acid** (2 : 6-*Dichloro*-8-*hydroxypurine*).



$C_5H_2ON_4Cl_2$. 205.

20 gms. (3 mols.) of dry potassium urate and 24 gms. (excesss) of phosphorus oxychloride are heated in a sealed tube for 6 hours at 160°–170°. When cold, the tube is carefully opened and the product poured into water. The precipitate formed is filtered off, dried and powdered. It is then

added slowly to 5 parts of conc. nitric acid and boiled for 20 minutes. Only a small portion of the dichlorouric acid goes into solution, and this is reprecipitated by diluting with water. The crude acid is collected, well washed with water, and while suspended in 24 parts of boiling alcohol is treated with ammonia solution until all save a slight impurity is dissolved. Animal charcoal is added and the whole boiled and filtered. The ammonium salt of the acid separates out in pale yellow leaflets on cooling, and further crops may be obtained by concentrating the mother liquors. The salt is redissolved in water, and the free acid obtained by precipitation with mineral acid.

$$3C_5H_4O_3N_4 + 2POCl_3 \longrightarrow 3C_5H_2ON_4Cl_2 + 2H_3PO_4.$$

Yield.—35% theoretical (7 gms.). Colourless crystalline powder which does not melt. (B., 30, 2208.)

PREPARATION 313.—**Diphenylchloroacetic Acid** (*Diphenylchloroethan Acid*).

$(C_6H_5)_2C(Cl).COOH$. $C_{14}H_{11}O_2Cl$. 246·5.

15 gms. benzilic acid (p. 118) and 15 gms. (excess) phosphorus oxychloride are gently warmed together until a slight red colour appears. The melt is then cooled and shaken with a litre of cold water until (1–2 hours) the product becomes quite solid. It is then filtered off, washed with benzene and dried. It is purified by recrystallisation from a mixture of benzene and petroleum ether.

$$3(C_6H_5)_2C(OH).COOH + POCl_3 \longrightarrow 3(C_6H_5)_2C(Cl)COOH + H_3PO_4.$$

Yield.—65% theoretical (11 gms.). Rhombic plates ; M.P. 118°–119°, with decomposition. (B., 36, 145.)

PREPARATION 314.—**β-Iodopropionic Acid** (3-*Iodo-pentan acid*).

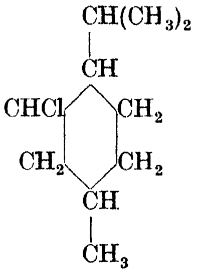
$CH_2I.CH_2.COOH$. $C_3H_5O_2I$. 200.

100 gms. (a little more than 1 mol.) of phosphorus di-iodide (see p. 519) are added in small quantities to 52 c.cs. (2 mols.) of glyceric acid (D. 1·26) in a large round flask, and the mixture gently heated till a violent reaction sets in. Should it become too violent the flask is cooled in water. The product, a dark brown syrupy liquid, is again heated, when a second less violent reaction occurs. A light yellow liquid, which, on cooling, solidifies to a crystalline mass, is formed. From this, iodopropionic acid is extracted with hot carbon disulphide (*caution!*) or petroleum ether (*caution!*). The solvent is distilled off and the discoloured residue recrystallised from carbon disulphide or petroleum ether.

$$CH_2(OH).CH(OH).COOH + 3HI = CH_2I.CH_2.COOH + 2H_2O + I_2.$$

Colourless pearly laminae ; slightly soluble in cold, readily in hot water and in alcohol ; M.P. 83·5°. (A., 131, 323 ; 166, 1 ; B., 9, 1902.)

Preparation 315.—**Menthyl Chloride** (*1-Methyl-4-isopropyl-3-chlorocyclohexane*).



$C_{10}H_{19}Cl$. 174·5.

50 gms. (1 mol.) phosphorus pentachloride are covered with dry petroleum ether in a flask and the whole well cooled in ice. 50 gms. (excess) of menthol are added in small portions to the cooled mixture, no fresh menthol being added until the evolution of hydrochloric acid has ceased. The petroleum ether is then distilled off, and the residue distilled with the aid of a fractionating column; crude menthyl chloride passes over at 205°–215°, and it may be purified by redistilling several times. In the crude state it may be used for Preparation 444.

$$C_{10}H_{19}OH + PCl_5 \longrightarrow C_{10}H_{19}Cl + POCl_3 + HCl.$$

Yield.—55% theoretical (30 gms.). B.P. 209·5°–210·5°. (B., 29, 317; 25, 686; J. C. S. 41, 54.)

Preparation 316.—**Glyceryl mono- and di-chlorohydrins.**

$CH_2OH.CH(OH).CH_2Cl$. $C_3H_7O_2Cl$. 110·5.

$CH_2Cl.CH(OH).CH_2Cl$. $C_3H_6OCl_2$. 129.

α-Monochlorohydrin.—100 gms. glycerol (previously dehydrated by heating to 175° on a sand bath) are cooled, mixed with 2 gms. glacial acetic acid in a flask provided with a two-holed stopper, and the whole weighed. A stream of hydrogen chloride, passed through conc. sulphuric acid and through an empty safety flask, is then led through the mixture, which is heated by an oil bath kept at 100°–110°. The absorption of the gas is very rapid, and when 30% increase in weight has occurred the passage of the gas is stopped. Crude monochlorohydrin is obtained by distilling the product under reduced pressure; and it may be purified by redistillation in this way.

Yield of Crude.—86% theoretical (100 gms.). B.P.^{1} 98°–100°; B.P.^{40} 141°. Colourless liquid. (C. V., I, 292.)

αγ-Dichlorohydrin.—*Method I.*—If the passage of the gas is continued beyond the monochlorohydrin stage absorption continues at a slower rate. The temperature of the oil bath should be raised to 130° and the operation continued until an increase, 25% in excess of the theoretical amount, has taken place (allowing for complete volatilisation of the water formed). Fractional distillation under reduced pressure of the product gives an 82% theoretical yield of relatively pure compound. Alternatively the product may be washed with small quantities of water and solid sodium carbonate until just alkaline to litmus, about 50 c.cs. water being necessary to dissolve the salt formed. It is then separated in a funnel and fractionated as before mentioned.

Method II.—125 gms. (less than 2 mols.) sulphur monochloride (p. 518) are slowly added in small quantities at a time from a tap funnel to 50 gms. of anhydrous glycerol (dehydrated, as in Method I) contained in a retort fitted with a reflux condenser. The experiment should be conducted in a fume chamber. The retort is occasionally shaken, and the reaction is completed by heating in a boiling brine bath until the evolution of hydrogen chloride from the condenser has almost ceased. The condenser is then removed and the mass again heated until all sulphur dioxide and hydrogen chloride are expelled. When cold, the semi-solid mass is twice extracted with twice its volume of ether. The ethereal extract is filtered free from sulphur, and the ether removed by distillation on a water bath. The residue is repeatedly fractionated until a fraction of boiling point 175°–178° is obtained.

$$CH_2(OH)CH(OH)CH_2(OH) + 2S_2Cl_2 \longrightarrow$$
$$CH_2Cl.CH(OH)CH_2Cl + 2HCl + SO_2 + 3S.$$

Colourless ethereal liquid ; easily soluble in ether ; B.P. 176° ; D. $^{0}_{4}$ 1·383. (J., 13, 456 ; A. Spl., 1, 221 ; A., 122, 73 ; 168, 42 ; C. & I., 49, 102 ; 50, 949, 970 ; C. V., I, 292.)

PREPARATION 317.—*n*-Butyl Bromide.

$CH_3CH_2CH_2CH_2Br$. C_4H_9Br. 137.

Hydrobromic-sulphuric Acid Mixture.—(This preparation must be carried out in a good fume cupboard.) 8 c.cs. bromine and 25 gms. crushed ice are placed in a 200 c.cs. round-bottomed flask, which is cooled in ice-water, and sulphur dioxide passed in until the red colour of bromine is discharged (1–2 hours).

18 gms. *n*-butyl alcohol followed by 6·5 c.cs. conc. sulphuric acid are now added, the latter dropwise with shaking. The flask is attached to an upright reflux condenser the top of which is connected by means of a bent delivery tube with an inverted funnel dipping below the surface of water in a beaker. (See also C. V., I, 97.) After being heated to gentle ebullition for 5–6 hours the contents of flask are distilled and the distillate separated in a separating funnel. The bottom layer is washed first with an equal volume of water, then with 5 c.cs. conc. sulphuric acid and finally with 10 c.cs. 10% sodium carbonate solution. The product is dried in contact with anhydrous calcium chloride (1–2 gms.) overnight, then decanted through a plug of glass wool in a funnel into a small distilling flask from which it is distilled and the fraction boiling at 99–104° collected.

$$C_4H_9OH + HBr \longrightarrow C_4H_9Br + H_2O.$$

Yield.—70% theoretical (33 gms.). Colourless liquid ; B.P. 100° ; D. ^{20} 1·279.

PREPARATION 318.—Ethyl Bromide (*Monobromoethan*).

$$CH_3.CH_2.Br. \qquad C_2H_5Br. \qquad 109.$$

Method I.—A General Method for the Preparation of Alkyl Bromides.—The details of this preparation are very similar to those given in the general method for the preparation of alkyl iodides (see p. 344). 10 gms. (excess) of red phosphorus and 50 gms. (excess) of ethyl alcohol are placed in a distilling flask, attached to a condenser and receiver. The receiver consists of a Buchner flask, attached by means of a cork to the end of the condenser, its side tube being connected with a soda-lime tower to trap any fumes of hydrobromic acid. A tap funnel containing 65 gms. (5 mols.) of bromine is fixed through a cork in the neck of the distilling flask. The flask is cooled in water, the bromine slowly added, the whole left for several hours, and the contents of the flask then distilled from the water bath at 50°, the receiver being cooled in ice. The distillate is purified as in the preparation of ethyl iodide, given on p. 344.

$$5ROH + P + 5Br = 5R.Br + H_3PO_4 + H_2O.$$

Yield.—Almost theoretical (80 gms.). Colourless, highly refractive liquid; characteristic odour; soluble in most organic solvents; insoluble in water; B.P. ^{760} 38·8°; D. $^{18}_{4}$ 1·47; D. $^{0}_{4}$ 1·485. (J., 1857, 441.)

Method II.—70 gms. of conc. sulphuric acid and 30 gms. of alcohol are mixed in a 500-c.c. distilling flask, cooled under the tap to ordinary temperature, and 100 gms. (1 mol.) of coarsely-powdered sodium bromide added. The flask is closed by a cork, and attached to a condenser leading, by means of an adapter, into a 250-c.c. conical flask, which serves as a receiver. Enough water is poured into the latter to close the end of the adapter. The distilling flask is then carefully heated on a sand bath and distillation slowly conducted until no more oil distils, the receiver being meanwhile cooled in ice. Should the reaction mixture threaten to froth over, the flask must be raised from the sand bath for a moment. The ethyl bromide is separated in a funnel, washed with an equal bulk of dilute sodium carbonate solution, and with water, dehydrated over calcium chloride, and distilled on a water bath, the fraction 35°–43° being retained. Ethyl bromide prepared by this method usually contains traces of ether.

$$C_2H_5OH + H_2SO_4 = C_2H_5.H.SO_4 + H_2O.$$

$$C_2H_5.H.SO_4 + NaBr = C_2H_5Br + NaHSO_4.$$

Yield.—80% theoretical (50 gms.). (Am. Soc., 38, 640; Bl., [iv], 9, 134; O. S., VIII, 120.)

PREPARATION 319.—Ethyl Chloride (*Monochloroethan*).

$$CH_3.CH_2Cl. \qquad C_2H_5Cl. \qquad 64·5.$$

Dry hydrogen chloride is passed through a trap into 200 gms. of absolute alcohol containing 100 gms. of fused coarsely-powdered zinc chloride, in a 500-c.c. round-bottomed flask heated on a water bath, and fitted with an upright condenser, from the top of which the vapour is led into a conical flask containing water. The inlet tube is cut off just above the surface of the water. Thence the vapour passes through a tower filled with soda-lime, and finally into a U-tube surrounded by ice, and fitted with an open tube at its lowest point. The condensed ethyl chloride drops from the bottom of the U-tube, and is collected in a small conical flask standing in ice. The upright condenser returns alcohol to the flask. The excess of hydrogen chloride which passes on is absorbed by the water in the conical flask, and the remainder removed in the soda-lime tower. A fairly rapid stream of gas must be maintained on starting or the alcohol will be sucked back into the trap. The passage of the gas is continued until a sufficient quantity of ethyl chloride has been obtained. It must be stored in a well-stoppered bottle, wrapped in a cloth, and placed in an ice chest. Owing to the risk of its breaking the bottle a quantity should only be kept when there is necessity for so doing.

$$C_2H_5OH + HCl = C_2H_5Cl + H_2O.$$

Yield.—Almost theoretical (280 gms.). Colourless liquid ; characteristic odour ; soluble in most organic solvents ; insoluble in water ; B.P. 12·5° ; D. $^{0}_{4}$ 0·9214. (A., 150, 216 ; 174, 372 ; Z. Ch., 1871, 147.)

PREPARATION 320.—**Methyl Iodide and Ethyl Iodide.**

Methyl iodide. CH_3I. 142.

Ethyl iodide. $CH_3.CH_2I$. C_2H_5I. 156.

A General Method for the Preparation of Alkyl Iodides.—36 gms. (excess) of methyl alcohol (52 gms. of ethyl alcohol) are placed in a 500-c.c. flask with an upright condenser, along with 10 gms. (excess) of red phosphorus. 100 gms. (5 mols.) of powdered iodine are slowly added during 1 hour with frequent shaking, the condenser being detached from the flask momentarily during the addition. The latter is cooled in cold water if necessary. The whole is then allowed to stand overnight, or should that time be not available, it is left for 3 hours with occasional shaking, and then gently boiled on a water bath under a reflux condenser for 1 hour. The former method, however, gives the better yield. The contents of the flask are then distilled off on a water bath into a receiver containing water and cooled in ice.

The distillation is continued till the greater part of the liquid has distilled over, and no oily drops are to be seen in the condenser. The residue consisting of a concentrated solution of phosphorus and phosphoric acids in addition to excess of red phosphorus is discarded. The distillate is shaken up with water to remove alcohol, and then with dilute caustic soda to remove free iodine. Enough alkali must be used to render the lower layer of alkyl halide colourless.* The latter is then separated off,

---

* Should difficulty be experienced in freeing the liquid from iodine, addition of a little sodium thiosulphate solution is effective.

dried over granular calcium chloride (6 gms.) and distilled. The preparation should be kept in the dark in a well-stoppered bottle. If exposed to light, iodine slowly separates, but may be prevented from so doing by adding a small quantity of colloidal silver to the liquid.

$$5ROH + P + 51 = 5RI + H_3PO_4 + H_2O.$$

Yield.—Almost theoretical (methyl iodide, 110 gms.; ethyl iodide, 120 gms.). Colourless, highly refractive liquids; characteristic odour; B.P. ^{760} methyl iodide, 42·8°; B.P. ^{760} ethyl iodide, 72·2°; D. $^{15}_{4}$ methyl iodide, 2·27; D. $^{0}_{4}$ ethyl iodide, 1·975. (A. Ch., [1], 91, 89; [2], 25, 323; 42, 119; A., 126, 250; J. C. S., 117, 1592; O. S., XIII, 60.)

Care should be taken not to raise the temperature too high, as there is a danger that the red phosphorus may take fire if air leaks in. To avoid this the distillation, if not done on a water bath, is best carried out in a current of carbon dioxide.

Reaction CLXIII. Addition of Halogen or Halogen Hydride to Unsaturated Compounds.—The ease of addition increases from iodine to chlorine and from hydrochloric to hydriodic acid, iodine and hydrogen chloride adding with difficulty except with terpenes to which hydrogen chloride adds readily. Fluorine acts violently and destructively. The halogen of halogen hydride normally adds on to the carbon atom which has the lesser number of hydrogen atoms (Markownikoff Rule, A., 1875, 305.)

$$R.CH{=}CH_2 + HX \longrightarrow R.CHXCH_3$$

though in presence of peroxides (often produced by action of air) hydrogen bromide generally adds the reverse way ("Peroxide Addition", Kharasch, Am. Soc., 1933, 2468, Chem. Rev., 27, 351.)

$$RCH{=}CH_2 + HBr\ (+\text{peroxide}) \longrightarrow RCH_2CH_2Br.$$

$\alpha\beta$-Unsaturated compounds generally add halogen to the β-carbon, possibly by 1 : 4 addition followed by migration of a proton.

$$CH_2{=}CH.COOH + HX \longrightarrow CH_2X.CH_2.COOH.$$

For a review of the reaction between olefines and halogens including reference to the *trans* addition of halogens see Chem. Rev., 33, 27.

PREPARATION 321.—**Ethylene Dibromide** (1 : 2-*Dibromoethan*).

$CH_2Br.CH_2Br.$ $C_2H_4Br_2.$ 188.

Ethylene is prepared by gently heating a mixture of 25 gms. ethyl alcohol, 150 gms. conc. sulphuric acid, and a little sand, in a 2-litre round flask on a sand bath till a steady stream of gas is evolved. A mixture of 1 part of alcohol and 2 parts by weight of conc. sulphuric acid is then slowly added through a tap funnel, the lower opening of which has been drawn out somewhat at such a rate that the gas is constantly evolved without frothing. The gas is purified by passing it through two wash-bottles in series containing dilute caustic soda solution, to which a little phenolphthalein has been added. The wash-bottles are fitted with safety tubes, and their contents must be renewed occasionally, the phenolphthalein serving to show when the alkali is exhausted. The gas is then bubbled slowly through two wash-bottles with ground-glass stoppers, each containing 15 gms. of bromine (1 mol.) and 50 c.cs. of water, and immersed in water, the temperature of which is kept at 20°–25°. Should the contents of the ethylene generating flask char too badly (some charring is inevitable) a fresh supply of gas must be made. When decolourisation of the bromine is complete (several hours) the crude ethylene bromide is washed with dilute caustic soda solution and with water, dried over calcium chloride and distilled, the fraction 130°–132° being collected separately.

$$CH_3CH_2OH \longrightarrow CH_2:CH_2 \longrightarrow CH_2Br.CH_2Br.$$

Yield.—85% theoretical (30 gms.). Colourless oil; insoluble in water; B.P. ^{760} 131·5; D. $^{15}_{4}$ 2·19. (A., 168, 64.)

PREPARATION 322.—**Cinnamic Acid Dibromide** (3-*Phenyl*-2 : 3-*dibromopropan acid*).

$$C_6H_5.CHBr.CHBr.COOH. \qquad C_9H_8O_2Br_2. \qquad 308.$$

Method I.—40 gms. (1 mol.) of finely-divided cinnamic acid are spread out on a large clock-glass and placed in a desiccator over concentrated sulphuric acid. A dish containing 45 gms. (slightly more than 1 mol.) of dry bromine is supported on a glass tripod above the cinnamic acid, the desiccator is closed, and allowed to stand until all the bromine has evaporated from the dish, and has been absorbed by the acid (about 3 days). The clock-glass is removed, the product exposed to the air for several hours, weighed in order to make sure that the theoretical amount of bromine has been absorbed, and recrystallised from dilute alcohol.

$$C_6H_5.CH:CH.COOH + Br_2 = C_6H_5CHBr.CHBr.COOH.$$

Yield.—Theoretical (90 gms.). Colourless leaflets; M.P. 195° (decomposition). (J. C. S., 83, 669.)

Method II.—12·5 gms. (1 mol.) of cinnamic acid are dissolved in 65 c.cs. of anhydrous ether, and the solution cooled to 0° in a freezing mixture. 4·3 c.cs. (1 mol.) of bromine are then slowly added from a burette while all but diffused daylight is excluded, as the reaction is very violent in direct sunlight. The ether is removed on a water bath, and the residue recrystallised from dilute alcohol.

Yield.—Theoretical (25 gms.). Colourless leaflets. (A., 195, 140.)

PREPARATION 323.—**Cinnamic Acid Dichloride** (3-*Phenyl*-2 : 3-*dichloropropan acid*).

$$C_6H_5.CHCl.CHCl.COOH. \qquad C_9H_8O_2Cl_2. \qquad 219.$$

Direct sunlight or some other source of ultra-violet rays is essential for this preparation (p. 56).

10 gms. finely-ground cinnamic acid are suspended in 80 gms. freshly-distilled carbon disulphide (*caution*) in a *quartz* flask. A stream of dry chlorine gas (p. 513) is passed in until the liquid assumes a greenish-yellow colour. The mixture is alternately shaken until this colour disappears, and resaturated with chlorine gas until an increase in weight of 5 gms. has taken place. The precipitate is filtered off and recrystallised from aqueous alcohol.

$$C_6H_5CH : CH.COOH + Cl_2 \longrightarrow C_6H_5CHCl.CHCl.COOH.$$

Yield.—90% theoretical (14 gms.). Colourless leaflets ; M.P. 162°–164° (slight decomposition). (B., 14, 1867.)

PREPARATION 324.—**β-Phenyl-β-Bromopropionic Acid** (3-*Phenyl*-3-*bromopropan acid*).

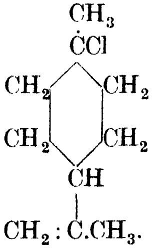
$$C_6H_5CHBrCH_2COOH. \qquad C_9H_9O_2Br. \qquad 229.$$

10 gms. (1 mol.) of finely-powdered cinnamic acid are heated in a sealed tube (see p. 47) for 2 hours at 100° with 10 gms. of glacial acetic acid which has been saturated with hydrogen bromide at ordinary temperature (1 gm. of glacial acetic acid dissolves about 0·6 gm. of hydrogen bromide, so there is an excess of the latter present.) The precipitate is recrystallised from *dry* carbon disulphide (the acid is readily decomposed by water) in which cinnamic acid is readily soluble even in the cold (*caution*).

$$C_6H_5CH : CHCOOH + HBr = C_6H_5CHBr—CH_2COOH.$$

Colourless crystals ; soluble in hot, slightly soluble in cold carbon disulphide ; M.P. 137°. (B., 11, 1221.)

PREPARATION 325.—**Dipentene Hydrochloride** (1-*Chloro*-Δ^8-*methene*).

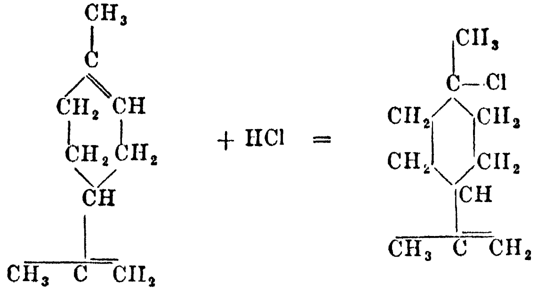


$$C_{10}H_{17}Cl. \qquad 172·5.$$

This reaction must be carried out in a fume cupboard.

20 gms. dipentene, which have been *thoroughly* dried over metallic sodium, are dissolved in an equal volume of *dry* carbon disulphide (*caution*), the solution placed in a dry distilling flask—the side tube of which is connected with a calcium chloride tube—and a current of dry hydrogen chloride (see p. 513) led into the solution through the neck of the flask, which is meanwhile surrounded with ice. After 8 hours the operation is interrupted, the carbon disulphide removed on a water bath (*caution*),

and the residue fractionated under reduced pressure, the fraction 97°–98° at 11–12 mms. being retained.



Colourless liquid ; B.P. ^{11} 97°–98°.

Note.—Moisture must be excluded in this preparation (A., 270, 188.)

PREPARATION 326.—Ethylene Dichloride (1 : 2-*Dichloroethan*).

$$\begin{array}{l} CH_2Cl \\ | \\ CH_2Cl. \end{array}$$

$C_2H_4Cl_2$. 99.

Ethylene is prepared from ethyl alcohol as in Prep. 9 or Prep. 436. The gas is passed first into an empty wash-bottle surrounded by a freezing mixture, and then through a second containing conc. sulphuric acid. The gas is next passed into antimony trichloride at 40°–50°, through which dry chlorine is also passed. The ethylene dichloride formed is distilled from the antimony trichloride.

Sweet smelling liquid ; B.P. 85°. (P. A., 13, 297.)

Reaction CLXIV. Replacement of Hydrogen by Nascent Halogen.—When nascent bromine is required, sodium bromide and bromate are added to the substance, and the amount of sulphuric acid required by the following equation is added :

$$5NaBr + NaBrO_3 + 6H_2SO_4 \longrightarrow 6NaHSO_4 + 3H_2O + 6Br.$$

An excess of bromate and sulphuric acid is often employed to react with the hydrobromic acid formed during the bromination of the substance.

$$R.H + 2Br \longrightarrow R.Br + HBr.$$

$$HBrO_3 + 5HBr \longrightarrow 6Br + 3H_2O.$$

Nascent chlorine or iodine can be generated from the corresponding salts in a similar manner. For the use of standard bromate in estimations, see p. 508.

PREPARATION 327.—*p*-Chloroacetanilide (1-*Chloro-4-acetaminobenzene*).

C_8H_8ONCl. **169·5.**

20 gms. of alcohol and 20 gms. glacial acetic acid are mixed, and to this is added 10 gms. (1 mol.) of acetanilide, which is dissolved by gentle heat.

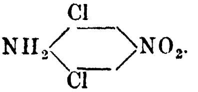
After 20 c.cs. of water have been added the solution is heated to 50°, when 200 c.cs. of a cold 10% solution (a slight excess) of bleaching powder are added gradually with continuous stirring. A white precipitate is formed which is filtered off, washed with water, and then recrystallised from alcohol, decolourising carbon being added, if necessary. N-Chloroacetanilide is formed as an intermediate product.

$$C_6H_5NH.COCH_3 \xrightarrow{Cl_2} C_6H_5NCl.COCH_3 \longrightarrow ClC_6H_4NH.COCH_3.$$

Colourless needles; M.P. 179°–180°; soluble in alcohol, ether, and carbon disulphide. (G., 28, II, 313.)

N-Chloroanilides (J. C. S., 99, 1185; 1928, 998), dibromodimethyldihydroresorcinol (J. C. S., 121, 1896), and N-bromosuccinimide (H. Acta., 1946, 1144), may be employed as halogenating agents (see J. C. S., 1939, 1774).

PREPARATION 328.—2 : 6-Dichloro-4-Nitroaniline.



$C_6H_4O_2N_2Cl_2$. 207.

35 gms. of *p*-nitroaniline are dissolved in 312 c.cs. conc. hydrochloric acid at 50°. A solution of 20·5 gms. of potassium chlorate in 437 c.cs. of water at about 25° are slowly added. When all the chlorate has been added the solution is diluted with a large quantity of water; the precipitate formed is removed by filtration and well washed. It can be further purified by crystallisation from glacial acid or from a mixture of glacial acetic acid and alcohol.

Yield.—87% theoretical (42 gms.). Lemon-yellow needles; M.P. 189°. (B., 36, 4391.)

Reaction CLXV. Replacement of Hydrogen by the use of Halogen Compounds.—The halogen compounds used are those of phosphorus, sulphur, antimony and iodine, and also sulphuryl chloride and bleaching powder. With phosphorus pentachloride the halogen does not enter the aromatic nucleus until the hydrogen of the side chain has been completely replaced. A mixture of red phosphorus and bromine is used in place of phosphorus bromide; with yellow phosphorus the reaction is much too vigorous. As red phosphorus generally contains traces of free phosphoric acid it should be previously washed with water or ammonia and dried before using. Sulphur bromide and iodide are used in presence of nitric acid; with these the halogen enters the nucleus, and only mono-derivatives are formed. Antimony pentachloride yields two atoms of halogen for chlorination. Iodine monochloride in glacial acetic acid or dilute hydrochloric acid replaces hydrogen by iodine. Sulphuryl chloride chlorinates aromatic compounds, both in the side chain and in the nucleus; when a carbonyl or carboxyl group is present the hydrogen in the α-position to this group is substituted. Bleaching powder is used as a chlorinating agent owing to the ease with which it gives up its available chlorine.

PREPARATION 329.—**α-Bromostearic Acid** (2-*Bromo-octadecan acid*).

$CH_3(CH_2)_{15}CHBrCOOH$. $C_{18}H_{35}O_2Br$. 363.

30 gms. (3 mols.) of stearic acid and 1·1 gms. (1 atom) of red phosphorus are placed in a flask fitted with a reflux condenser and dropping funnel. The flask is immersed in a water bath containing water at 60°–70°, so that the stearic acid melts, and 22·5 gms. (4 mols.) of dry bromine are added gradually from the dropping funnel. When addition is complete the mixture is heated on a boiling water bath for about 3 hours. The product is poured into water, and the monobromostearic acid filtered off and dried on a porous plate. It is recrystallised from carbon disulphide (*caution*).

$$3CH_3(CH_2)_{16}COOH + P + 4Br_2 = 3CH_3(CH_2)_{15}CHBrCOBr + HPO_3 + 2HBr.$$

$$CH_3(CH_2)_{15}CHBrCOBr + H_2O \longrightarrow CH_3(CH_2)_{15}CHBrCOOH.$$

Colourless plates ; M.P. 61° ; the materials used in this preparation must be pure and dry (see next preparation). (B., 24, 2903 ; 25, 482.)

PREPARATION 330.—**Monobromoacetic Acid** (*Bromo-ethan Acid*).

$CH_2BrCOOH$. $C_2H_3O_2Br$. 139.

The materials for this preparation must be pure and dry. The acetic acid is purified, as on p. 244 ; the bromine is shaken with conc. sulphuric acid, and the phosphorus warmed with dilute ammonia, washed well with water, and dried in a steam oven. (Work in a fume cupboard.)

20 gms. (3 mols.) of pure glacial acetic acid and 3 gms. (1 atom) of red phosphorus are placed in a round-bottomed flask of about 300 c.cs. capacity. (*N.B.*—Use ground glass joints and not rubber.)

71 gms. (4 mols.) of bromine are added from a dropping funnel very gradually at first, the flask being cooled by immersion in cold water. The reaction proceeds with great vigour, but moderates after about half of the bromine has been added, when the remainder may be run in more quickly. The flask is then warmed on a boiling water bath until the colour of bromine vapour in the interior of the flask disappears. After cooling, the bromo-acetyl bromide is poured into a distilling flask and distilled under diminished pressure.

The product is weighed, and the theoretical amount of water required to convert it into bromoacetic acid gradually added (1·8 gms. for 20 gms. of the acyl bromide). The mixture solidifies to a white crystalline mass. This is purified by distilling under ordinary pressure from a small distilling flask provided with an air condenser, the portion distilling at 190°–210° being retained.

$$3CH_3COOH + P + 8Br = 3CH_2BrCOBr + HPO_3 + 2HBr.$$

$$CH_2BrCOBr + H_2O \longrightarrow CH_2BrCOOH.$$

Colourless crystals ; M.P. 50°–51° ; B.P. 208°.

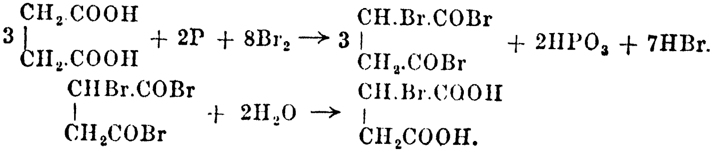
Note.—The bromoacetyl bromide and bromoacetic acid must not be allowed to touch the hands as they cause serious wounds.

(B., 20, 2026 ; A., 242, 141 ; O. S., 23, 37.)

Preparation 331.—**Monobromosuccinic Acid** (*2-Bromo-butan-diacid*).

$COOH.CH_2.CHBrCOOH$. $C_4H_5O_4Br$. 197.

A tubulated retort is sealed to a Liebig's condenser, and the latter connected to an apparatus to absorb hydrobromic acid. 18 gms. (3 mols.) of carefully dried succinic acid are intimately mixed with 3·5 gms. (excess) of red phosphorus. This is placed in the retort, and 80 gms. (excess) of bromine are added slowly from a dropping funnel through the tubulus. The bromine must be very carefully added at the beginning as the reaction is violent, and again added only when the reaction subsides. When all the bromine has been added, the whole is heated on a water bath until the bromine disappears. The retort now contains monobromosuccinyl bromide; the free acid is obtained by pouring *slowly* the contents of the retort into 100 c.cs. of boiling water, the flame being withdrawn. It is then filtered, and repeatedly extracted with ether, the latter removed on the water bath, and the residue recrystallised from water.



$$3\begin{array}{l}\mathrm{CH_2.COOH}\\|\\\mathrm{CH_2.COOH}\end{array} + 2P + 8Br_2 \rightarrow 3\begin{array}{l}\mathrm{CH.Br.COBr}\\|\\\mathrm{CH_2.COBr}\end{array} + 2HPO_3 + 7HBr.$$

$$\begin{array}{l}\mathrm{CHBr.COBr}\\|\\\mathrm{CH_2COBr}\end{array} + 2H_2O \rightarrow \begin{array}{l}\mathrm{CH.Br.COOH}\\|\\\mathrm{CH_2COOH.}\end{array}$$

Yield.—85% theoretical (25 gms.). Colourless crystals; M.P. 160°; soluble in water. (A., 242, 145; B., 14, 892.)

Preparation 332.—**2 : 4 : 1-Iodonitroaniline** (*1-Amino-2-iodo-4-nitro-benzene*).

$C_6H_3(NH_2)(NO_2)I$. $C_6H_5O_2N_2.I$. 264.

15 gms. (1 mol.) of finely-ground *p*-nitroaniline are agitated with cold glacial acetic acid in quantity just sufficient to bring all into solution. A solution of 26·5 gms. (1 mol.) of iodine monochloride in glacial acetic acid is then slowly added to the well-stirred solution, which after the addition is allowed to stand 1 hour. It is then poured into 1·5 litres of boiling water, filtered and allowed to cool. After some time crystals of iodonitroaniline separate which are filtered off and dried.

$$C_6H_4(NH_2)(NO_2) + ICl \longrightarrow C_6H_3(NH_2)(NO_2)I + HCl.$$

Long yellow needles; soluble in hot water; M.P. 105°. (B., 34, 3344.)

Preparation 333.—**Monochloromalonic Acid** (*2-Chloro-propan-diacid*).

$CH.Cl(COOH)_2$. $C_3H_3O_4Cl$. 138·5.

8 gms. (1 mol.) of malonic acid from a sample which has been dried in a steam oven and cooled in a desiccator are dissolved in 250 c.cs. of anhydrous ether. The solution is cooled in ice-water, and 10 gms. (1 mol.) of sulphuryl chloride slowly added. The ether is removed on a water bath, and the residue left in a vacuum desiccator containing sulphuric acid until crystallisation of mono-chloromalonic acid is complete.

$$CH_2(COOH)_2 + SO_2Cl_2 \longrightarrow CHCl(COOH)_2 + HCl + SO_2.$$

Yield.—Theoretical (10·5 gms.). Colourless crystals; M.P. 133°. (B., 35, 1814.)

Reaction CLXVI. Replacement of the Amino Group by Halogen.—This group in aryl compounds can easily be replaced by halogen :

(*a*) By means of the Sandmeyer reaction. The amine is diazotised and the resulting diazonium solution added to a warm solution of cuprous halide. (Ann. Rep., 1939, 231 ; See Hodgson, J. C. S., 1946, 745.)

$$R.NH_2 \longrightarrow R.N_2Cl \longrightarrow R.Cl + N_2.$$

(*b*) By Gattermann's method, in which copper powder is added to an acid solution of the diazonium salt.

(*c*) By heating a solution of the diazonium compound with hydriodic acid or potassium iodide.

PREPARATION 334.—*o*-**Bromotoluene.**

$C_6H_4(CH_3).Br.$ $C_7H_7Br.$ 171.

6 gms. *ortho*-toluidine are dissolved in a mixture of 35 c.cs. hydrobromic acid of constant boiling point, and 40 c.cs. of water. The solution is cooled to 0°, and diazotised by the addition of 5 gms. sodium nitrite dissolved in 12 c.cs. of water ; during this addition a drop is frequently removed, diluted with water on a watch-glass, and tested with starch-iodide paper for free nitrous acid (see p. 380). Copper powder (prepared from 40 gms. copper sulphate, see p. 515) is then added in small quantities at a time to the diazonium solution, which should be continuously stirred ; an effervescence—due to the escape of nitrogen—takes place. When addition of copper produces no further effervescence, the bromo-toluene forms the lower layer. This layer is separated, steam distilled and the distillate extracted with ether. The ethereal solution is dried over solid calcium chloride, and fractionated.

$$CH_3.C_6H_4.NH_2 \rightarrow CH_3.C_6H_4N_2Br \rightarrow CH_3.C_6H_4.Br.$$

Yield.—70% theoretical (6 gms.). B.P. 181°. O. S., IX, 22 ; C. V., I, 136, describes preparation of *p*-bromotoluene.)

PREPARATION 335.—*p*-**Chlorotoluene** (1-*Methyl*-4-*chlorobenzene*).

$CH_3.C_6H_4.Cl.$ $C_7H_7Cl.$ 126·5.

20 gms. (1 mol.) of *p*-toluidine are dissolved in 100 c.cs. of a mixture of equal volumes of water and conc. hydrochloric acid and diazotised in the usual way (see p. 380) with sodium nitrite. 15 gms. of moist copper powder (see p. 515) are then added in small portions to the well-stirred solution. When the evolution of nitrogen has ceased, the product is steam distilled, the distillate extracted with ether, and the ethereal solution dried over anhydrous sodium sulphate. The sodium sulphate is filtered off and the filtrate distilled. *p*-Chlorotoluene passes over at 163°.

$$CH_3.C_6H_4.NH_2 \longrightarrow CH_3.C_6H_4N_2Cl \longrightarrow CH_3.C_6H_4Cl + N_2.$$

Yield.—70% theoretical (17 gms.). Colourless oily liquid ; M.P. 7·4° ; B.P. 163°. (B., 23, 1218 ; O. S., III, 33.)

PREPARATION 336.—**Chlorobenzene.**

$C_6H_5.Cl.$ 112·5.

20 gms. aniline are dissolved in 130 c.cs. water and 37 c.cs. conc. hydrochloric acid, and diazotised (see Preparation 379) at 0°–5° by the addition of 15 gms. sodium nitrite dissolved in 40 c.cs. water. 140 c.cs. of a 10% solution of freshly-prepared cuprous chloride (p. 515) are cooled to 0° and the diazonium chloride run in with stirring. The contents of the flask while still being stirred are allowed to reach room temperature. At about 15° the yellow complex is decomposed yielding nitrogen and chlorobenzene. The temperature is raised to 60° to complete the decomposition. The chlorobenzene is separated, washed with cold conc. sulphuric acid and dried over calcium chloride.

$$C_6H_5N_2Cl \longrightarrow C_6H_5.Cl + N_2.$$

Yield.—75% theoretical (18 gms.). Colourless liquid; B.P. 132°. (B., 23, 1628, 1880; A., 272, 141.) See D.D.T., p. 453.

For preparation of *o*- and *p*-chlorotoluene, see C. V., I, 170.

PREPARATION 337.—**p-Iodotoluene.**

$CH_3.C_6H_4.I.$ $C_7H_7I.$ 218.

20 gms. *p*-toluidine are boiled with 70 c.cs. conc. hydrochloric acid and sufficient water to dissolve the hydrochloride. The solution is diazotised as usual (p. 380), and 31 gms. potassium iodide dissolved in water are then run in from a tap funnel with continuous stirring. The mixture is allowed to stand for a time when a dark brown mass is formed which is filtered off and recrystallised from alcohol.

$$CH_3C_6H_4NH_2 \longrightarrow CH_3C_6H_4N_2Cl \longrightarrow CH_3C_6H_4I.$$

Yield.—80% theoretical (25 gms.). Yellow plates; M.P. 35°; B.P. 211°. (C. V., II, 351, gives preparation of iodobenzene.)

PREPARATION 338.—**Fluorobenzene.**

$C_6H_6F.$ 96.

40 gms. aniline are diazotised as described in Prep. 378. 20 gms. boric acid are added in small portions to 42 gms. 60% hydrofluoric acid in a wax-coated flask which is shaken and cooled in ice-water. The solution of fluoboric acid is added with good stirring to the diazonium solution, the temperature being kept below 10°. After 30 minutes the yellow crystalline solid is filtered, washed with ice-water, then with methyl alcohol, and with ether. The solid is air-dried and placed in a large flask fitted with a condenser attached to three distillation flasks arranged in series in a fume cupboard and ice-cooled, a delivery tube from the third flask leading off the fumes of boron trifluoride. The solid is carefully heated at a point near its surface with a small flame until decomposition begins. When it slackens, heat is again carefully applied, until fuming ceases. The combined distillate is washed with 10% caustic soda solution until washings are almost colourless, then once with water. The fluorobenzene

is then dried over calcium chloride and distilled, the fraction B.P. 84°–85° being collected.

$$C_6H_5N_2Cl + HBF_4 \longrightarrow C_6H_5N_2BF_4 + HCl.$$

$$C_6H_5N_2BF_4 \longrightarrow C_6H_5F + N_2 + BF_3.$$

Yield.—50% theoretical (16 gms.). Colourless liquid, with odour of benzene ; B.P. 85°. (C. V., II, 295.)

Reaction CLXVII. Replacement of Halogen by Halogen.—The substitution of bromine by chlorine can be effected through the use of the pentachlorides of antimony or phosphorus. Iodine is still more readily replaced by chlorine, not only by direct action of the latter, but also by double decomposition with certain metallic chlorides ($HgCl_2$, $SbCl_5$, AgCl) or iodine trichloride.

The substitution of chlorine by the direct action of bromine is rarely effected. Aluminium bromide, cupric bromide in alcoholic solution or boron tribromide under pressure, convert many alkyl chlorides into alkyl bromides. Mono-chloroacetic acid heated to 150° in a sealed tube with hydrobromic acid or potassium bromide yields mono-bromoacetic acid.

Iodine may be replaced by bromine by direct action or by heating under pressure with bromides of copper, mercury, silver or boron.

Bromine and chlorine can be replaced by iodine through double decomposition with hydriodic acid or iodides of potassium, calcium or aluminium.

Fluorine can be introduced into an aliphatic molecule (1) by action of fluorides on alkyl halides, e.g. the refrigerant, Freon, CCl_2F_2, from carbon tetrachloride, (2) by addition of hydrogen fluoride to olefines, (3) direct action of fluorine on saturated compounds, and (4) replacement of hydroxyl by interaction with hydrogen fluoride. Complete surveys of organic fluorine compounds are given in *Organic Reactions*, Adams, Vol. II, 49, and in *Preparative Organic Chemistry*, Rochemüller, pp. 229, 593. (J.S.C.I., 1947, 427.)

Diazonium salts and fluoboric acid yield aromatic fluoro compounds (C. V., II, 295, 299.) See Prep. 338.

PREPARATION 339A.—Acetyl Fluoride.

CH_3COF. C_2H_3OF. 62.

50 gms. acetyl chloride are placed in a rubber-stoppered pressure bottle (see p. 52) and cooled to −15° (see p. 12). 3 gms. anhydrous zinc fluoride are introduced, the bottle restoppered and the temperature allowed to rise to room temperature with shaking. It is again cooled, a further 3 gms. anhydrous zinc fluoride added and the temperature again allowed to rise. When 33 gms. of the salt have been added in this way the temperature is allowed to rise to 50°. The contents are then cooled and distilled using an efficient condenser.

$$2CH_3COCl + ZnF_2 \longrightarrow 2CH_3COF + ZnCl_2.$$

Yield.—80% theoretical (32 gms.). Colourless liquid ; B.P. 20°.

PREPARATION 339.—**Iodoacetic Acid.**

$CH_2I.COOH$. $C_2H_3O_2I$. 186.

25 gms. (1 mol.) of chloroacetic acid dissolved in 125 c.cs. of absolute alcohol and 50 gms. (excess) of finely-powdered potassium iodide are refluxed on a water bath for 1 hour. The product is well cooled in ice-water, and filtered from potassium chloride and iodide. The filtrate is decolourised (if necessary), by passing in a stream of sulphur dioxide, and afterwards evaporated to a small bulk on a water bath. On cooling, a product separates which is collected, dried by exposure in air, and recrystallised from a large volume of petroleum ether.

Colourless leaflets ; M.P. 84° ; the solid causes painful blisters in contact with the skin, and the vapours irritate the eyes. (B., 41, 2853.)

PREPARATION 340.—**Glyceryl Tribromide** (1 : 2 : 3-*Tribromo-propan*).

$CH_2.Br.CHBr.CH_2Br$. $C_3H_5Br_3$. 281.

75 gms. (slight excess) of bromine are slowly added to 50 gms. (1 mol.) of allyl iodide contained in a flask, fitted with an air condenser, and well cooled in a freezing mixture, the whole apparatus being set up in a fume cupboard. The liquid is allowed to stand 24 hours, and filtered from the iodine which has crystallised out. The brown filtrate is repeatedly washed with dilute caustic soda, with sodium thiosulphate solution, and with water ; it is then dried over fused calcium chloride and distilled. The distillate is again treated with sodium thiosulphate solution and with water, dried and distilled. The fraction 200°–220° is allowed to stand in a freezing mixture, and the mother liquor is then poured off from the crystals which form. The product is purified by repeated distillations.

Colourless glistening prisms ; insoluble in water ; M.P. 16° ; B.P. 219°–220°. (C. r., 70, 638 ; A., 156, 168 ; C. V. I, 521.)

Reaction CLXVIII. Replacement of Hydrogen by Halogen. (*Organic Preparations*, Weygand, p. 71.)—Chloro- and bromo-derivatives of the aliphatic hydrocarbons are obtained by the action of chlorine and bromine on these hydrocarbons in presence of light, the reaction being more energetic in sunlight than in diffused light. The corresponding iodo-derivatives cannot be obtained in this way, due it is supposed, to the energetic reducing action of hydriodic acid, which converts the iodo-derivative into the original paraffin. Iodination of aromatic hydrocarbons, however, takes place in presence of oxidising agents (e.g. nitric acid) (O. S., IX, 46).

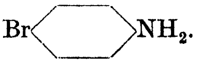
In the case of aromatic bodies the temperature has an important influence on the point of attack in the molecule by chlorine or bromine ; in the cold in the presence of carriers, the halogen enters the nucleus, while at the boiling point the side chain is attacked. The carriers most frequently used are : iron, aluminium-mercury couple, iodine, halides of phosphorus, antimony, iron, aluminium, sulphur or pyridine. The halogen is always more active in sunlight, or in ultra-violet light.

The presence of hydroxyl-, amino- or substituted amino-groups in the aromatic nucleus facilitates halogenation (cf. Preps. 352 and 353).

A solvent is frequently employed, either to dissolve the compound or to moderate the action of the halogen ; those commonly employed are carbon tetrachloride, glacial acetic acid, carbon disulphide, ethylene dichloride, chloroform, ether, water, hydrochloric acid, sulphuric acid.

In some cases the operation has to be conducted in a sealed tube under pressure, and if a solvent is also employed carbon tetrachloride is generally the most suitable. For direct halogenation under pressure, see Ann. Chim. App., 1935, 163.

PREPARATIONS 341 and 342.—***p*-Bromoaniline** (1-*Amino*-4-*bromobenzene*).



C_6H_6NBr. 172.

p-Bromoacetanilide.—34 gms. bromine are slowly added with stirring to a solution of 27 gms. acetanilide in 100 c.cs. glacial acetic acid. After 10 minutes the solution is poured into stirred cold water. The precipitated *p*-bromoacetanilide is filtered and washed with water containing a little sodium bisulphite, and crystallised from alcohol.

p-Bromoaniline.—The *p*-bromoacetanilide is dissolved in 40 c.cs. boiling alcohol in a flask fitted with reflux condenser. 10 gms. potassium hydroxide in 12 c.cs. water are added through the reflux and refluxing continued for 40 minutes. 150 c.cs. water is added and the mixture distilled until 100 c.cs. distillate is collected. The residue is poured into 200 c.cs. cold water when the *p*-bromoaniline separates as an oil which solidifies on keeping. The crude product is filtered, dissolved by heating with 10 c.cs. conc. hydrochloric acid in 150 c.cs. water, decolourising carbon being added. It is filtered and poured slowly into 10% caustic soda solution and ice. The crystalline product is filtered, and dried.

$$BrC_6H_4NHCOCH_3 \longrightarrow BrC_6H_4NH_2.$$

Yield.—30% theoretical (10 gms.) calculated on acetanilide. Colourless crystals; M.P. 66°. (G., 58, 233.)

PREPARATION 343.—**Bromobenzene** (*Phenylbromide*).

C_6H_5Br. 157.

To a mixture of 30 c.cs. benzene and 20 c.cs. bromine in a 200-c.c. round-bottomed flask are added ten drops of purified pyridine. The flask is attached to an upright condenser the upper opening of which is connected by a good cork and delivery tube to an inverted filter funnel dipping under water in a beaker. The mixture is warmed in a bath of water at 25°–30° until the vigorous reaction, which sets in, subsides. It is then warmed to 70° and maintained at this temperature until the evolution of hydrogen bromide ceases. The product is then cooled, transferred to a funnel, and treated by shaking with dilute caustic soda solution until just alkaline. The heavier layer of bromobenzene is separated, dried with solid calcium chloride, decanted and distilled. The fraction boiling at 140°–170° is redistilled and the fraction boiling at 150°–160° retained.

$$C_6H_6 + Br_2 \longrightarrow C_6H_5Br + HBr.$$

Yield.—50% theoretical (28 gms.). Colourless liquid; B.P. 154°; insoluble in water; miscible with organic solvents.

PREPARATION 344.—**Benzyl Chloride** (*Phenyl-chloro-methan*).

$C_6H_5.CH_2.Cl$. C_7H_7Cl. 126·5.

50 gms. toluene are placed in a tared retort (Fig. 50 or 56), the neck of which is sloped upwards and connected to a water reflux condenser carrying a straight calcium chloride tube at the end. 2 gms. phosphorus pentachloride or phosphorus trichloride to act as chlorine carrier are also placed in the retort. The toluene is boiled and a stream of dry chlorine is led through the liquid by a delivery tube fixed by a cork (an ordinary cork, previously soaked in melted paraffin wax should be used) in the neck of the retort. The retort is weighed periodically, and the stream of chlorine continued until an increase in weight of 18·5 gms. takes place.

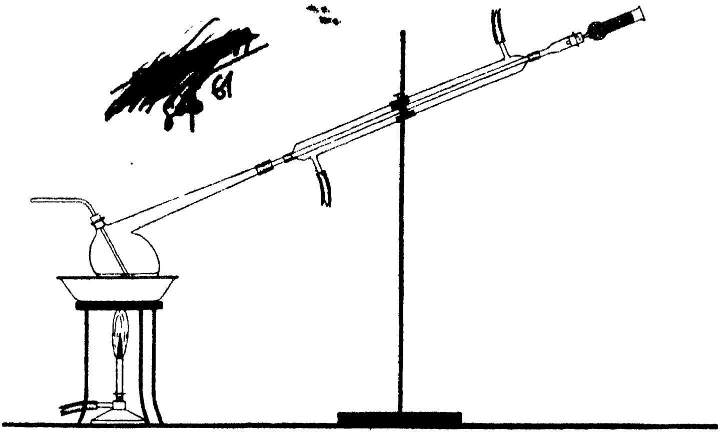


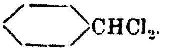
FIG. 56.

The product is distilled, the fraction 165°–185° being collected; this is redistilled, collecting the fraction 176°–180°, which is practically pure benzyl chloride.

$$C_6H_5.CH_3 + Cl_2 \longrightarrow C_6H_5CH_2Cl + HCl.$$

Yield.—60% theoretical (40 gms.). B.P. 176°; D. $^{15}_{15}$ 1·04. (A., 1853, 88, 129; B., 18, 606; A., 272, 149.) See also J. C. S., 1936, 337.

PREPARATION 345.—**Benzylidene Chloride** (*Benzal chloride*).

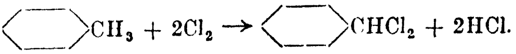


$C_7H_6Cl_2$. 161.

445 gms. toluene and 10 gms. phosphorus pentachloride are heated to boiling in a litre flask provided with a reflux and agitator (Fig. 56). Dry chlorine is passed into the liquid until the increase in weight is 355 gms. The chlorination is facilitated by bright sunlight, or by ultra-violet light.

The chlorination mixture is then fractionally distilled and the fraction between 160°–225° collected. The latter is further fractionated and the portion between 200°–210° collected and purified by distillation.

The impurities present after chlorination are unchanged toluene, benzyl chloride and benzotrichloride.



Yield.—85% theoretical (660 gms.). Colourless liquid; B.P. 212°; D. 1·2557. (A., 116, 336; 146, 322; 139, 318.)

PREPARATION 346.—*p*-Nitrobenzyl Bromide.

$NO_2.C_6H_4.CH_2Br.$ $C_7H_6O_2NBr.$ 216.

Method I.—5 gms. pure *p*-nitrotoluene, 2 c.cs. of bromine, and a crystal of iodine are placed in a sealed tube. The tube is placed in a bomb furnace and gradually heated up during 40 minutes to 130°, at which temperature it is kept for 160 minutes. After cooling, the tube is opened (p. 49) and the product extracted with about 60 c.cs. of hot alcohol. From the resulting solution crystals separate on cooling, which are filtered off; a second crop is obtained after concentrating and cooling the mother liquor. Water is added to the final mother liquor to precipitate a small quantity of the nitrobenzyl bromide, which is filtered off, dried, and purified by recrystallisation from petroleum ether. The first and second crops should be washed with cold petroleum ether.

Yield.—75% theoretical (6 gms.).

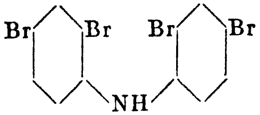
Method II.—10 gms. of *p*-nitrotoluene and a crystal of iodine dissolved in 100 c.cs. of carbon tetrachloride are placed in a silica flask provided with a reflux condenser. The solution is covered with water (about 50 c.cs.) and heated to gentle boiling, while situated about 15 cms. from a mercury vapour lamp (Fig. 46). A solution of 15 gms. bromine in 50 c.cs. carbon tetrachloride is then run in drop by drop from a dropping funnel at the top of the condenser. When all the bromine is in, boiling is continued until the solution becomes almost colourless. The contents of the flask are cooled, transferred to a separating funnel, and the lower carbon tetrachloride layer run into a distilling flask. Carbon tetrachloride is distilled off over a water bath, and the residue of *p*-nitrobenzyl bromide recrystallised from alcohol or petroleum ether.

$$NO_2.C_6H_4CH_3 + Br_2 \longrightarrow NO_2C_6H_4CH_2Br + HBr.$$

Yield.—80% theoretical (12·6 gms.). Needles; M.P. 99°–100°. (See also Am. Soc., 40, 406; J. R. T. C., I, 58; C. V., II, 443.) A useful reagent for the identification of phenols and acids.

It is worthy of note that *o*-nitrotoluene is not brominated by this method even at temperatures up to 200°—an interesting example of "steric hindrance". The *m*-compound, on the other hand, gives a 20% yield of the bromo-compound.

Preparation 347.—Tetrabromodiphenylamine (2 : 4 : 2′ : 4′-*Tetrabromo*-1 : 1′-*diphenylamine*).



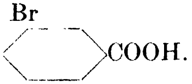
$C_{12}H_7NBr_4$. 485.

4 gms. (1 mol.) of finely-powdered diphenylamine are agitated with a sufficient quantity of cold glacial acetic acid to dissolve. The solution is stirred while 5 c.cs. (4 mols.) of bromine dissolved in 50 c.cs. glacial acetic acid are slowly run in. The tetrabromodiphenylamine formed separates as a precipitate, which is filtered off and recrystallised from alcohol.

$$(C_6H_5)_2NH + 4Br_2 \longrightarrow (C_6H_3Br_2)_2NH + 4HBr.$$

Yield.—Theoretical (12 gms.). Colourless needles ; M.P. 182°. (A., 132, 166 ; B., 8, 825.)

Preparation 348.—*m*-Bromobenzoic Acid (1-*Carboxy*-3-*bromobenzene*).



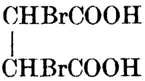
$C_7H_5O_2Br$. 201.

6 gms. (1 mol.) of benzoic acid, 8 gms. (1 mol.) of bromine, and 40 gms. of water are heated together in a thick-walled sealed tube to about 140°–150° in a Carius furnace (p. 49) for 9 hours. After cooling, the tube is opened with the usual precautions, and the colourless crystals of bromobenzoic acid washed out, filtered, and boiled with 100 c.cs. of water in a basin for 1 hour to remove unchanged benzoic acid. The residual bromobenzoic acid is then recrystallised twice from hot water.

$$C_6H_5.COOH + Br_2 = C_6H_4(Br)CO.OH + HBr.$$

Yield.—80% theoretical (8 gms.). Colourless needles ; soluble in hot water ; M.P. 155°. (A., 149, 131.)

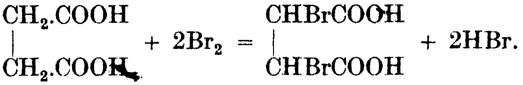
Preparation 349.—Dibromosuccinic Acid (2 : 3-*Dibromo-butan-diacid*).



$$\begin{array}{l} CHBrCOOH \\ | \\ CHBrCOOH \end{array}$$

$C_4H_4O_4Br_2$. 276.

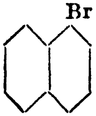
12 gms. (1 mol.) of succinic acid, 32 gms. (1 mol.) of bromine, and 12 gms. of water are heated in a sealed tube for 6 hours at 170° (see p. 48). The tube is then opened with care (p. 49) The greyish-white mass with which the tube is now filled is recrystallised from boiling water, with the addition of a little decolourising carbon.



$$\begin{array}{l} CH_2.COOH \\ | \\ CH_2.COOH \end{array} + 2Br_2 = \begin{array}{l} CHBrCOOH \\ | \\ CHBrCOOH \end{array} + 2HBr.$$

Yield.—Theoretical (27 gms.). Colourless glistening crystals ; soluble in hot water, in alcohol and in ether ; decomposes at 200° with formation of hydrobromic acid and bromo-maleic acid. (A., 117, 120 ; A. Spl., 1, 351 ; Bl., 18, 168.) C. V., II, 177, gives preparation from fumaric acid.

PREPARATION 350.—α-Bromonaphthalene.



$C_{10}H_7Br$. 207.

116 gms. of naphthalene (flakes) and 125 c.cs. of water are placed in a pot fitted with a good mechanical agitator and heated to 40°–50°. 145 gms. (45 c.cs.) of bromine are then gradually dropped in from a dropping-funnel dipping to the bottom of the pot at such a rate that the temperature is maintained at 40°–50°. The addition takes 8–9 hours. After all the bromine has been added, stirring is continued until the colour has practically disappeared. The mixture is allowed to cool, and a heavy oil separates. The oil is steam distilled on an oil bath at 145°–150°, this process removing the hydrobromic acid and some unchanged naphthalene. The oil is distilled *in vacuo*, the fraction 132°–133° at 12 mms. (145°–148° at 20 mms.) being collected. The lower fractions contain naphthalene, and the higher, 1 : 4-dibromonaphthalene.

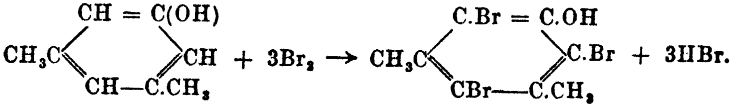
$$C_{10}H_8 + Br_2 = C_{10}H_7Br + HBr.$$

Yield.—55–60% theoretical (100–110 gms.). B.P. 281°; M.P. 4°. (A., 135, 40; 147, 166; O. S., I, 35; X, 14.)

PREPARATION 351.—Tribromo-*s*-xylenol.

$(CH_3)_2C_6Br_3(OH)$. $C_8H_7OBr_3$. 359.

A few gms. of *s*-xylenol are placed in a large test tube or small beaker, and covered with about 20 times their weight of water. Bromine is gradually added drop by drop until an excess is indicated by a reddish-brown colour which does not disappear. Sulphur dioxide, either as aqueous solution or gas, is added until the excess of bromine is removed. The precipitate is filtered off, washed with water, and recrystallised from alcohol.



Yield.—90% theoretical. Fine needles; M.P. 166°. (B., 18, 2679, A., 281, 122.)

PREPARATION 352.—Tribromophenol (1-*Hydroxy*-2 : 4 : 6-*tribromobenzene*).

$C_6H_2(OH)Br_3$. $C_6H_3OBr_3$. 331.

5 gms. (1 mol.) of phenol are dissolved in 100 c.cs. of water, and to the cold solution 8·3 c.cs. (3 mols.) of bromine in aqueous solution are added. The precipitate, which is almost insoluble in water, is filtered off, washed with water, and recrystallised from dilute alcohol.

$$C_6H_5(OH) + 3Br_2 \longrightarrow C_6H_2Br_3(OH) + 3HBr.$$

Yield.—Theoretical (17 gms.). Colourless needles; M.P. 95°. (A., 43, 212; 137, 208.) For estimation of phenol by bromination, see p. 508.

PREPARATION 353.—**p-Bromodimethylaniline.**

$C_6H_4BrN(CH_3)_2$. $C_8H_{10}NBr$.   200.

10 gms. dimethylaniline are dissolved in glacial acetic acid, and 6·6 gms. bromine dissolved in glacial acetic acid gradually added. When the solution is diluted with water, the p-bromo-dimethylaniline is precipitated, filtered off, and recrystallised from alcohol.

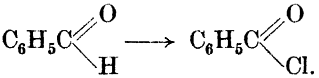
$$C_6H_5N(CH_3)_2 \longrightarrow C_6H_4Br.N(CH_3)_2.$$

Yield.—Almost theoretical (16–17 gms.). White plates; M.P. 55°. (B., 8, 715.)

PREPARATION 354.—**Benzoyl Chloride.**

C_6H_5COCl. C_7H_5OCl.   140·5.

Dry chlorine is led into cold benzaldehyde (for apparatus, see p. 69). The chlorine is easily absorbed with evolution of heat, torrents of hydrochloric acid being given off. When the reaction has moderated somewhat, heat is applied in order to keep the liquid boiling briskly, the stream of chlorine being continued until the evolution of hydrochloric acid ceases. The excess chlorine is removed by passing a stream of dry air or carbon dioxide through the apparatus. The product is then distilled.



$$C_6H_5C{\overset{\displaystyle /\!\!/ O}{\underset{\displaystyle \backslash H}{}}} \longrightarrow C_6H_5C{\overset{\displaystyle /\!\!/ O}{\underset{\displaystyle \backslash Cl.}{}}}$$

Yield.—Almost theoretical. Colourless, fuming liquid, with irritating smell; B.P. 198°; D. $^{19}_{19}$ 1·214. (A., 3, 262.)

PREPARATION 355.—**Chloral** (*Trichloroacetaldehyde*).

CCl_3CHO. C_2HOCl_3.   147·4.

100 c.cs. absolute alcohol are placed in a retort, with the side tube on the slant, and attached to a reflux. A current of dry chlorine is passed into the alcohol, the temperature being kept at 5°–10° by external cooling. The gas is quickly absorbed at first, but the absorption slackens off. The contents of the retort are heated to 60°, while chlorine is still passed, as long as it is absorbed. The liquid is then boiled gently and cooled—its specific gravity should now be 1·400. An equal volume of conc. sulphuric acid is then cautiously added, ethyl chloride and hydrochloric acid being evolved. The mixture is distilled from a water bath. The distillate is neutralised with chalk and again distilled, and finally fractionated, the fraction boiling at 95°–100° being retained.

$$CH_3CH_2OH \xrightarrow{Cl} CH_3CHO \xrightarrow{Cl} CCl_3CHO \rightarrow CCl_3CH(OH)OC_2H_5 \rightarrow CCl_3CHO.$$

Colourless liquid; characteristic odour; B.P. 98°. (A., 279, 293.) For preparation of bromal, see C. V., II, 87.

When chloral is mixed with $\frac{1}{8}$ its weight of water, the mixture gradually solidifies to a crystalline mass of chloral hydrate, $CCl_3CH(OH)_2$. M.P. 57°; B.P. 97°.

Chloral condensed with chlorobenzene in presence of oleum or hydrogen fluoride gives *p-p'*-dichlorodiphenyl-trichloroethane, D.D.T. (See Prep. 494.)

$$ClC_6H_4.CH(CCl_3).C_6H_4Cl,$$

PREPARATION 356.—**Monochloroacetic Acid.**

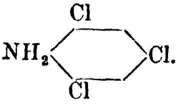
$CH_2Cl.COOH$. $C_2H_3O_2Cl$. 94·5.

100 gms. glacial acetic acid and 10 gms. of sulphur are placed in a small flask, and the whole weighed. The flask is fitted with a two-holed cork, one hole being fitted with an adapter, to which is attached a reflux condenser, while the other is fitted with a delivery tube reaching down into the acid. The flask is heated on a boiling water bath, and a steady current of chlorine passed into the acid until (about 6 hours) a gain in weight of 50 gms. has taken place. It is important to place the apparatus in direct sunlight as this has a catalytic accelerating effect on the operation. When the required increase has taken place, the liquid is decanted from the sulphur into a distilling flask and distilled through an air condenser. Acetyl chloride, sulphur chloride and acetic acid come over at first. The fraction 150°–190°, collected separately, yields crystals of mono-chloroacetic acid, on cooling ; the liquid is drained off from the crystals, the latter redistilled, and the fraction 180°–190° collected.

$$CH_3.COOH + Cl_2 \longrightarrow CH_2Cl.COOH + HCl.$$

Yield.—45–60% theoretical (75–100 gms.). Colourless crystals. Useful reagent for phenols with which it forms phenoxy acetic acids. M.P. 62°–63° ; B.P. 185°–187°. (B.I, [3], 2, 145 ; Z. a., 40, 973.) C. V., II, 181, gives preparation of dichloroacetic acid from chloral hydrate.

PREPARATION 357.—**Trichloroaniline** (1-*Amino*-2 : 4 : 6-*trichlorobenzene*).

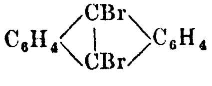


$C_6H_4NCl_3$. 196·5.

10 gms. of dry aniline are dissolved in 200 gms. dry carbon tetrachloride and placed in a flask fitted with a mechanical agitator (see Fig. 50). The flask is surrounded by an efficient freezing mixture, so that the temperature is about − 10°. Through one of the side tubes is passed dry chlorine mixed with dry carbon dioxide (equal volumes). A white crystalline deposit of trichloroaniline is thrown down, but if the temperature is allowed to rise or the materials are not absolutely dry, the product is contaminated with aniline black. The crystals are filtered off and recrystallised from alcohol.

Yield.—Almost theoretical (21 gms.). White needles ; M.P. 77·5° ; B.P. 262°. (J. S. C. I., 45, 355.)

PREPARATION 358.—**9 : 10-Dibromoanthracene.**



$C_{14}H_8Br_2$. 336.

50 gms. of anthracene (80–85%) and 500 c.cs. of carbon tetrachloride are placed in a flask with mechanical agitator and reflux condenser affixed. 95 gms. of bromine are slowly added with vigorous agitation, and the dibromo compound separates. The hydrogen bromide evolved is led from the top of the condenser to a fume duct or is absorbed in water. The addition of bromine takes about 30 minutes. The mixture is then gently raised to boiling and maintained there for 1 hour. It is cooled, allowed to stand for some hours, and the dibromo compound filtered off, washed with carbon tetrachloride, and dried. A further yield is obtained by concentrating the mother liquor. The product is crystallised from carbon tetrachloride or from toluene.

$$C_{14}H_{10} + 2Br_2 \longrightarrow C_{14}H_8Br_2 + 2HBr.$$

Yield.—85% theoretical (70 gms.). Yellow needles; M.P. 217°. (O. S., III, 41.)

CHAPTER XXIII

THE LINKING OF HYDROGEN TO NITROGEN

AMINO COMPOUNDS

Reaction CLXIX. Action of Metals on Nitro Compounds in Acid Media.—Primary amines are formed.

$$R.NO_2 + 3M'' + 6HCl \longrightarrow R.NH_2 + 3M''.Cl_2 + 2H_2O.$$

The metals used are iron, zinc, tin ; and the acids, hydrochloric, sulphuric, and in some cases acetic. As a rule, the best temperature for the reduction is about 100°, and in some cases the nitro compound may be dissolved in a suitable solvent. In all cases, good mechanical agitation is essential to prevent the metal settling to the bottom of the pot.

The amine is obtained in the form of its salt, the base being liberated by caustic soda. The amine, if volatile in steam, is separated by steam distillation ; solid amines are separated by filtration. Sometimes the amines may be extracted with ether, but before this is done the metal should first be removed.

Where zinc and tin are used, double salts of the general formula, $R.NH_2.HCl.MCl_2$, sometimes separate out when the reduction is complete. These salts may be decomposed by excess of caustic soda, and the base isolated as before.

When iron is used along with hydrochloric acid, the acid acts as a catalyst, and very little need be used in the reaction (see note under aniline). Further, steam distillation can be effected without the addition of alkali.

PREPARATION 359.—**Aniline** (*Aminobenzene*).

$$C_6H_5NH_2. \quad C_6H_7N. \quad 93.$$

This compound should be made in a pot, as shown in Fig. 37, to which is attached a reflux condenser. The metal used in this reduction is iron, and should be in as fine a state as possible. The agitation should be very efficient.

60 c.cs. of water and 120 gms. of iron powder are placed in the reduction pot, agitation being maintained during the addition. The pot is then heated to 90°–95°, and 10 c.cs. conc. hydrochloric acid (D. 1·8) are poured in ; 100 gms. nitrobenzene are then added, a few c.cs. at a time. The temperature must be held at 100°, and this can be conveniently done by regulating the addition of the nitrobenzene. When all the latter has been added, the reduction is continued at about 100° until no smell of nitrobenzene remains, or until a sample dissolves completely in dilute hydrochloric acid.

If the agitation is not powerful enough to carry through this process, the following may be adopted : 100 gms. of nitrobenzene and 60 c.cs. water and 10 c.cs. of conc. hydrochloric acid (D. 1·18) are heated in the pot up to 95°. 120 gms. iron powder are then added carefully, the temperature being maintained at about 100°. After all the iron has been added, the temperature is maintained at 100° by external heat, and agitation continued until all the nitrobenzene has been reduced.

Steam Distillation.—If direct steam can be led into the reduction pot, this process is simplified, for, by merely altering the condenser to the usual sloping position, the aniline can be distilled off. If direct steam cannot be led into the reduction pot, the contents, after the reduction is finished, are poured into a large round-bottomed flask, and steam from a steam generator led into it, the products of vaporisation being condensed in the usual way (see Fig. 14).

Separation.—The condensate is poured into a separating funnel and allowed to stand until separation into two layers is complete. This may be assisted by applying heat or by adding salt. The aniline is then poured off, dried over solid caustic soda and distilled.

$$C_6H_5NO_2 + 3Fe + 6HCl \longrightarrow C_6H_5NH_2 + 3FeCl_2 + 2H_2O.$$

Yield.—95% theoretical (70 gms.). B.P. 184° ; D. 1·026 ; important intermediate for dyestuffs.

Note.—The quantity of hydrochloric acid used in an acid reduction where iron is employed is only about $\frac{1}{40}$ of the quantity required by theory.

Several theories have been advanced to explain this reaction. Ferrous chloride is formed at the outset, according to equation (1), while ferric hydroxide appears early in the reduction. At the end of the reduction the iron is almost completely in the form of Fe_3O_4. These two reactions may be explained by equations (2) and (3), and it is probable that the ferrous chloride catalyses both.

$$(1) \qquad Fe + 2HCl \longrightarrow FeCl_2 + H_2.$$

$$(2) \qquad R.NO_2 + 2Fe + 4H_2O \longrightarrow R.NH_2 + 2Fe(OH)_3.$$

$$(3) \qquad 4R.NO_2 + 9Fe + 4H_2O \longrightarrow 4R.NH_2 + 3Fe_3O_4.$$

(A., 55, 200 ; B., 19, 903 ; 13, 1298 ; 19, 2916.)

Second Method (using tin and hydrochloric acid).

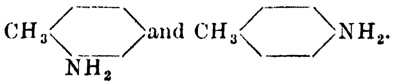
25 gms. nitrobenzene and 50 gms. granulated tin are placed in a flask fitted with a reflux condenser. Through the condenser are added 20 c.cs. conc. hydrochloric acid and the flask shaken regularly. If the reaction becomes too vigorous the flask may be cooled in cold water. A further 20 c.cs. of acid is added when the reaction slackens and this procedure repeated until 100 c.cs. of acid have been added. The reduction is completed and any unchanged nitrobenzene removed by heating on a boiling water bath for 20 minutes in the open flask. The flask is cooled and excess of strong aqueous caustic soda added to liberate the aniline and redissolve the hydroxide. The mixture is then steam-distilled until 175 c.cs. of distillate have been collected. To the distillate, consisting of two layers, water and aniline, common salt is added to reduce the solubility of the latter in water (3%). 40 c.cs. ether are added and the mixture shaken in a separating funnel, pressure being released from time to time by partially opening the stop-cock when the funnel is inverted. The ethereal extract is separated and the process repeated with 40 c.cs. fresh ether. The combined extract is dried over solid caustic potash for some hours, filtered and

distilled in portions (*caution!*) in apparatus using a Buchner flask with rubber tube attached as receiver (see p. 21). The aniline is finally distilled using an air condenser, the fraction B.P. 180°–184° being collected.

$$2C_6H_5NO_2 \xrightarrow[HCl]{Sn} (C_6H_6NH_2)_2.H_2SnCl_6 \xrightarrow{NaOH} 2C_6H_5NH_2.$$

Yield.—90% theoretical (17 gms.).

PREPARATION 360.—*o*- **and** *p*-**Toluidines** (1 : 2- *and* 1 : 4-*Methyl-amino benzenes*).

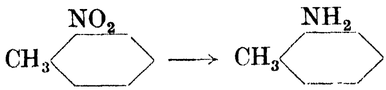


C_7H_9N. 107.

The reduction of nitrotoluene is similar to that given for nitrobenzene under aniline (p. 365). The steam distillation is similar, the *ortho*- and *para*-compounds formed in the reduction passing over.

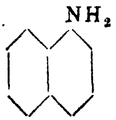
Separation of o- and p-Toluidine (*a*).—The oil is separated from the water, ice and salt added, and the mixture stirred. A whitish-yellow crystalline compound appears, which is the hydrate of the *p*-compound. This is filtered through an ice filter (Fig. 4), and the hydrate well pressed to remove any adhering oily *o*-compound. The *ortho*-compound passes through the filter along with the water, and is separated. The *para*-compound is recrystallised from alcohol. (J. S. C. I., 27, 258.) For separation by means of SO_2, see E.P. 355018.

Separation of Pure o-Toluidine (*b*).—The mixture of the *o*- and *p*-compounds is treated with conc. hydrochloric acid until slightly acid to Congo red, and water added until the solution is saturated at ordinary temperature. Saturated aqueous sodium ferrocyanide is then gradually added with shaking, when the greenish-white needles of *o*-toluidine hydro-ferrocyanide come down. The solution, after precipitation is complete, is still slightly acid. The *o*-compound is filtered off, washed with a little water, and a very little dilute hydrochloric acid. It is dried, and the base obtained from it by decomposing with caustic soda and extraction with ether. After drying the ethereal solution with potassium carbonate, and removing the ether, the base distils at 198°.



Yield.—90–95% theoretical (total *o* and *p*). *o*, B.P. 198° ; D. 1·003 ; *p*, M.P. 45° ; B.P. 200° ; D. 1·046. (J. C. S., 121, 1294.) For preparation of *m*-toluidine, see J. S. C. I., 51, 283.

ION 361.—**α-Naphthylamine.**



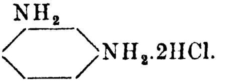
$C_{10}H_9N$. 143.

The reduction is similar to that of nitrobenzene (Preparation 359), but no condenser need be used in this case. 120 gms. iron powder and 60 c.cs. water are placed in the reduction pot, and the temperature raised to 95°. 10 c.cs. of conc. hydrochloric acid are then poured in and 100 gms. α-nitronaphthalene added gradually. The reduction is continued until a sample is completely soluble in hydrochloric acid.

Separation.—The steam distillation is carried out as in Preparation 359, using in this case superheated steam. A convenient apparatus for producing superheated steam is shown in Fig. 15. The naphthylamine is then filtered off, and crystallised from benzene or toluene.

Yield.—80–85% theoretical (65–70 gms.). M.P. 51° ; B.P. 300° ; D. 1·23. A small percentage of β-naphthylamine is formed in the reduction. (J. pr., 27, 140 ; A., 92, 401 ; 275, 217.)

PREPARATION 362.—*m*-**Phenylenediamine Hydrochloride.**



$C_6H_{10}N_2Cl_2$. 181.

This process is carried out in the usual reduction pot with reflux attached (see Fig. 37).

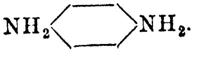
150 c.cs. water are placed in the reduction pot and heated up to 95°, and 100 gms. of *m*-dinitrobenzene are then added. 10 c.cs. of conc. hydrochloric acid and about 120 gms. of fine iron powder are added gradually, care being taken that the contents do not froth over. This process is carried on until the solution loses its yellow colour, as may be shown by spotting on filter paper. A solution of sodium carbonate is then added until an alkaline reaction is obtained. It is boiled and filtered from the iron residue. The iron residue is again boiled with water and filtered. The combined filtrates are evaporated to a convenient bulk and conc. hydrochloric acid added to precipitate the hydrochloride. This is allowed to cool, and is filtered and dried.

The crude base obtained on evaporation of the above filtrate is too soluble to be crystallised from water, and is purified by vacuum distillation.

Yield.—90% theoretical (77 gms.). M.P. 61° ; B.P. 283°. Very soluble in water. (J., 1861, 512 ; 1863, 422 ; Z. Ch., 1865, 51.)

C. V., II, 160, describes similar preparation of *m*-tolylenediamine.

PREPARATION 363.—*p*-**Phenylenediamine.**



$C_6H_8N_2$. 108.

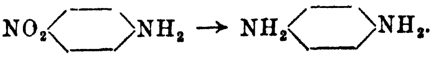
The process is similar to that used for making the *meta*-compound. In this case, however, *p*-nitroaniline is added to the mixture of iron powder, water, and acid. The following quantities are used :

100 gms. iron powder ; 5 c.cs. conc. hydrochloric acid ; 100 c.cs. water.

These are heated to 95° and 100 gms. *p*-nitroaniline gradually added. Cooling may have to be applied to regulate the action.

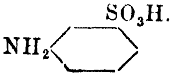
The reduction is continued as in Preparation 362 until the liquid loses its yellow colour.

Sodium carbonate is added, as before, until alkaline. After the iron residue is filtered off the filtrate is concentrated until the base crystallises.



Yield.—80% theoretical (60 gms.). M.P. 147°; B.P. 267°. (J., 1863, 422; B., 7, 871; 28, 250.)

PREPARATION 364.—**Metanilic Acid** (*Aniline-m-sulphonic acid*).

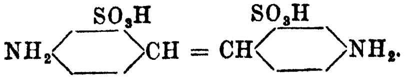


$C_6H_7O_3NS$. 173.

123 gms. nitrobenzene are sulphonated as in Prep. 288 and the mixture reduced, using iron, as in H-acid (p. 322). After the reduction mixture is neutralised, the filtrate is concentrated to about 600 c.cs. Hydrochloric acid is added until an acid reaction to Congo is obtained. The metanilic acid then crystallises out. The separation may be assisted by adding common salt.

Yield.—80% theoretical. Crystallises with $\frac{1}{2}H_2O$; intermediate for dyestuffs. (Z. a., 9, 686.)

PREPARATION 365.—**4 : 4′-Diaminostilbine-2 : 2′-disulphonic Acid.**



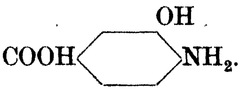
$C_{14}H_{14}O_6N_2S_2$. 370.

The sodium salt of the dinitro acid from Preparation 288 is dissolved in 300 c.cs. hot water, and hydrochloric acid is added to neutralise any free sodium carbonate. The solution is run on to 200 gms. of iron turnings. which have been previously etched by standing in 20 c.cs. of 40% acetic acid. The reduction proceeds in the normal way.

The solution is made strongly acid to Congo red with hydrochloric acid, and the diaminostilbinedisulphonic acid separates as yellow crystals After 10 hours it is filtered off and washed.

Yield.—About 40% (calculated on *p*-nitrotoluene). Important intermediate for dyestuffs. (B., 30, 3100.)

PREPARATION 366.—**4-Amino-3-hydroxybenzoic Acid.**



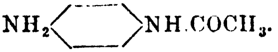
$C_7H_7O_3N$. 153.

10 gms. 4-nitro-3-hydroxy benzoic acid (see p. 274) and 200 c.cs. conc. hydrochloric acid are heated on a water bath and 30 gms. of tin slowly added. After the reaction is complete the double tin salt separates out, and is filtered. The precipitate is dissolved in 200 c.cs. of warm water and hydrogen sulphide passed until all the tin is separated. The filtrate from the tin is concentrated until crystals of the hydrochloride begin to separate.

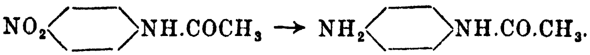
When cold, the hydrochloride is filtered, dissolved in a little water, and the free base precipitated by the addition of a conc. solution of sodium acetate. It is filtered, washed with water, and recrystallised from hot water or dilute alcohol.

Yield.—60% theoretical (5 gms.). M.P. 115°–116°. (J. C. S., 119, 1429.)

PREPARATION 367.—***p*-Aminoacetanilide.**


$C_8H_{10}ON_2$. 150.

93 gms. of aniline are converted into acetanilide, and then to nitroacetanilide, as shown in the preparations of *p*-nitroaniline (p. 280). The moist nitro compound is then added in small portions to a vessel fitted with good agitation (see Fig. 37), and containing 125 gms. iron filings, 8 c.cs. 40% acetic acid and 500 c.cs. water heated to boiling. Boiling is continued for 10 minutes after the last addition, when the solution "spotted" on filter paper should be colourless. The liquid is then cooled to 70°, and sodium carbonate is added until the reaction is alkaline.* The precipitation of the iron is completed by adding the minimum quantity of ammonium sulphide until a drop on filter paper gives no coloration with sodium sulphide. The whole is then filtered, and the filtrate evaporated to 400 c.cs. when, on cooling, the aminoacetanilide crystallises in long needles. A further crop of crystals may be obtained by evaporating the mother liquor.



Yield.—55% theoretical (80—90 gms.). M.P. 162·5°; on hydrolysis gives *p*-phenylenediamine. (B., 17, 343; A., 293, 373.)

PREPARATION 368.—***p*-Phenetidine** (1-*Ethoxy*-4-*aminobenzene*).


$C_8H_{11}ON$. 137.

1. *p-Nitrophenetole.*—140 gms. *p*-nitrophenol are dissolved in 400 gms. of 10% caustic soda solution, and the solution is placed in an enamel-lined autoclave fitted with a stirrer. 70 gms. ethyl chloride are introduced, and the mixture heated for 7–8 hours at 90°–100°. After cooling, the *p*-nitrophenetole is filtered off and washed with dilute caustic soda to remove unchanged nitrophenol, and then with water.

2. *p-Phenetidine.*—100 gms. *p*-nitrophenetole, 200 c.cs. water and 10 c.cs. conc. hydrochloric acid are placed in a flask or a sulphonating pot fitted with a good mechanical agitator (see Fig. 37). The temperature is raised to 60°, and iron filings (100 gms.) are gradually introduced over 3–4 hours. When all the iron has been added the temperature is raised to 90°, where it is maintained until the reduction is complete. The supernatant aqueous liquor is poured or siphoned off, and the sludge is steam distilled with

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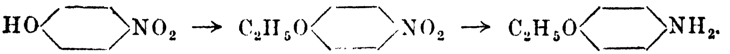
* If the sodium carbonate is added at 100° or in excess, hydrolysis of the aminoacetanilide takes place.

superheated steam at 160°–180° (p. 29), when the *p*-phenetidine distils, and is separated from the aqueous distillate by extraction with ether, and purified by distillation.



Liquid; B.P. 244°. (Am. Soc., 1, 272; B., 22, 1782; U.S.P., 1890430.)

Reaction CLXX. Action of Metals on Nitro Compounds in Alkaline Media.—The metal usually employed is zinc, although iron powder can be used in some cases. The reaction is usually carried out in presence of caustic soda.

$$Zn + 2NaOH \longrightarrow Zn(ONa)_2 + H_2,$$

and the reaction takes place in several stages.

$$\begin{array}{llll} RNO_2 & & R.N{=}N.R & \\ & + 6H \longrightarrow & \quad\downarrow & \text{azoxy—} \\ RNO_2 & & \quad O & \\ & + 2H \longrightarrow & R.N{=}N.R & \text{azo—} \\ & + 2H \longrightarrow & R.NH.NH.R & \text{hydrazo—} \end{array}$$

Sodium arsenite may be used for reduction to the azoxy stage (C. V., II, 57).

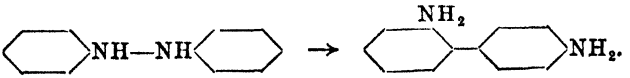
$$4RNO_2 + 3As_2O_3 + 18NaOH \longrightarrow 2RN{=}\underset{\substack{\downarrow \\ O}}{N}R + 6Na_3AsO_4 + 9H_2O.$$

A slight excess of metal is required, and each stage can be isolated by using the required amount of metal, e.g. 3 atoms for the azoxy-, 4 for the azo-, and 5 for the hydrazo-stage. A certain amount of primary amine is also formed. O. S., 22, 28, describes the isolation of azobenzene.

Good agitation is essential, and a solvent may be used in some cases. This, however, is not always necessary if the agitation is efficient. The compounds are isolated by dissolving out the zinc with *ice-cold* hydrochloric acid. The hydrazo compounds, when heated with mineral acids, undergo a rearrangement (benzidine transformation).

$$C_6H_5.NH—NH.C_6H_5 \longrightarrow NH_2C_6H_4—C_6H_4NH_2.$$

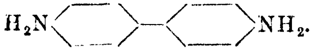
the NH_2 groups taking the *p*-position, although a certain amount of *o-p*-compound is formed, as well as *o*- and *p*-semidines (see p. 166).



The sulphates of these last compounds are soluble in water, and they can, therefore, be separated from the *p-p′*-compounds by means of sodium sulphate or sulphuric acid.

For mechanism of benzidine conversion, see J. C. S., 1946, 406, 638

PREPARATION 369.—Benzidine (4 : 4'-*Diamino-diphenyl*).



$C_{12}H_{12}N_2$. 184.

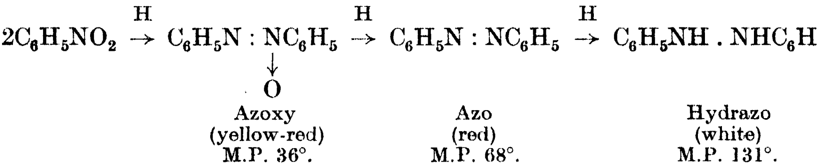
1. *Hydrazobenzene.*—100 gms. nitrobenzene, 100 gms. of conc. caustic soda (30% solution) and 100 gms. water are placed in the reduction pan (see Fig. 37) and heated to 95°, and all external heat cut off. Zinc dust of good quality (over 85% Zn, p. 518) is then added, a few gms. at a time. The heat of reaction will raise the temperature to 100°, and when it cools to 98° a few more gms. of zinc dust are added, the temperature being allowed to drop to 98° before any further addition of zinc is made.

During the course of the reduction small samples are abstracted by means of a rod. It will be noticed that first a yellowish-red crystalline solid (azoxybenzene), then a red crystalline solid (azobenzene), and ultimately a lemon-yellow crystalline solid (hydrazobenzene) are formed. When this stage is reached further addition of zinc is stopped, and the whole is allowed to run for ½ hour, external heat being applied. In all about 160 gms. of zinc dust will be necessary, the amount, of course, depending on the metallic content of the dust.

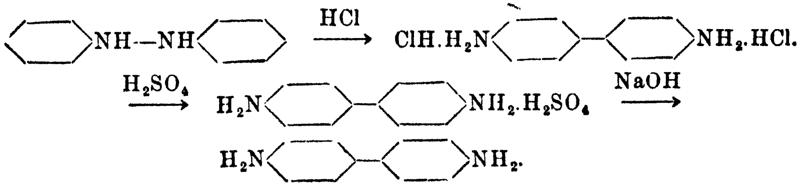
The whole is quickly cooled by adding a large bulk of cold water to the reduction pot, agitation being maintained.

When cooled to 30°, the contents of the pot are poured into a large enamelled bucket. A large quantity of ice is added, and conc. hydrochloric acid is poured in, with stirring. The temperature should not rise above 5°. Acid is added until the liquid in the bucket gives an acid reaction to Congo red paper. The hydrazobenzene is then filtered off and washed with cold water.

2. *Benzidine.*—Hydrazobenzene is removed to a basin, boiled slowly with 500 c.cs. water and 120 c.cs. conc. hydrochloric acid and filtered from zinc residue. A saturated solution of sodium sulphate is then added until the benzidine sulphate is completely precipitated (test). This is filtered off and is well washed with warm water until free of acid. The moist benzidine sulphate is removed, heated to 50° with a little water, and caustic soda solution (30%) added with stirring until the liquid is just alkaline (test with phenolphthalein). When cold, the free base is filtered off and dried at 50°. It may be crystallised from benzene, alcohol or from hot water (see p. 499).

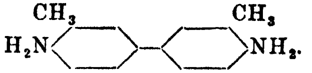


$$2C_6H_5NO_2 \xrightarrow{H} \underset{\underset{O}{\downarrow}}{C_6H_5N : NC_6H_5} \xrightarrow{H} C_6H_5N : NC_6H_5 \xrightarrow{H} C_6H_5NH\,.\,NHC_6H_5$$



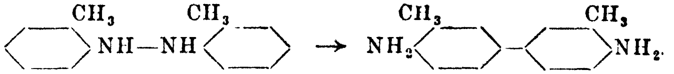
Yield.—75–80% theoretical (55–60 gms.). Lustrous plates ; M.P. 128° ; monohydrate M.P. 105° ; B.P. over 400°, with decomposition ; slightly soluble in hot water ; soluble in alcohol and in benzene. Important intermediate for dyestuffs. (Z. a., 6, 67 ; O. S., 22, 28.)

PREPARATION 370.—*o*-**Tolidine** (4 : 4′-*Diamino*-3 : 3′-*dimethyldiphenyl*).



$C_{14}H_{16}N_2$. 212.

The process is exactly the same as for benzidine, except that 100 gms. of distilled *o*-nitrotoluene (containing not more than 4% *p*-nitrotoluene) are used.



Yield.—65% theoretical (48 gms.). Plates ; M.P. 128° ; slightly soluble in water ; soluble in alcohol and in benzene ; salts about 5 times more soluble than those of benzidine ; intermediate for dyestuffs. (B., 17, 467 ; 20, 2017.)

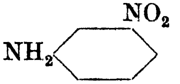
Reaction CLXXI. Action of Sulphides or of Polysulphides on Nitro Compounds.—Sulphides of sodium or ammonium are employed—the former industrially—in aqueous or aqueous alcoholic solution for the reduction of poly-nitro compounds to nitroamines :

$$C_6H_4(NO_2)_2 + Na_2S_2 + H_2O \longrightarrow C_6H_4(NO_2)NH_2 + Na_2S_2O_3.$$

Mono-nitro compounds react, but less readily, especially with sodium sulphide.

$$ArNO_2 + Na_2S + H_2O \longrightarrow ArNH_2 + Na_2SO_3.$$

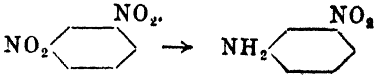
PREPARATION 371.—*m*-**Nitroaniline.**



$C_6H_6O_2N_2$. 138.

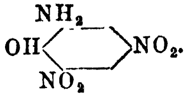
This experiment should be performed in a good fume cupboard. 20 gms. *m*-dinitrobenzene and 900 c.cs. water in a large beaker are maintained at 85° and briskly stirred whilst a previously-prepared and warm solution of 30 gms. crystalline sodium sulphide and 8 gms. finely-divided sulphur in 120 c.cs. water is added dropwise from a tap funnel. The dinitrobenzene must be maintained in the form of a fine, oily dispersion throughout the addition. Boiling is continued until reduction is complete. This is ascertained by spotting copper sulphate solution on filter paper alongside a drop of reaction product withdrawn from time to time. Formation of copper sulphide indicates completion of reaction.

The product is filtered to remove sulphur and the filtrate cooled. When the separation of crystals is complete they are filtered, washed with water, and recrystallised therefrom.



Yield.—70% theoretical (58 gms.). M.P. 112·4°; B.P. 285°; intermediate for azo dyestuffs. (C. Z., 37, 299.)

PREPARATION 372.—Picramic Acid (2-*Amino*-4 : 6-*dinitrophenol*).



$C_6H_5O_5N_3$. 199.

10 gms. picric acid and 3·5 gms. of caustic soda are dissolved in 600 c.cs. water in a large flask and heated up to 55° with vigorous stirring, when a solution of 40 gms. crystalline sodium sulphide ($Na_2S.9H_2O$) in 100 c.cs. water is gradually added.

127·5 gms. of powdered picric acid are then gradually added concurrently with 220 gms. sodium sulphide in 400 c.cs. of water. The addition of the picric acid should end at the same time as the sulphide solution. The temperature should not rise above 65°, ice being added, if necessary. Stirring is continued for about 10 minutes after this addition, and then 400 gms. ice are introduced. The sodium salt of picramic acid is immediately precipitated. After standing for 10 hours it is filtered off and washed with brine.

The free acid is obtained by stirring up the sodium salt with 500 c.cs. water, heating to 80°, and acidifying with dilute sulphuric acid until just acid to Congo red.

Yield.—90% theoretical (100 gms.). Red needles, soluble in water; M.P. 168°–169°. (See also A., 88, 281; 96, 83; J. Soc. Dyers, 46, 365.)

Reaction CLXXII. Action of Reducing Agents on Azo Compounds.—

$$X\text{—}N{=}N\text{—}Y \xrightarrow{H_2} X.NH_2 + H_2N.Y.$$

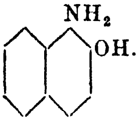
This reaction is useful for determining the constitution of azo dyes and for preparing amines. The reducing agents employed are metal and acid, zinc dust and water or ammonia, stannous chloride, or sodium hydrosulphite ($Na_2S_2O_4$) in alkaline solution. The last mentioned is the most commonly used and reacts as follows:

$$Na_2S_2O_4 + 2H_2O \longrightarrow 2NaHSO_3 + 2H.$$

(See J. Soc. Dyers, 37, 206.)

The reaction is carried out with or without heat, until the suspended or dissolved colour gives place to a colourless product containing one or two primary amines.

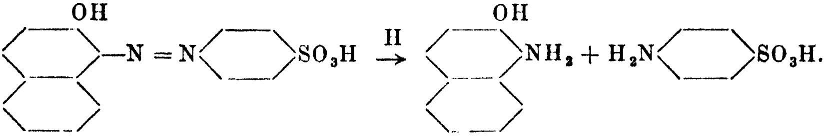
PREPARATION 373.—α-Amino-β-Naphthol.



$C_{10}H_9ON$. 159.

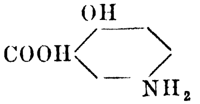
50 gms. Orange II (see Preparation 386) are dissolved in 500 c.cs. boiling water, and to this are added 65 gms. tin dissolved in 375 c.cs. conc. hydrochloric acid. When decolourisation is complete the solution

is filtered quickly and on cooling the hydrochloride of amino-naphthol separates out as colourless crystals.



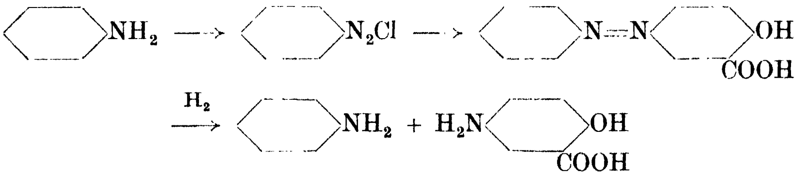
Fine needles, slightly soluble in dilute hydrochloric acid and in alcohol. See also C. V., II, 33, for preparation from α-nitroso-β-naphthol. (Prep. 242.)

Preparation 374.—**Aminosalicylic Acid** (*2-Hydroxy-5-aminobenzoic Acid*).



$C_7H_7O_3N$. 153.

A mixture of 50 gms. of aniline hydrochloride, 60 gms. conc. hydrochloric acid, and 300 gms. ice is diazotised (p. 380) by adding a solution of 29 gms. of sodium nitrite in 100 c.cs. of water to the mixture. After 15 minutes the diazonium salt is run into a solution of 53·3 gms. of salicylic acid in 220 gms. of crystallised sodium carbonate and a litre of water. The sodium salt separates, is filtered and washed with a little water. The azo compound is next boiled with about a litre of water, sodium hydroxide solution added until alkaline and dry sodium hydrosulphite ($Na_2S_2O_4$, about 135 gms.) added until reduction is complete. After aniline is removed by steam distillation acid is added and the free amino-salicylic acid separates.



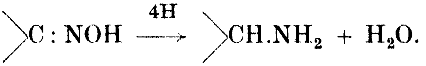
Decomposes at 280°. (B., 32, 81.) See also Abs. B., 1936, 440.

Reaction CLXXIII. Action of Reducing Agents on Nitroso Compounds.

$$R.NO \longrightarrow R.NH_2.$$

This reduction to a primary amine is usually carried out in acid solution, or with bisulphite. For example, see Preparation 393, also C. V., II, 33.

Reaction CLXXIV. Reduction of Oximes to Amines with Metallic Sodium or Sodium Amalgam.



$$>C:NOH \xrightarrow{4H} >CH.NH_2 + H_2O.$$

The reaction serves for the production of amines from aldehydes or ketones through the oximes of these compounds.

Reduction with metallic sodium is usually carried out in absolute alcoholic or moist ethereal solution. Methyl, ethyl or amyl alcohol may be used, but for various reasons absolute ethyl alcohol is the most frequently employed, the reaction being conducted at or near the boiling point of the alcohol. When ordinary alcohol (about 90%) is used, the sodium spurts about on the surface of the liquid, and most of the hydrogen escapes as gas. With the absolute alcohol, the sodium—with the exception of the first portions added—melts to a ball which remains largely, and at times completely, immersed in the liquid, and hence the hydrogen generated is more liable to react. In some cases the sodium alcoholate formed also acts as a reducing agent, and is thereby converted into the sodium salt of the corresponding acid.

When the reduction is carried out with sodium amalgam the oxime is dissolved in aqueous alcohol, and acetic acid and amalgam added at intervals so that the solution is slightly acid throughout the reduction.

PREPARATION 375.—α-**Phenylethylamine** (1-*Phenyl*-1-*amino-ethan*).

$C_6H_5CH(NH_2)CH_3$. $C_8H_{11}N$. 121.

50 gms. acetophenone oxime dissolved in 100 c.cs. absolute ethyl alcohol are placed in a litre round-bottomed flask having a long neck. The flask is fitted with a cork carrying an addition tube (p. 56), and the sloping limb of the latter is attached to a reflux water condenser, while the vertical limb is closed with a cork. A bottle containing benzene and pieces of bright sodium (about 50 gms.) of such a size that they slip easily down the addition tube is prepared. The flask is heated on a water bath until the alcohol boils. Pieces of sodium (one at a time) are introduced through the vertical limb of the addition tube, a piece of drawn-out glass rod being used to remove the sodium from the bottle, and the benzene adhering need not be removed with filter paper. The first pieces of sodium cause vigorous reaction, but the reaction soon becomes moderate. The alcohol is kept actively boiling all the time. When the reaction becomes sluggish a further 100 c.cs. absolute alcohol are added, and addition of sodium to the boiling solution is continued, as before. Altogether about 500 c.cs. absolute alcohol and 40 gms. sodium are required. The addition of sodium is continued until a test, carried out in the following way, shows that reduction is complete :—

A sample (about 2 c.cs.) is withdrawn, diluted with an equal volume of water, and about 2 c.cs. conc. hydrochloric acid added. The mixture is boiled for a minute with Fehling's solution (I) prior to the addition of an excess of Fehling's solution (II). If no reduction of the Fehling's solution takes place the reduction of the oxime is complete.

When reduction is complete and all the sodium dissolved, the flask is cooled, and 200 c.cs. water added to decompose the ethoxide. A sloping condenser is then attached and heating continued on a water bath until distillation slackens. A further 200 c.cs. water are then added and heating continued on a sand bath until all the alcohol has passed over and a thermometer inserted in the neck of the flask registers 96°. The contents of the flask, consisting of a layer of amine and a layer of caustic soda, are cooled and poured into a separating funnel. A little ether is used to complete the transference of the amine. The total distillate, containing alcohol, water, and α-phenylethylamine, is made strongly acid with hydrochloric acid and evaporated to small bulk, after which the residual aqueous solution of amine hydrochloride is added to the contents of the separating funnel, where the excess of caustic soda liberates the base. After some time the lower layer of caustic soda is run off, the upper layer of amine is agitated with 20 c.cs. 0·720 ether, and the final traces of caustic soda separated. The products from the reduction of a number of 50 gms. instalments of acetophenoneoxime may with advantage be united at this stage. The ethereal solution along with ethereal washings is dried over anhydrous sodium sulphate and distilled. At first ether containing some amine passes over—this portion of distillate which is alkaline to litmus is kept separate for recovery as carbamate. The temperature then rises rapidly to 186°–187°, at which the amine distils; the condenser, which should be long, is only half-filled with water at this stage. Owing to the avidity of the amine for carbon dioxide it should be collected in a flask having a soda-lime side tube.

$$C_6H_5C(NOH).CH_3 \rightarrow C_6H_5.CH(NH_2).CH_3.$$

$$2C_6H_5CH(NH_2)CH_3 + CO_2 \rightarrow C_6H_5CH(CH_3)NHCOONH_3CH(CH_3).C_6H_5.$$

Yield.—90% theoretical (40 gms.). Dry carbon dioxide passed into the dry ethereal distillate causes precipitation of a quantity of carbamate which increases the yield to 95%.

α-Phenylethylamine.—B.P. 186°; easily soluble in organic solvents; moderately soluble in water; strong base; absorbs carbon dioxide when exposed to air. (J. C. S., 83, 1147; 1928, 2483; J. R. T. C., 1926, 59). See also C. V., II, 503; O. S., XXIII, 68. (For resolution, see p. 416.)

α-Phenylethylamine Carbamate.—M.P. 101°–102°; easily soluble in water or in alcohol; on heating, dissociates into amine and carbon dioxide.

Catalytic Reduction of Oximes.—Oximes may be reduced to primary amines in good yield by hydrogen in presence of nickel-keiselgühr (p. 178). (Am. Soc., 55, 1669.)

CHAPTER XXIV

HYDROGEN TO NITROGEN

HYDROXYLAMINES AND HYDRAZINES

Reaction CLXXV. Action of Metallic Zinc on Nitro Compounds in Neutral Media.

$$R.NO_2 + 4H \longrightarrow R.NHOH.$$

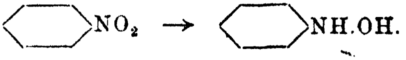
This is a standard method of preparing hydroxylamines, e.g. nitrobenzene gives phenylhydroxylamine. Although the reaction may be carried out by generating the hydrogen by the interaction of zinc and water, better yields are obtained by adding a neutral salt, such as ammonium chloride. In order to prevent the reduction going beyond this stage it is necessary to keep down the temperature. (B., 27, 1432, 1548 ; D.R.P., 84, 138.)

If the reduction is carried out in presence of alcohol at 70°–75°, azoxy-, azo-, and, in some cases, hydrazo-compounds can be obtained. These reductions take place *via* intermediate organo-zinc salts which decompose yielding the azoxy-compound, etc., and a double basic zinc salt of the formula, $2NH_4Cl, 5Zn(OH)_2$. (J. C. S., 123, 2466 ; 125, 1108 ; J. R. T. C., 1929, 43 ; 1930, 191.)

PREPARATION 376.—**Phenylhydroxylamine** {*(Hydroxy-amino)-benzene)*}.

$$C_6H_5NHOH. \quad C_6H_7ON. \quad 109.$$

12 gms. of nitrobenzene are mixed in a beaker with 250 c.cs. of water containing 6 gms. of ammonium chloride and well stirred, the temperature being kept at 10°–15°. 18 gms. of good zinc dust are added in four equal parts after intervals of ¼ hour. When the smell of nitrobenzene has disappeared the stirring is stopped. The mixture is filtered at the pump the filtrate being put on one side, and the precipitate washed, by adding 200 c.cs. of water at 45° while the pump is not working, and then the water gradually sucked through by means of the pump. The filtrate and the washings are separately saturated with sodium chloride, and cooled to 0°. After a short time the phenylhydroxylamine separates out ; it is filtered and dried without washing.



Yield.—65% theoretical (7 gms.). Colourless crystals ; M.P. 81°. (D.R.P., 89978 ; J. C. S., 123, 2464 ; Am. Soc., 45, 1784 ; O. S., IV, 56.)

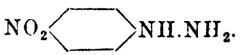
Reaction CLXXVI. Reduction of Diazonium Salts to Hydrazines.

$$RN_2Cl + 4H \longrightarrow RNH.NH_2.HCl.$$

Certain reducing agents (e.g. stannous chloride or alkali sulphites) reduce diazonium salts to hydrazines. This action may be contrasted with the reduction of diazonium salts to hydrocarbons (p. 384) and of azo-compounds to amines (Reaction CLXXII).

The reaction is somewhat similar to that (CLXXII) of reducing agents on azo-compounds. The hydrazines are universally obtained by this reaction, the same reducing agents being used as in the case of azo-compounds.

PREPARATION 377.—*p*-**Nitrophenylhydrazine.**



$C_6H_7O_2N_3$. **153.**

10 gms. *p*-nitroaniline dissolved in 20 c.cs. of conc. hydrochloric acid are diazotised (p. 380) at 5°–10° with 6 gms. sodium nitrite dissolved in 12 c.cs. water. The filtered solution, neutralised with aqueous sodium carbonate and diluted to 100 c.cs., is slowly added, with stirring, and while still cold to 50 c.cs. of an ice-cold solution previously prepared by saturating a solution of 6 gms. caustic potash in 30 c.cs. water with sulphur dioxide and then adding 10 gms. potassium carbonate. The potassium nitrophenyl disulphonate, which possibly has the structure (*A*) below is filtered, washed with a little cold water, and is then, while undried, treated with 20 c.cs. conc. hydrochloric acid and 20 c.cs. water. This mixture is heated in a boiling water bath for 5 minutes. *p*-Nitrophenylhydrazine hydrochloride, which separates on cooling, is disolved in a small amount of water and treated with a saturated solution of sodium carbonate (6 gms.) containing sodium acetate (5 gms.) until neutral. The free *p*-nitrophenylhydrazine may be crystallised from boiling water.

$NO_2C_6H_4N_2Cl \longrightarrow NO_2C_6H_4N_2SO_3Na \longrightarrow$

$NO_2C_6H_4N(SO_3H)NHSO_3Na$ (*A*)

$\xrightarrow{HOH} NO_2C_6H_4NH.NHSO_3Na \longrightarrow$

$NO_2C_6H_4NHNH_2HCl \longrightarrow NO_2C_6H_4NH.NH_2$.

Yield.—50% theoretical (4·5 gms.). Orange-red needles ; M.P. 157°, with decomposition ; soluble in alcohol and in ligroin. (J. C. S., 121, 719.)

PREPARATION 378.—**Phenylhydrazine.**

$C_6H_5NH.NH_2$. $C_6H_8N_2$. 108.

Method I.—10 gms. freshly-distilled aniline are added to a solution of 30 gms. conc. hydrochloric acid in 75 c.cs. water and diazotised with 8 gms. sodium nitrite in 30 c.cs. water, the temperature being kept about 0°. 30 gms. common salt are added with shaking, and the solution cooled in a freezing mixture. 60 gms. stannous chloride in 25 gms. conc. hydrochloric acid are then added, and after standing for some hours the hydrochloride of phenylhydrazine separates, is filtered off and washed with a little saturated salt solution. It is transferred to a flask and treated with excess of caustic soda solution, when the free base is extracted with ether The ethereal solution is dried with caustic potash, and the ether removed by evaporation. The phenylhyrazine may be purified, if desired, by freezing or by distilling *in vacuo*.

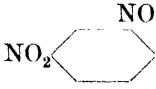
$$C_6H_5NH_2 \longrightarrow C_6H_5N_2Cl \xrightarrow{H_2} C_6H_5NH.NH_2.HCl.$$

Yield.—90% theoretical (10 gms.).

Method II.—10 gms. aniline are dissolved in acid and water and diazotised as before. The diazonium solution is poured into a saturated solution of sodium sulphite containing 34 gms. Na_2SO_3. The liquid is now heated with zinc dust and a little acetic acid till it becomes colourless, when it is filtered hot. Sodium phenylhydrazine sulphonate passes into the filtrate, and is immediately mixed with one-third of its volume of fuming hydrochloric acid (*caution!*). This converts it into phenylhydrazine hydrochloride, which is thrown out of solution, filtered, and well pressed. The free base is liberated as before.

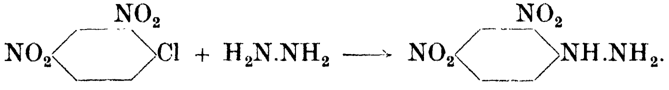
Yield.—75% theoretical (8 gms.). Colourless crystals; M.P. 23°; B.P. ^{760} 243·5° (decomposition); B.P. ^{12} 120°; soluble in alcohol, ether, benzene. (B., 16, 2976; 26, 19; 31, 346; O. S., II, 71.)

PREPARATION 379.—**2 ; 4-Dinitrophenylhydrazine.**



$C_6H_6.N_4O_4$. 198.

14 gms. hydrazine sulphate are agitated with 50 c.cs. hot water and 35 gms. potassium acetate added. The mixture is boiled for 5 minutes, then cooled to about 70° and 30 c.cs. alcohol added to precipitate potassium sulphate which is collected on a filter and washed with 25 c.cs. alcohol. The filtrate and washings are heated under reflux with 20 gms. 2 : 4-dinitrochlorobenzene in 100 c.cs. alcohol. After 1 hour the mixture is cooled, dinitrophenylhydrazine collected and washed with a little warm alcohol. A second crop may be obtained by concentrating the mother liquor.



Yield.—80% theoretical (16 gms.). Red needles. M.P. 198°, with decomposition. Almost insoluble in dilute acids. Important reagent for identification of aldehydes and ketones (see below). C. V., II, 228.

Preparation of 2 : 4-*dinitrophenylhydrazones.*—A stock solution (Brady's reagent) is made as follows: 2 gms. dinitrophenylhydrazine are dissolved in 4 c.cs. conc. sulphuric acid and 30 c.cs. methyl alcohol added slowly with cooling. After warming to dissolve, 10 c.cs. water are carefully added.

About 0·1 gm. of the carbonyl compound dissolved in the minimum of methyl alcohol is treated with 3–5 c.cs. reagent. The dinitrophenylhydrazone separates at once or on heating for 5 minutes. In difficult cases dil. sulphuric acid facilitates separation. The dinitrophenylhydrazones may be crystallised from alcohol or glacial acetic acid and serve for the identification (by melting point) of carbonyl compounds.

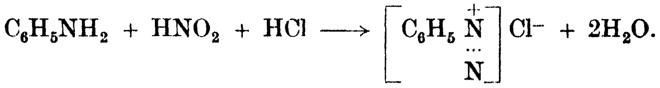
CHAPTER XXV

THE LINKING OF NITROGEN TO NITROGEN

DIAZONIUM COMPOUNDS

Reaction CLXXVII. Action of Nitrous Acid on Primary Aromatic Amines.

Diazonium compounds are formed in this way.



$$C_6H_5NH_2 + HNO_2 + HCl \longrightarrow \left[C_6H_5 \overset{+}{N} \overset{\vdots}{\underset{}{}} N \right] Cl^- + 2H_2O.$$

Diazonium compounds are usually prepared in mineral acid solution, and the nitrous acid generated from sodium nitrite. Sufficient acid must be used to generate nitrous acid and to form the salt of the base, and still leave the solution acid. In practice $2\frac{1}{4}$–$2\frac{1}{2}$ mols. of hydrochloric acid are generally employed. In most cases it is essential that the reaction be carried out at about 0°, as many diazonium solutions decompose above this temperature. The reaction goes very readily in some cases ; but in others, and especially where an acid group is present, e.g. naphthylamine sulphonic acids, the reaction is only carried out with difficulty. It is possible to diazotise a solid in suspension, but the reaction is usually very slow. If the solid is dissolved and reprecipitated in a fine state of division the action goes much more quickly.

In the case of acidic substances, the compound is dissolved in sodium carbonate or caustic soda solution, and reprecipitated with the requisite amount of acid and then diazotised.

Commercial sodium nitrite contains 1–3% sodium nitrate, the harmful effect of which on diazonium compounds may be obviated by adding to the amine solution or the nitrite solution an amount (1·5–4·5% of the weight of nitrite used) of sodium metabisulphite slightly in excess of that necessary to reduce the nitrate. Diazonium compounds prepared in this way or with pure sodium nitrite are much more stable (J. Soc. Dyers, 41, 275).

Diazotisation.—In the ordinary process of diazotisation the base is dissolved in the requisite quantity of acid, with heating if necessary, and excess of ice is added to bring the temperature down to 0°–5°. Sodium nitrite in the form of a 10% solution is then run in until the end point is reached.

The End Point.—The reaction is complete when on stirring after each addition, and testing with starch-iodide solution or paper, a distinct blue colour is obtained at once. A drop of the solution is removed on a glass rod at intervals and placed on the starch-iodide paper, or on a piece of dry filter paper near a drop of starch-iodide solution (see p. 512). Whenever the blue colour is obtained, and this colour persists when another test is made after 3 minutes, the reaction is complete. A blue colour developed on the paper after a time is disregarded. The nitrite should be added at such a rate that no free nitrous acid is evolved. It is essential that the starch-iodide solution or paper should be tested with a very dilute acidified solution of sodium nitrite before use.

It is not usually necessary to isolate the diazonium salt from solution, although in some cases this separates out as the reaction proceeds. If sufficient acid is not present, an aminoazo compound may be precipitated, due to the " coupling " (see p. 387) of the diazonium compound with the excess of base. In fact, this is one method of forming aminoazo compounds—by diazotising in presence of about half the quantity of acid necessary for the complete diazotisation.

In certain instances when negative substituents are present it is necessary to use other acids in place of hydrochloric to bring about diazotisation, e.g. nitrosylsulphuric acid, in presence of conc. sulphuric (J. pr., 56, 48), glacial acetic (J. C. S., 1933, 1620), or phosphoric acid (Am. Soc., 1933, 4531).

Stabilised diazo compounds can be prepared as diazonium sulphates (J. C. S., 1947, 325), diazonium aryl sulphonates (J. C. S., 1940, 207), diazonium cobaltinitrites (J. C. S., 1944, 22), zinc chloride double salts. Some of these, known as " Fast Salts " are commercially applied, the fabric being first impregnated with an alkaline solution of a naphthol and then immersed in a separate bath of the diazonium compound.

For printing, a mixture of naphthol and stable diazo salt can be applied to the cloth and coupled as required. For this the Fast Salt type of compound is unsuitable and other types are used :

1. Nitrosoamines or anti-diazotates, formed by action of caustic soda on diazonium salt solutions.

2. Diazoamino or diazoimino compounds formed by action of diazonium compounds on certain primary or secondary amines, respectively, are used in the form of mixtures with sodium salts of naphthols ("Rapidogen " dyes). They are developed by steaming in an acid atmosphere, e.g. acetic acid vapour. They are stable in neutral or alkaline conditions, but yield diazonium salts and amines on acidification.

Preparation of Diazonium Compounds (in Solution).

1. *From Aniline,* $C_6H_5N_2Cl$.

9·3 gms. aniline are run into 100 gms. of water and 45 gms. conc. hydrochloric acid. 100 gms. ice are added, and the whole is stirred till temperature reaches 0°. 7 gms. sodium nitrite (as a 10% solution) are then gradually added, preferably by a tube leading under the surface of the solution.

The temperature should not rise above 7°–8°. Slow stirring is continued all the time, except when tests are being made. When a distinct blue colour is obtained on starch-iodide paper at once, which persists after another test in 3 minutes, the diazotisation is complete.

2. *From Benzidine,* $ClN_2C_6H_4—C_6H_4N_2Cl$, *or Tolidine.*

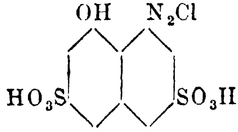
The process is similar to above, 18·4 gms. benzidine or 21·2 gms. tolidine being dissolved by heating in 300 gms. water and 90 gms. conc. hydrochloric acid. After cooling to 0°, the diazotisation is carried out as before. In these cases tetrazonium compounds are formed.

3. *From p-Nitroaniline,* $NO_2C_6H_4N_2Cl$.

(*a*) 13·8 gms. *p*-nitroaniline are powdered and added to a mixture of 150 gms. water, 45 gms. conc. hydrochloric acid, and 150 gms. ice, and stirred for 15 minutes, the temperature being under 5°. 7 gms. sodium nitrite (10% solution) are introduced *quickly*, the usual test with starch iodide being applied after all of the nitrite solution has been added.

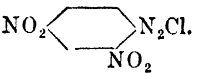
(*b*) 13·8 gms. *p*-nitroaniline are added to 70 gms. water and 45 gms. conc. hydrochloric acid, and heated to dissolve. The solution is then cooled and diazotised, as before.

4. *From H Acid,*



34·1 gms. H-acid are introduced into 400 gms. water and 6 gms. sodium carbonate at a temperature of 40°–50°. The solution should be alkaline. This is run into a mixture of 55 gms. hydrochloric acid and 500 gms. water. The mixture is cooled to 5°, and 7 gms. sodium nitrite (10% solution) are then added (see p. 380).

5. *From Dinitroaniline,*



8 gms. sodium nitrite are dissolved in conc. sulphuric acid by heating to about 50°. The solution is cooled to 20°, and 18·3 gms. finely-powdered dinitroaniline are gradually added. When all has been added, stirring is continued for 2 hours at 20°–30°. The solution is then poured on to ice and filtered. The diazonium compound is thus isolated as a paste.

PREPARATION 380.—**Diazoaminobenzene** (*Benzeneazoanilide*).

$C_6H_5N{=}N.NH.C_6H_5$. $C_{12}H_{11}N_3$. 197.

10 c.cs. sulphuric acid, 600 c.cs. water, and 20 gms. of aniline are warmed to 30°, and a solution of 7·5 gms. sodium nitrite in a little water added with constant stirring. 50 gms. sodium acetate in 200 c.cs. water are added and the solution maintained at 30° for 15 minutes, and cooled. The diazoaminobenzene is then filtered off, washed with water, and dried on a porous plate. It may be recrystallised from warm petroleum, but the solution should not be boiled for any length of time as the compound is thereby decomposed.

$$C_6H_5N\,(:N).HSO_4 + NH_2.C_6H_5 \longrightarrow C_6H_5N : N.NHC_6H_5 + H_2SO_4.$$

Yield.—80% theoretical (17 gms.). Golden-yellow plates; M.P. 96°; explodes when heated slightly above its M.P.; O. S., XIV, 24.

PREPARATION 381.—**Diazobenzene Sulphate** (*Benzene Diazonium Sulphate*).

$C_6H_5.N\ (:\ N).SO_4H.$ $C_6H_6O_4N_2S.$ 202.

15 gms. (1 mol.) of aniline and 140 gms. of *absolute* alcohol are mixed, and 30 gms. (2 mols.) of conc. sulphuric acid run in, slowly, and with constant shaking. The precipitate of aniline sulphate, which first appears, redissolves. The mixture is kept at 30°–35° (thermometer in liquid), out of direct sunlight, while 20 gms. (1 mol.) of amyl nitrite are dropped in from a tap funnel. The whole is then left in ice-water for $\frac{1}{2}$ hour, and the crystals which have separated filtered off at the pump and washed with a little alcohol. As diazobenzene sulphate is explosive the precipitate must be kept moist. In that state it can be used for the various reactions described below.*

$$(C_6H_5NH_2)_2H_2SO_4 + 2C_5H_{11}ONO + H_2SO_4$$
$$= 2C_6H_5N\ (:\ N)SO_4H + 2C_5H_{11}OH + 2H_2O.$$

Colourless needles ; soluble in water ; decomposes explosively at about 100°. (B., 1930, 1666.)

For general method of preparing solid aryldiazonium sulphates, see J. C. S., 1947, 325.

PREPARATION 382.—**Diazobenzene Nitrate** (*Benzene Diazonium Nitrate*)

$C_6H_5.N(:\ N).NO_3.$ $C_6H_5O_3N_3.$ 167.

Owing to the highly explosive nature of the diazobenzene nitrate, its preparation should never be undertaken except the compound is wanted for research or some special purpose. 20 gms. of aniline are placed in a beaker, well cooled, and "boiled-out" nitric acid, previously diluted with half its volume of water, carefully added till the mixture sets to a thick crystalline paste—aniline nitrate. The crystalline mass is filtered off at the pump, and washed with a little cold water. 5 gms. of the moist salt are finely-powdered and placed in a small flask with enough water just to cover the substance. The flask is now well cooled in ice-water, and nitrous fumes (for preparation, see p. 520) are led in with frequent agitation until all the aniline nitrate has disappeared. At no time must the temperature of the flask rise above 10°. (Should there not be sufficient water to keep all the diazobenzene nitrate formed in solution, its crystalline form will easily enable it to be distinguished from the aniline salt.) When the reaction is finished the contents of the flask are poured into 3 times their volume of absolute alcohol, and ether is added to this mixture as long as crystals separate. If too much water has been added to the aniline nitrate from the beginning, a thick aqueous solution of diazobenzene nitrate separates out in place of the crystals. If this occurs, the ether-alcohol is decanted off, and the residue redissolved in absolute alcohol, and reprecipitated with ether. On no account must large quantities of the preparation be allowed to dry. If it has to be preserved it must be kept moist, or, better, in

---

* Any of the diazonium compound which remains over should be dissolved in water and poured away.

aqueous solution. The usual diazo reactions can be carried out with the latter.

$$C_6H_5.NH_2 + HNO_3 = C_6H_5NH_3.NO_3.$$

$$2C_6H_5.NH_3.NO_3 + NO + NO_2 = 2C_6H_5.N(:N).NO_3 + 3H_2O.$$

Colourless needles ; extremely explosive in the dry state ; very soluble in water ; insoluble in ether ; on heating decomposes explosively. (A., 137, 41.)

Diazobenzene Chloride.—Aniline is diazotised with amyl nitrite in dry alcohol through which hydrogen chloride is passed. On the addition of ether the diazonium chloride is precipitated. The salt is explosive in the dry form.

Reactions of Diazonium Compounds

The following reactions are performed with about 1 gm. of moist diazobenzene sulphate (Prep. 381). Some of the reactions are illustrated by preparations.

1. The substance is heated with a few c.cs. of ethyl alcohol, when vigorous effervescence takes place, and the liquid turns red. On adding water an oil consisting of benzene and a little phenetole separates on the surface. See *Organic Reactions*, Adams, Vol. II, 262.

$$C_6H_5.N_2.SO_4H + C_2H_5OH = C_6H_6 + N_2 + CH_3.CHO + H_2SO_4.$$

$$C_6H_5.N_2.SO_4H + C_2H_5OH = C_6H_5.O.C_2H_5 + N_2 + H_2SO_4.$$

2. A solution of about 1 gm. of the substance in a little water is cooled in ice, made alkaline with caustic soda, and treated with a cold, alkaline solution of stannous hydrate, made by treating about 4 gms. of stannous chloride in twice its weight of water, and adding 40% caustic soda solution until the precipitate redissolves. Effervescence occurs, nitrogen is liberated, and benzene separates on the surface of the liquid.

$$C_6H_5.N_2.ONa + Sn(ONa)_2 + H_2O = C_6H_6 + O:Sn(ONa)_2 + N_2 + NaOH.$$

3. An aqueous solution of the substance is gently warmed, when a vigorous evolution of nitrogen occurs, and a dark-coloured oil, smelling strongly of phenol, separates. It can be extracted with ether and tested for phenol (see Preparation 352).

If a solution of diazobenzene nitrate be used, the liberated nitric acid acts on the phenol as it is formed, and nitrophenol is produced.

$$C_6H_5.N_2.SO_4H + H_2O = C_6H_5OH + H_2SO_4 + N_2.$$

$$C_6H_5.N_2.HNO_3 + H_2O = C_6H_5OH + HNO_3 + N_2.$$

$$C_6H_5OH + HNO_3 = C_6H_4(OH)(NO_2) + H_2O.$$

4. An aqueous solution of the substance is mixed with a solution of bromine in hydrobromic acid or potassium bromide, when a reddish-brown oil separates. This solidifies to a mass of leafy crystals, if the aqueous layer is poured off the oil, and the latter washed with a little ether. The crystals are diazobenzene perbromide.

$$C_6H_5.N_2.SO_4H + KBr + Br_2 = C_6H_5NBr.NBr_2 + KHSO_4.$$

$$C_6H_5.N_2.SO_4H + HBr + Br_2 = C_6H_5.NBr.NBr_2 + H_2SO_4.$$

If a sufficient quantity of the crystals has been prepared, it may be divided into two portions. One portion is covered with conc. ammonia. A violent reaction sets in, the crystals disappear, and a dark oil, possessing a peculiar narcotic odour, is produced, consisting principally of benzene diazoimide.

$$C_6H_5NBrNBr_2 + NH_3 = C_6H_5N_3 + 3HBr.$$

The other portion of the perbromide is warmed with a little alcohol. Nitrogen and bromine are given off, and bromobenzene is formed.

$$C_6H_5.NBr.NBr_2 = C_6H_5Br + N_2 + Br_2.$$

5. Potassium iodide solution is added to an aqueous solution of the diazonium salt. Nitrogen is evolved, and a dark-coloured oil, iodobenzene, separates.

$$C_6H_5.N_2.SO_4H + KI = C_6H_5I + N_2 + KHSO_4.$$

For large scale reaction, see Preparation 338.

6. The solution of the diazonium salt is mixed with an aniline salt and excess of sodium acetate, or the solution is shaken up with a few drops of aniline. In either case a yellow crystalline precipitate of diazoaminobenzene is obtained.

$$C_6H_5.N_2.SO_4H + C_6H_5NH_2.HCl + CH_3COONa$$
$$= C_6H_5N:N.NHC_6H_5 + NaHSO_4 + CH_3COOH + HCl.$$

$$C_6H_5.N_2.SO_4H + C_6H_5NH_2 = C_6H_5N_2.NHC_6H_5 + H_2SO_4.$$

For Preparation, see p. 382.

7. A solution of phenol in caustic soda is added drop by drop to an aqueous solution of the substance. An orange crystalline precipitate of sodium hydroxyazobenzene is formed. If β-naphthol be used in place of phenol a scarlet precipitate of sodium hydroxy-β-naphthaleneazobenzene is obtained.

$$C_6H_5.N_2.SO_4H + C_6H_5(ONa) = C_6H_5N:NC_6H_4(ONa) + Na_2SO_4 + 2H_2O.$$
$$C_6H_5.N_2SO_4H + C_{10}H_7(ONa) = C_6H_5N:NC_{10}H_6(ONa) + Na_2SO_4 + 2H_2O.$$

8. An acetic acid solution of dimethylaniline is added to a solution of the substance. A magnificent red colour is produced in a short time through the formation of dimethylaminoazobenzene sulphate.

$$C_6H_5N_2SO_4H + C_6H_5N(CH_3)_2.HOOC.CH_3$$
$$= C_6H_5N:N.C_6H_4N(CH_3)_2.H_2SO_4 + CH_3COOH.$$

A sulphuric acid solution of *m*-phenylene diamine is added to the solution of the diazonium salt. The orange colour is due to diaminoazobenzene sulphate (Chrysoidine). Preparation 385.

$$C_6H_5N_2SO_4H + C_6H_4(NH_2)_2(H_2SO_4)$$
$$= C_6H_5N:NC_6H_3(NH_2)_2(H_2SO_4) + H_2SO_4.$$

9. A ¼ gm. at the most of the moist diazobenzene sulphate is allowed to dry spontaneously on filter paper in a safe place, and when dry exploded by kindling the paper.

10. Concentrated sodium borofluoride solution is added to a solution of diazobenzene chloride. The fluoborate is precipitated. On cautious heating this is converted to the fluorobenzene. See Prep. 338.

$$C_6H_5N_2Cl \longrightarrow C_6H_5N_2BF_4 \longrightarrow C_6H_5F + BF_3 + N_2.$$

For further information see " Aromatic Diazo Compounds " (Saunders).

Reaction CLXXVIII. Action of Alkaline Reducing Agents on Aromatic Nitro Compounds.—Azoxy, azo, and hydrazo compounds are formed.

The reducing agents employed, other than metals (see Reaction CLXX) are sodium methoxide or ethoxide, alcoholic caustic soda or potash, sodium amalgam, alkaline stannous chloride. The last reducing agent is usually employed for the isolation of azo compounds, while the others yield azoxy compounds, and, in some cases, hydrazo compounds.

$$4C_6H_5NO_2 + 3CH_3ONa \longrightarrow 2C_6H_5.N_2O.C_6H_5 + 3H.COONa + 3H_2O.$$

Better yields of azo and hydrazo compounds are sometimes obtained by reducing the azoxy compound in preference to the nitro compound. Certain hydrazo compounds, e.g. hydrazo-naphthalenes, undergo the " benzidine conversion " (see p. 166) in alkaline as well as in neutral solution, so that the product finally isolated in the reduction is a diamino base. (J. C. S., 125, 1108.)

CHAPTER XXVI

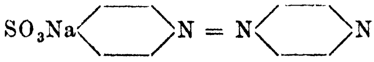
DYES

1. AZO DYES

THESE dyes are formed by coupling diazonium compounds with phenols or aromatic bases. The characteristic group is —N=N—, and the general formula X—N=N—Y. Mono-azo dyes contain one —N=N— group, while dis-azo dyes contain two, and so on. For the general laws of coupling, see Reaction CXXII. Mono-azo dyes are acid or basic in reaction, according to the nature of the auxochrome present (see p. 288). They are soluble in alkali if they contain a phenolic group *para* to the azo link. They are decomposed by conc. nitric acid and halogens. Reducing agents decompose them, with the formation of amines, a reaction which serves to determine their composition and constitution (see p. 373).

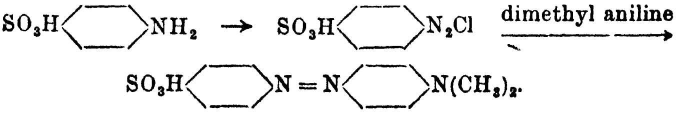
Special attention is directed to the test for completion of the " coupling " process on p. 288.

PREPARATION 383.—**Methyl Orange** (*4-Dimethylamino-4'-azobenzene-Na-sulphonate*). C.I., 142.



$C_{14}H_{14}O_3N_3SNa$. **327.**

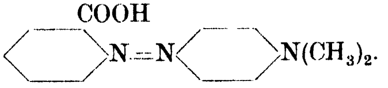
17·3 gms. of sulphanilic acid are dissolved in 150 c.cs. water containing 6 gms. sodium carbonate in solution. To this solution are added 7·2 gms. of sodium nitrite in 10% solution. The mixture is cooled by adding ice, and 25 c.cs. of hydrochloric acid in the form of a 15% solution (see p. 380), slowly added with stirring. 12·1 gms. of dimethylaniline are dissolved in an equal quantity of hydrochloric acid as above, and added to the diazonium compound. Caustic soda solution is then added till the solution is just alkaline. The methyl orange separates at once. A further yield may be obtained by adding common salt until the solution is saturated. The dye is filtered off, and is recrystallised from water.



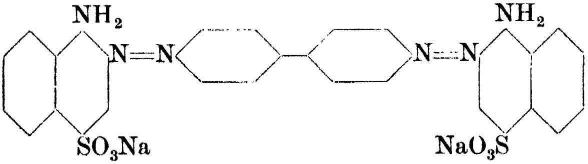
Yield.—Almost theoretical. (B., 10, 528.)

The sodium salt consists of yellow crystals dissolving in water to a yellow solution which turns red on addition of mineral acid. The dye is used as an indicator in acidimetry and alkalimetry.

If anthranilic acid is used in place of sulphanilic, the dyestuff formed is *Methyl Red*. C.I., 211. (O. S., II, 47.)



PREPARATION 384.—**Congo Red.** C.I., 370.



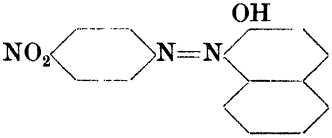
$C_{32}H_{22}O_6N_6S_2Na_2$. 696.

18·4 gms. benzidine are dissolved in 300 c.cs. of water and 20 c.cs. conc. hydrochloric acid, heat being applied, if necessary. Ice is added till the temperature is below 5°. 30 c.cs. conc. hydrochloric acid are then added, and about 14·4 gms. sodium nitrite in 10% solution until diazotisation is complete (see p. 380). 150 gms. sodium naphthionate are dissolved in as little water as possible. The diazonium solution is run into the sodium naphthionate, with stirring, and after ½ hour a solution of 35 gms. sodium carbonate is added gradually, so that during further stirring the solution is always alkaline. The contents of the beaker will appear brown at this stage. The whole is then slowly heated up to about 80° and common salt added to saturate the solution. After cooling, the reddish-brown Congo red is filtered off, washed with saturated common salt solution, and dried. Dyes cotton, direct from neutral or alkaline bath, red.

In order to obtain a good yield a large excess of sodium naphthionate is employed, the excess being recovered as the free acid on acidifying the mother liquor after filtering off the dyestuff. (B., 19, 1719.)

If *o*-tolidine is used in place of benzidine, the dyestuff formed is *Benzopurpurin 4B*. C.I., 448. (D.R.P., 84893.)

PREPARATION 385.—**Para Red** (*p-Nitrobenzeneazo-β-naphthol*). C.I., 44.

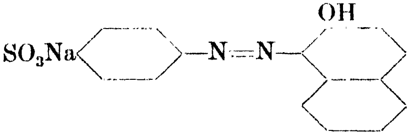


$C_{16}H_{11}O_3N_3$. 293.

13·8 gms. *p*-nitroaniline are diazotised as described on p. 382 and added slowly with stirring to 14·5 gms. β-naphthol dissolved in 100 c.cs. 10% caustic soda, until coupling is complete (see p. 280). The insoluble dye is filtered, washed with water and dried.

Para red is applied to cotton by impregnation with β-naphthol followed by drying, and immersion in the diazonium solution. The azoic or " ice " dyes are formed from derivatives of β-naphthol, e.g. anilides of 2-hydroxy-3-naphthoic acid.

Preparation 386.—Orange II. C.I., 151.

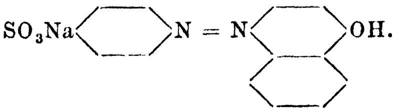


$C_{16}H_{11}O_4N_2SNa.(5H_2O)$. 350.

17·3 gms. sulphanilic acid are dissolved in water containing a little caustic soda and ice to cool below 5°. 30 c.cs. conc. hydrochloric acid are then added, and about 7·2 gms. sodium nitrite in 10% solution gradually run in until diazotisation is complete (see p. 380). The diazo compound usually separates out as fine needles, but these are not isolated. 14·4 gms. β-naphthol are dissolved in 15 c.cs. water, to which 4·5 gms. caustic soda have been added. This solution is made up to about 180 c.cs. by adding water. It is then cooled if necessary. The diazonium solution is carefully added, with stirring, until coupling is complete (see p. 288), the temperature not being allowed to rise above 8°. The mass should now give a slight alkaline reaction. After stirring for about an hour the dyestuff separates out, a little salt being added to complete the precipitation. The orange powder is filtered off and dried.

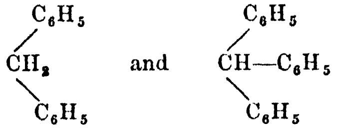
Dyes wool orange from an acid bath. (J. S. C. I., 6, 591.)

If α-naphthol is used in place of β-naphthol, the dyestuff formed is Orange I. C.I., 150. (J. S. C. I., 6, 591.)



2. Di- and Tri-Aryl Methane Dyes

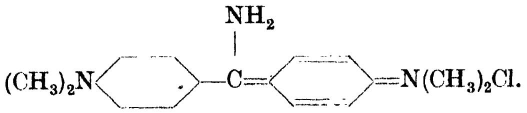
These dyes may be regarded as derivatives of



Diphenylmethane. Triphenylmethane.

The dyes are obtained from their amino, alkylamino and hydroxy derivatives, these groups being usually present in the *p*-position.

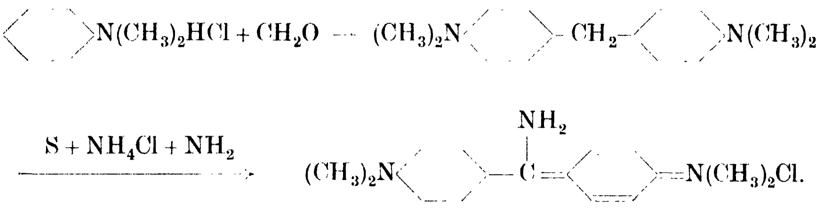
Preparation 387.—Auramine. C.I., 655.



242 gms. pure dimethylaniline are mixed with 140 c.cs. water an 260 gms. conc. hydrochloric acid, and heated to 30°. 60 gms. 40

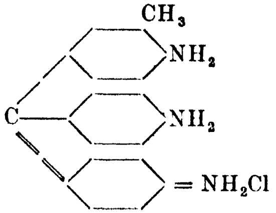
formaldehyde solution are then added, and the mixture heated to 85°, with stirring, for 5 hours. The base is then precipitated by adding 120 gms. sodium carbonate dissolved in a little water. The product, tetramethyl-diamino-diphenylmethane, is filtered after cooling to 20°, and washed with water. It is dried at 50°. The yield of this base is almost quantitative. 127 gms. diamino base, 32 gms. sulphur, 70 gms. ammonium chloride, and 1,000 gms. common salt are heated to 110° in an autoclave provided with stirrer and exit tube. The substances should be finely powdered and dried. The temperature is raised to 130° during 2 hours, and a rapid stream of *dry* ammonia passed through. At 140° a vigorous evolution of hydrogen sulphide begins, which lasts from 5–7 hours, according to the speed of the stream of ammonia. The temperature is raised to 145° during 5 hours, stirring being continued. The ammonia stream should pass at a speed of about 5 bubbles per second, and it is advisable to have a slight excess pressure of $\frac{1}{5}$ atm. measured by a manometer, which can be conveniently done by throttling the exit tube.

When the evolution of hydrogen sulphide has ceased, the contents of the autoclave are placed in a large basin and treated with 3 litres of water to dissolve out the salt. The dye is then filtered off, and dissolved in $1\frac{1}{2}$ litres of water at 60°. The solution is filtered, and a litre of saturated salt solution added, when the auramine comes down in glistening, golden leaflets. It is filtered and dried.



Yield.—Up to 175 gms. Dyes cotton mordanted with tannin or tartar emetic a pure yellow. (B., 33, 318.)

PREPARATION 388.—**Magenta** (*Fuchsine*). C.I., 677.

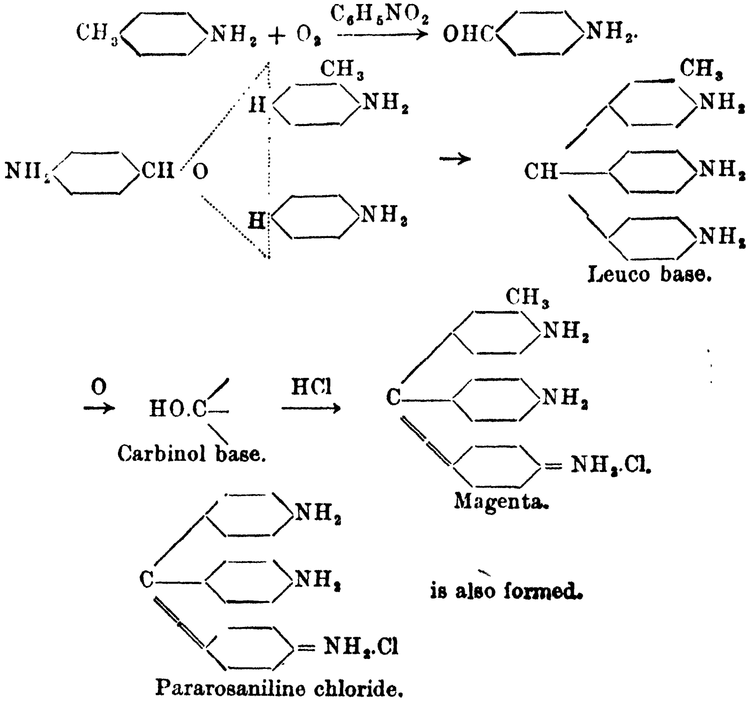


$C_{20}H_{20}N_3Cl$. 337·5.

7 gms. aniline and 27 gms. commercial toluidine (containing 64% *ortho* and 36% *para*) are heated with 34 gms. conc. hydrochloric acid to 130° in a 250-c.c. flask. 3 gms. aniline, 13 gms. commercial toluidine, and 27·5 gms. nitrobenzene are then added. The flask is transferred to an oil

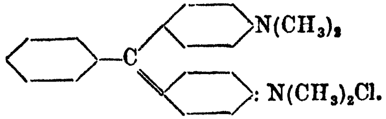
bath at 100°, and 1·5 gms. iron powder dissolved in the minimum quantity of hydrochloric acid (2 mols.) slowly added. An air condenser is attached, and the temperature raised to 180°, and maintained at this temperature for about 5 hours. When a sample, withdrawn on a glass rod, solidifies on cooling, the action is finished. The mixture is then steam distilled to remove the nitrobenzene and excess amines. The melt is then poured into 250 c.cs. boiling water, with stirring, and 6 c.cs. conc. hydrochloric acid added slowly. As soon as an acid reaction is obtained, 13 gms. common salt are added, and the whole boiled for a few minutes. The aqueous solution (containing the hydrochlorides of aniline and toluidine) is poured off and the residue allowed to cool, when it solidifies to a green mass. This mass is broken up and extracted with 750 c.cs. boiling water containing 6 c.cs. conc. hydrochloric acid, which dissolves the magenta. The solution is filtered hot, and, after cooling to 60°, is again filtered. The magenta is then "salted out" with common salt, and after standing some time is filtered off and recrystallised from water containing a little hydrochloric acid.

The hydrochloride forms green, glistening crystals, giving a red solution in water. It dyes silk and wool bluish-red directly, and tannin- and tartar emetic-mordanted cotton.



(J. S. C. I., 5, 163; 7, 118.)

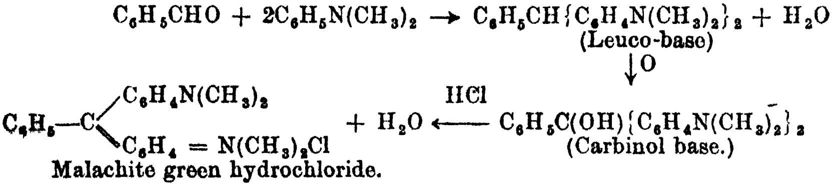
PREPARATION 389.—**Malachite Green.** C.I., 657.



$C_{23}H_{25}N_2Cl$. 364·5.

Method I.—50 gms. dimethylaniline, 20 gms. of benzaldehyde and 20 gms. of pulverised anhydrous zinc chloride (see p. 517) are heated in a porcelain dish, with frequent stirring, on a water bath for 4 hours. The mass is then melted by the addition of hot water and transferred to a large flask, where it is steam distilled until no more dimethylaniline passes over. The leuco-base of the dye remains in a viscous form on the sides of the flask after cooling ; the aqueous solution is decanted and the base washed a few times by decantation with cold water. The base is dissolved in boiling alcohol, the solution filtered hot, and the filtrate left overnight in an ice-chest. Colourless crystals separate, which are collected and dried in air on filter paper. A second crop may be obtained by concentrating the mother liquor. If the base separates as an oil, instead of crystals, more alcohol should be added, and heat applied until the oil redissolves.

A small portion of the leuco-base is weighed, dried at 100°, and weighed again in order to determine its moisture content. The equivalent of 10 parts by weight of the anhydrous base is dissolved by heating with a quantity of dilute hydrochloric acid. corresponding to 2·7 parts by weight of hydrogen chloride. The colourless solution of the leuco-base is diluted in a large beaker with 800 parts of water, and 10 parts of 40% acetic acid added. The solution is cooled to about 0° by the addition of lumps of ice, and a freshly-prepared lead dioxide paste (for preparation and estimation, see p. 515), corresponding to 7·5 parts PbO_2, added gradually during the course of 10 minutes, the mixture being stirred and cooled during the addition. Stirring is continued for 2 hours, after which the unchanged lead peroxide is filtered off, and the lead in the filtrate precipitated by the addition of 10 parts of sodium sulphate dissolved in 50 parts of water. Lead sulphate is filtered off, the filtrate is heated to boiling, and 15 gms. of sodium chloride added for each 100 c.cs. of dye solution ; while still hot, 8 parts of zinc chloride, dissolved in a small quantity of water, are also added. On cooling, the zinc chloride double salt of the dye is filtered off, washed with saturated sodium chloride solution, and dried on a porous plate. If the mother liquors are coloured, owing to some of the dye still remaining in solution, a further crop may be obtained by adding more sodium chloride and zinc chloride.



$$C_6H_5CHO + 2C_6H_5N(CH_3)_2 \longrightarrow \underset{\text{(Leuco-base)}}{C_6H_5CH\{C_6H_4N(CH_3)_2\}_2} + H_2O$$

$$\big\downarrow O$$

$$\underset{\text{Malachite green hydrochloride.}}{C_6H_5{-}C\begin{cases} C_6H_4N(CH_3)_2 \\ C_6H_4 = N(CH_3)_2Cl \end{cases}} + H_2O \xleftarrow{HCl} \underset{\text{(Carbinol base.)}}{C_6H_5C(OH)\{C_6H_4N(CH_3)_2\}_2}$$

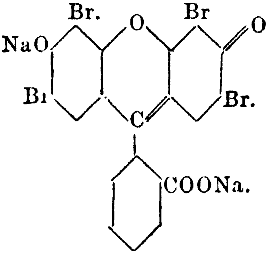
The formula of the zinc chloride double salt is $2C_{23}H_{25}N_2Cl$, $2ZnCl_2$, H_2O.

Brass yellow prismatic needles ; soluble in hot water to a bluish-green solution ; dyes silk, wool, jute and leather, a bluish-green directly and cotton which has been previously mordanted with tannin and tartar emetic.

Method II.—50 gms. dimethylaniline, 20 gms. benzaldehyde, and 45 gms. of conc. hydrochloric acid are placed in a flask fitted to a reflux condenser, and the mixture heated at 100° for 24 hours. The product is then made alkaline with caustic soda, and steam distilled to remove traces of benzaldehyde and dimethylaniline. After this the procedure is the same as in Method I. (J. S. C. I., 6, 433.)

3. Phthalein Dyes

PREPARATION 390.—**Eosin** (*Tetrabromofluorescein*). C.I., 768.

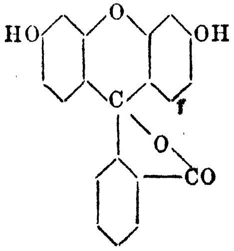


$C_{20}H_6O_5Br_4Na_2$. 692.

Into a mixture of 15 gms. of fluorescein and 60 gms. of alcohol (about 95%), contained in a flask, are added with frequent shaking 11 c.cs. of bromine, drop by drop, from a burette. When half the bromine has been added the dibromide which is then formed is in solution ; on further addition of bromine the tetrabromide separates out in the form of brick-red leaflets. After all the bromine has been added, the mixture is allowed to stand for 2 hours. The precipitate is filtered off, washed first with alcohol, then with water, and converted into the sodium salt by mixing with a little hot water, carefully neutralising with caustic soda (avoiding excess), and evaporating to dryness on a water bath.

Bluish-red crystals or brownish-red powder. In water, bluish-red solution ; dilute solution has green fluorescence. In alcohol, easily soluble, with bluish-red colour and yellowish-green fluorescence. Dyes wool and silk yellowish-red. (J. S. C. I., 12, 513.)

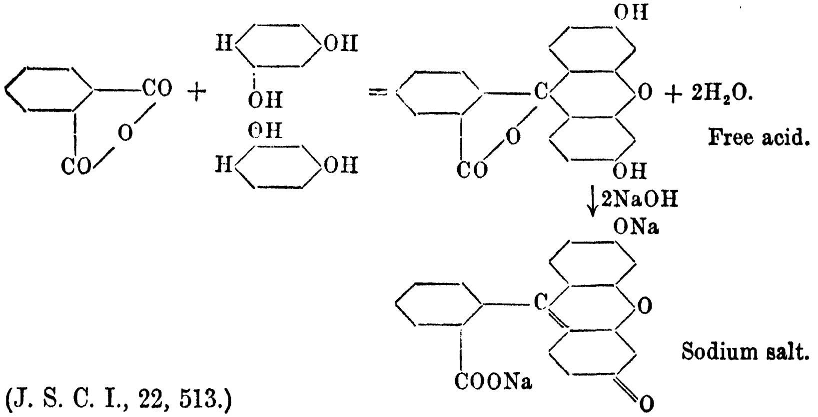
PREPARATION 391.—**Fluorescein.** C.I., 766.



$C_{20}H_{12}O_5$. **332.**

A mixture of 15 gms. of phthalic anhydride and 22 gms. of resorcinol is ground in a mortar. It is then transferred to a nickel or cast-iron vessel, and heated in an oil bath to 180°. At this temperature 7 gms. of powdered fused zinc chloride (see p. 517) are added, with stirring, during the course of 10 minutes. The temperature is raised to 210°, and maintained at this point until the liquid, which gradually thickens, becomes solid, for which 1–2 hours are required. The cold melt is removed from the vessel with a knife or chisel, powdered, and boiled 10 minutes with 200 c.cs. of water and 10 c.cs. of conc. hydrochloric acid. This treatment causes the solution of zinc oxide and basic zinc chloride. The fluorescein is filtered off, washed with water until the filtrate no longer shows an acid reaction ; it is dried on a water bath.

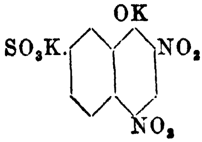
Yield.—Almost theoretical (32 gms.). Red powder ; slightly soluble in water ; soluble in alcohol ; soluble in alkali with intense green fluorescence ; dyes animal fibres yellow.



(J. S. C. I., 22, 513.)

4. Nitro Dyes

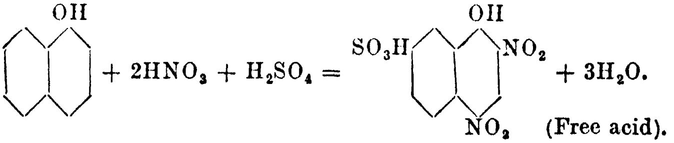
Preparation 392.—**Naphthol Yellow S.** (2 : 4-*Dinitro*-1-*naphthol*-7-*sulphonic acid*). (**K salt**). C.I., 10.



$C_{10}H_4O_8N_2SK_2$. **390.**

100 gms. of conc. sulphuric acid are warmed to 100° in a small flask, and 50 gms. of powdered α-naphthol added in one instalment. The mixture is raised to 120° by heating in an oil or sand bath and maintained at this temperature for 3–4 hours. The sulphonation mixture is then poured into 600 c.cs. of water. which are stirred mechanically. When the temperature of the mixture falls to 30° it is poured into a mixture of 23 gms. of conc. nitric acid and 8 c.cs. of water, which is well stirred mechanically ; the temperature is kept below 35° by cooling in water,

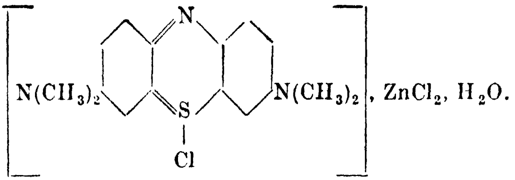
if necessary. A further 21 gms. of conc. nitric acid are added at such a rate that the temperature does not rise above 40°. The nitration mixture is filtered through woollen cloth and washed free from acid with 10% sodium chloride solution. The drained precipitate is stirred with 200 c.c. of hot water at 80°, solid sodium carbonate added until neutral, and the dyestuff precipitated by adding 20 gms. potassium chloride.



Orange-yellow powder ; dyes wool and silk from an acid bath. (A., 152, 299.)

5. Thiazine Dyes

PREPARATION 393.—**Methylene Blue** (*Tetramethylthionine Chloride*) **(Hydrated zinc double chloride).** C.I., 922.



Nitrosodimethylaniline.—16 gms. of dimethylaniline are dissolved in 53 gms. of conc. hydrochloric acid (30%) and 100 gms. ice added. 10·5 gms. of sodium nitrite previously dissolved in 40 c.cs. water are then slowly run in from a dropping funnel, the solution being agitated during the addition. The temperature must be kept at 0°–5° by the addition of ice, when necessary. When the nitrite is added, the agitation is stopped, and a test for the presence of free nitrous acid applied. A sample of the liquor is withdrawn, diluted with 3 times its volume of water, and tested with starch-iodide paper. If test does not indicate free nitrous acid, more nitrite must be added until a positive indication is obtained. The solution should be acid to Congo red paper, and yellow ; if not acid it is somewhat green. After the addition of all the nitrite the mixture is allowed to stand for 2 hours, and at the end of this time it should just give a slight indication of free nitrous acid. The greater part of the nitrosodimethylaniline separates out as yellow crystals.

p-Aminodimethylaniline.—The above mixture is well agitated, 100 c.cs. of water and 70 gms. of conc. hydrochloric acid added ; this is followed by 20 gms. iron filings, and sufficient ice added from time to time to keep the temperature below 30°. The reduction is complete when a drop spotted on filter paper is quite colourless. The liquor, which is generally acid is treated with lime-paste until only faintly acid to Congo red paper ; the neutralisation is completed by the addition of chalk until frothing stops. The residue of iron and chalk is filtered off and washed, the washings being added to the filtrate.

Thiosulphonic Acid and Dye.—Before entering on this stage of the preparation the following solutions are prepared :

Solution I.—33·5 gms. sodium thiosulphate in 40 c.cs. water.

Solution II.—26·4 gms. sodium bichromate in 40 c.cs. water.

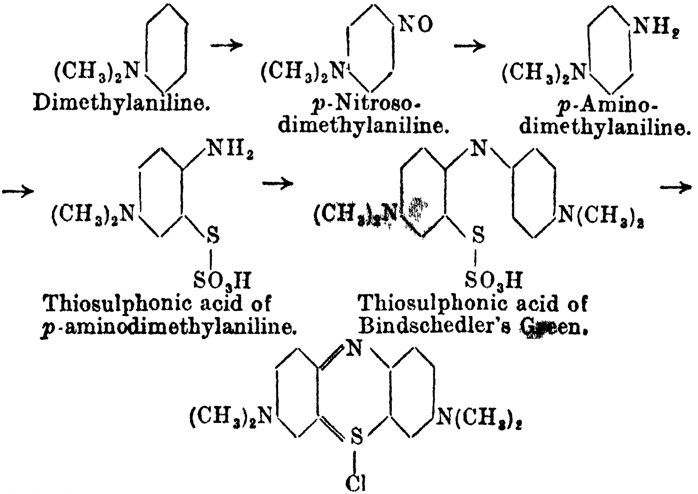
Solution III.—14 gms. dimethylaniline in 24 gms. conc. hydrochloric acid.

Solution IV.—26·4 gms. sodium bichromate in 40 c.cs. water.

Solution V.—1·5 gms. copper sulphate in 20 c.cs. water.

The clear neutral solution of *p*-aminodimethylaniline is vigorously agitated. Solution I is added all at once, and immediately following it Solution II during the course of 2 minutes. After an interval of 2 minutes Solution III is added all at once, and immediately following it Solution IV during the course of 2 minutes. Agitation is continued for 7 minutes before Solution V is added. The mixture is then transferred to a large vessel and heated ; it soon assumes a bronze appearance, and much frothing takes place. Heat is withdrawn until the froth settles ; when this occurs, the mixture is heated up again and filtered almost boiling. The black precipitate of chromium hydroxide is washed with boiling water until the filtrate is only faintly coloured. The total filtrate is heated almost to boiling, then treated with 150 gms. common salt, 40 gms. of 50% zinc chloride solution and 10 gms. conc. hydrochloric acid. On cooling, the double zinc salt of methylene blue separates out as a coppery powder, which is filtered off and washed with a little 10% brine solution ; it is dried at a temperature not exceeding 50°, a yield of about 30 gms. being obtained.

If " zinc-free " methylene blue is desired, the filtrate from the chromium hydroxide is heated to 80°, 15 gms. of common salt added for each 100 c.cs. of solution, also 10 c.cs. of conc. hydrochloric acid. On cooling, the " zinc-free " methylene blue separates in fine crystals.



Dimethylaniline. *p*-Nitroso-dimethylaniline. *p*-Amino-dimethylaniline.

Thiosulphonic acid of *p*-aminodimethylaniline. Thiosulphonic acid of Bindschedler's Green.

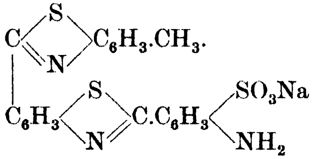
(A., 251, 1.) Methylene Blue.

Methylene blue is of a very pure shade, and is used for dyeing tannined cotton ; the " zinc-free " dye is used for medicinal purposes, and also for the production of discharge effects in silk printing.

PREPARATION 394.—**Methylene Green** (*Nitromethylene Blue*). C.I., 924. 30 gms. methylene blue (Zn salt) are made into a paste with 35 c.cs. water and 16 gms. of 60% nitric acid ; to this are added at 25°, 3·5 gms. of sodium nitrite dissolved in the minimum quantity of water. The temperature is raised slowly to 50° (rate 1° per minute) with good agitation and kept there for 2 hours. 160 gms. of saturated brine are then added, and the precipitate filtered off after 12 hours. The product is purified by dissolving in 800 c.cs. water at 60°, filtering to remove residue, and reprecipitating the dye with 105 gms. common salt along with 35 gms. of 50% zinc chloride solution. After standing for 12 hours, the dye is filtered off, pressed, and dried at 45°.

Yield.—About 25 gms. Used in conjunction with iron-mordanted logwood, or with tin phosphate for dyeing black on silk, also for cotton and calico printing. (E.P., 8992 (1886).)

PREPARATION 395.—**Primuline.** C.I., 812.



$C_{21}H_{14}O_3N_3S_3Na$. 475.

20 gms. *p*-toluidine and 14 gms. sulphur are well mixed together and heated in a jar in an oil bath to 250°. The mass turns yellow, and the reaction is finished when no more H_2S is evolved. (See p. 332.)

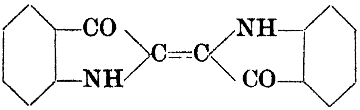
The mass, after cooling, is powdered and heated with 4 times its weight of fuming sulphuric acid (30% SO_3) to 70°–80° for a few minutes until a sample dissolves in caustic soda. The sulphonation mixture is poured into ice-water (*caution*), and the sulphonic acid of the base which is precipitated filtered and washed free of acid.

The paste is stirred up with dilute ammonia until alkaline, filtered and washed with cold water. The residue is the ammonium salt of dehydrothio-*p*-toluidinesulphonic acid (p. 332), and the filtrate contains the primuline. The filtrate is saturated with common salt, when the primuline separates out and is filtered and dried.

Dyes cotton direct from alkaline or neutral bath primrose-yellow (see Preparation 302). (D.R.P., 56606.)

6. Indigoid Dyes

PREPARATION 396.—**Indigo.** C.I., 1247.

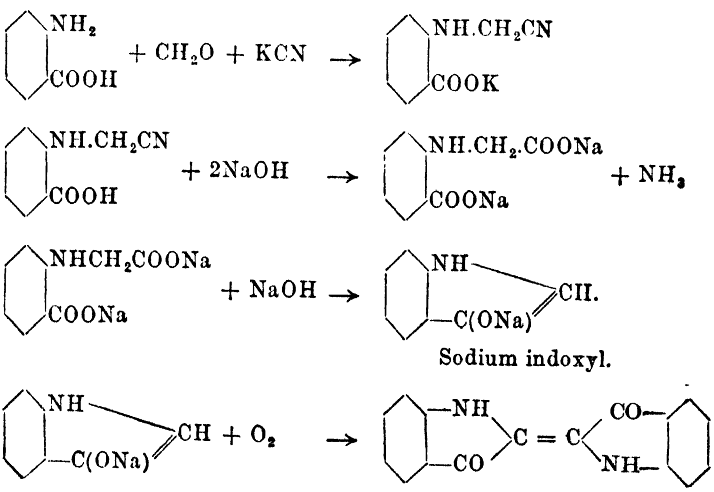


$C_{16}H_{10}O_2N_2$ 262

14 gms. anthranilic acid are suspended in 50 c.cs. benzene. 7 gms. finely-powdered potassium cyanide are added, and after shaking, 7·5 c.cs. of 40% formaldehyde. The temperature rises, and the potassium salt of ω-cyanomethyl anthranilic acid is formed in the aqueous liquid.

The benzene is removed, and 20 c.cs. of 40% caustic soda solution are added. The mixture is carefully heated over a wire gauze until ammonia begins to be evolved. After the reaction has subsided, heating is continued until all the ammonia is driven off, water being added, if necessary, to prevent the contents of the flask becoming solid. The mixture, when cold, is carefully neutralised with conc. hydrochloric acid (using phenolphthalein as indicator), and then acidified with about 15 c.cs. of glacial acetic acid. The yellowish-white precipitate of phenyl-glycine-*o*-carboxylic acid is filtered off, washed with water, and dried on a porous plate.

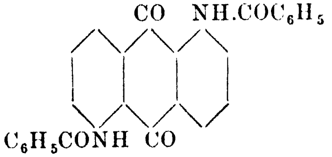
10 parts of phenyl-glycine-*o*-carboxylic acid, or the corresponding amount of the sodium potassium salt, are added to a solution of 10–12 parts of pure caustic soda in 4–6 parts of water. The mixture is then quickly evaporated, being stirred continuously until dry. It is powdered, and added to 8–14 parts of solid paraffin (M.P. about 160° F.). The mixture is heated to 250°–270°, and stirred with the thermometer, steam being evolved. The end of the reaction is indicated by the strong yellow colour of the fusion. The homogeneous paste is cooled, and boiled with water containing a little hydrosulphite, $Na_2S_2O_4$, to prevent oxidation. The liquid is cooled, filtered from paraffin, and oxidised by passing air, when indigo is precipitated as a dark blue powder.



Indigo dissolves in most alkaline reducing agents to give a colourless leuco-compound. Cotton, wool and silk are dyed by soaking in the leuco-compound and exposing to air. (D.R.P., 125916.)

7. Anthraquinone Dyes

PREPARATION 397.—**Algol Yellow R** (1 : 5-*Di-(benzoylamino)-anthraquinone*). C.I., 1131.



$C_{28}H_{18}O_4N_2$. 446.

7 gms. of 1 : 5-dinitroanthraquinone (Preparation 234) are added to a solution of 35 gms. sodium sulphide ($Na_2S.9H_2O$) in 200 c.cs. water, and heated gradually to boiling. The mass becomes dark blue and thick, owing to the separation of sulphur and diamino-anthraquinone. The precipitate is filtered off and extra yield recovered by adding common salt to the filtrate.

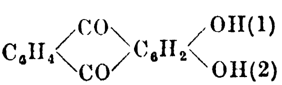
The diamino compound is then extracted from the precipitate by boiling with alcohol and filtering from sulphur. The diamine is precipitated from the alcoholic solution by adding water. It is filtered and dried on the water bath.

Scarlet red powder ; M.P. 262°. J. C. S., 1932, 83.

Benzoylation.—1 gm. of the diamino compound is treated with 4 gms. benzoyl chloride and 10 gms. dimethylaniline and boiled for 1 hour, when the benzoyl derivative separates out as a yellow-brown powder. The unchanged base and the dimethylaniline are extracted with dilute hydrochloric acid. The product is then filtered.

Yellowish powder ; M.P. 234°.

PREPARATION 398.—**Alizarin** (1 : 2-*Dihydroxyanthraquinone*). C.I., 1027.

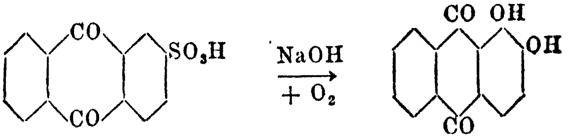


$$C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle C_6H_2\left\langle\begin{matrix}OH(1)\\OH(2)\end{matrix}\right.$$

$C_{14}H_8O_4$. 240.

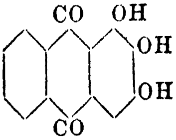
10 gms. 100% β-anthraquinone sulphonate " silver salt " (see p. 321) are mixed with 260 gms. 100% caustic soda, 28 gms. sodium chlorate, and sufficient water to make volume up to 670 c.cs. The mixture is placed in an autoclave and heated up to 185° with continuous stirring, the pressure attaining 5–6 atms. After 48 hours, the melt is allowed to cool, and the following test applied ; 2 c.cs. of the melt are treated with sufficient conc. hydrochloric acid to precipitate the alizarin. The filtrate is then extracted twice with a little ether to remove traces of alizarin. The liquid is now diluted to 15 c.cs., and the fluorescence, which is due to unchanged silver salt and the monohydroxysulphonic acid, observed. If the reaction is complete, only a very faint fluorescence should develop. If the reaction is not complete, the mixture is heated up again in the autoclave to 190° for 24 hours. It is then diluted with 2 litres of water, and the alizarin precipi-

tated *at the boil* with 50% sulphuric acid. It is cooled to 50°, filtered and washed. It is not dried, as when once dry it no longer dyes properly.



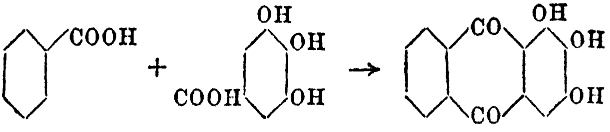
Yield.—About 70 gms. M.P. 289°. A polygenetic dyestuff, i.e., dyes mordanted cotton various colours, depending on the mordant used, e.g. iron oxide gives a violet colour, alumina a red colour, chromium a brown colour, etc. (J. S. C. I., 2, 213 ; E.P., 1948 (1869).)

PREPARATION 399.—**Anthragallol** (1 : 2 : 3-*Trihydroxyanthraquinone*). C.I., 1035.



$C_{14}H_8O_5$. 256.

36 gms. pure benzoic acid are dissolved in 300 gms. sulphuric acid (monohydrate, p. 316) in a glass or porcelain beaker with good stirring. The mixture is heated slowly to 90°, at which temperature 50 gms. pure, dry gallic acid* (dried at 110°) are added in small portions during an hour. The temperature is then raised to 118°, and kept there for 6 hours, after which the melt is allowed to drop cautiously into a litre of boiling water, with continuous stirring. The product is filtered boiling through a hot filter, and the dye well washed with hot water. The excess benzoic acid crystallises out in the mother liquor.



Yield.—70–80% theoretical (70–80 gms.). Dyes wool brown with chrome mordants, chromium fluoride giving the best shades. (J. S. C. I., 3, 141.)

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* Good quality gallic acid may be obtained by hydrolysing tannin with 40% caustic soda solution at 70° with the addition of a little sodium bisulphite to protect the acid from oxidation. The gallic acid is then precipitated by conc. hydrochloric acid and crystallised from water. (*Note.*—Sulphuric acid must not be used.)

CHAPTER XXVII

DRUGS

PREPARATION 400.—Chloral Formamide (1-*Formylamino*-2 : 2 : 2-*trichloroethanol*).

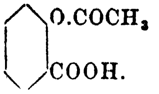
$CCl_3.CH(OH)NH.CHO.$ $C_3H_4O_2NCl_3.$ 192·5.

74 gms. freshly-distilled chloral are added, with stirring to 22·5 gms. cooled formamide. Much heat is evolved, and the mixture sets on cooling to a crystalline mass of chloral formamide. It is purified by recrystallisation from dilute alcohol, the solution not being heated above 48° (see below).

$$CCl_3CHO + HCONH_2 \longrightarrow CCl_3CH(OH).NH.CHO.$$

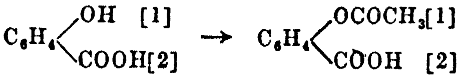
Colourless crystals; M.P. 114°–115°; a hypnotic; above 48°, is reconverted to chloral and formamide. (D.R.P., 50586; E.P., 7391 (1886).)

PREPARATION 401.—Acetylsalicylic Acid (*Aspirin*).



$C_9H_8O_4.$ 180.

100 gms. acetyl chloride in 25 gms. glacial acetic acid are added to 69 gms. salicylic acid in a retort. The retort is gently heated until the reaction commences, when heating is discontinued. Hydrochloric acid is evolved, and acetyl chloride commences to pass over. When the reaction slackens, the temperature is raised gradually to 60°, and when the action has ceased, to 70°, to remove acetyl chloride as far as possible. This can be much facilitated by a slight reduction of pressure. When the distillation has ceased the contents of the retort are poured into an enamelled basin and allowed to crystallise. The crystals are then filtered off, washed with water, and dried at 30°–40°. They are recrystallised by dissolving in ethyl alcohol at about 40°, and initiating the separation by the addition of cold water.



$$C_6H_4\begin{cases}OH\ [1]\\COOH[2]\end{cases} \rightarrow C_6H_4\begin{cases}OCOCH_3[1]\\COOH\ [2]\end{cases}$$

Rhombic plates; M.P., which varies according to rate of heating, is given by British Pharmacopoeia as 135°–138°; should give no violet coloration with ferric chloride; an important analgesic and antipyretic. (B., 17, 186.)

PREPARATION 402.—**Chloramine-T.**

$CH_3.C_6H_4SO_2N(Na)Cl + 3H_2O$. $C_7H_{13}O_5NClSNa$. 245·5.

p-Toluene-sulphonyl chloride (see Preparation 287) is treated with 4 times its weight of dilute ammonia solution, and stirred for several hours, until all the powdered sulphonyl chloride is converted into the crystalline sulphonamide. A little of the mixture is filtered, and the crystals boiled with water. When no acidity is developed the reaction is complete. The crystals are then filtered off, washed with a little water, and recrystallised from a small quantity of water. Needles ; M.P. 64°.

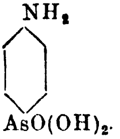
$$CH_3C_6H_4SO_2Cl \longrightarrow CH_3C_6H_4SO_2NH_2.$$

171 parts of *p*-sulphonamide are treated with 525 parts of a 2N solution of sodium hypochlorite (see p. 519) containing 40 parts NaOH. A white precipitate is immediately formed, which, on heating and subseq[illegible] cooling, deposits crystals of Chloramine-T, which are washed with b[illegible] and recrystallised from water.

$$CH_3C_6H_4SO_2NH_2 + NaOCl \longrightarrow CH_3C_6H_4SO_2N(Na)Cl.$$

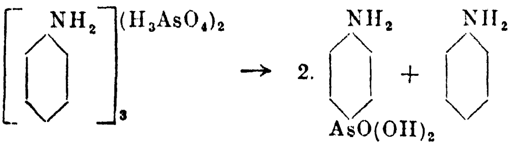
Colourless needles ; powerful disinfectant. (J. S. C. I., 37, 288.)

PREPARATION 403.—**Arsanilic Acid** (*p-Aminophenylarsinic acid*).



$C_6H_8O_3NAs$. 217.

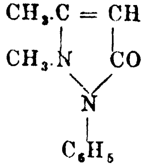
Syrupy arsenic acid (85% ; D. 2·00) is prepared by dissolving 36 gms. of commercial arsenic acid in 16 c.cs. water (check specific gravity). This is placed in an evaporating dish, and 40 c.cs. aniline added in 10 c.c. portions, the solid formed being broken up with a glass rod. The aniline arsenate is then transferred to a round-bottomed flask and an additional 40 c.cs. aniline added, and the mixture heated on an oil bath at 170°–175° until completely melted. The melt is then maintained at 155°–160° for 5 hours with continuous stirring, and poured into 35 c.cs. water. The flask is washed out with a portion of previously prepared solution of 17 gms. caustic soda in 70 c.cs. water, and the washings added with the remainder of the alkali to the reaction mixture, with stirring. The mixture is cooled and separates into two dark-coloured layers, the top layer consisting chiefly of aniline, and the bottom of an aqueous solution of sodium arsanilate. The two layers are carefully separated in a funnel, warming if necessary, to keep the arsanilate in solution. The aqueous solution is then boiled with decolourising carbon and filtered. The filtrate is treated with conc. hydrochloric acid until it is just acid to Congo red, and allowed to stand for 24 hours, occasionally scratching the sides of the vessel, if necessary, with a glass rod to induce crystallisation. The crystals are then filtered off, and recrystallised from about 125 c.cs. of water.



Cf. Sulphanilic acid. *Yield.*—12 gms.

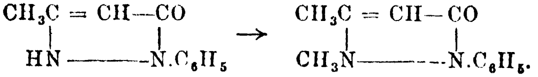
The sodium salt, $NH_2.C_6H_4.AsO(OH)(ONa)+5H_2O$, prepared by neutralising 1 mol. of the acid with 1 mol. caustic soda, is known as "Atoxyl". (Am. Soc., 41, 451; O. S., III, 13.)

PREPARATION 404.—**Antipyrine, Phenazone** (*1-Phenyl-2 : 3-dimethyl-5-pyrazolone*).



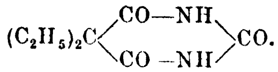
$C_{11}H_{12}ON_2$. 188.

Phenylmethyl pyrazolone (see Preparation 252) is methylated with a methyl alcoholic solution of methyl chloride or bromide at 90°–100°, a slight excess of methylating agent being employed. The methylation can be conveniently carried out in an autoclave fitted with an agitator. The alcohol is distilled off, and the reaction product dissolved in water made slightly alkaline with caustic soda. The antipyrine is then extracted with benzene, and crystallised from benzene, and finally from water, decolourising carbon being used.



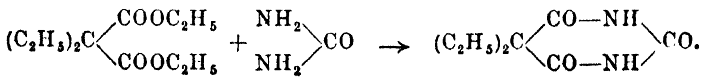
White crystalline scales; M.P. 113°; odourless; possesses bitter taste; a valuable analgesic and antipyretic. (D.R.P., 69883, 26429.)

PREPARATION 405.—**Veronal, Barbitone** (*Diethylmalonyl urea, 5 : 5-diethyl-barbituric acid*).



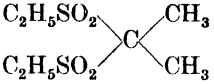
$C_8H_{12}N_2O_3$. 184.

16 gms. sodium are dissolved in 300 gms. absolute alcohol. To the cooled solution are added 20 gms. dry urea and 50 gms. diethyl malonic ester (see Reaction XLIV (*a*)). The mixture is heated in an autoclave for 4–5 hours at 100°–110°. On cooling, the sodium salt of diethyl barbituric acid separates, is filtered off, dissolved in water, and the free acid precipitated by the addition of hydrochloric acid. The acid is filtered and recrystallised from water, using decolourising carbon if necessary.



Colourless crystals ; M.P. 191° ; an important hypnotic. (C. V., II, 60, gives preparation of barbituric acid.

PREPARATION 406.—**Sulphonal** (*Diethylsulphonedimethylmethane*).



$(C_2H_5SO_2)_2C(CH_3)_2$

$C_7H_{16}O_4S_2$. 228.

1. *Acetone Ethyl Mercaptol.*—50 gms. ethyl mercaptan (see Preparation 306) are added to 20 gms. acetone and 6 gms. anhydrous calcium chloride. Dry hydrochloric acid gas is passed in, the temperature being kept below 25° by external cooling. When saturated with acid the mixture is allowed to stand overnight, and washed with water. The layer of mercaptol is separated and dried over calcium chloride, and fractionally distilled. Unchanged ethyl mercaptan passes over first, and then the mercaptol at 190°.

$$2C_2H_5SH + OC.(CH_3)_2 \longrightarrow (C_2H_5S)_2C(CH_3)_2 + H_2O.$$

2. *Sulphonal.*—33 gms. acetone ethyl mercaptol are added with brisk agitation to 1 litre of 5% potassium permanganate solution. The mixture gradually warms up as oxidation proceeds. About 85 gms. solid permanganate are gradually added at intervals. Stirring is continued until the permanganate is reduced, when the solution is boiled and decolourising carbon added. Sulphonal separates out on cooling, is filtered, and recrystallised from aqueous alcohol.

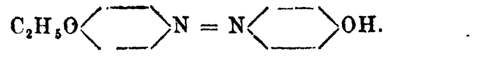
$$(C_2H_5S)_2.C(CH_3)_2 \longrightarrow (C_2H_5SO_2)_2.C.(CH_3)_2.$$

Colourless, odourless, tasteless, prismatic crystals ; M.P. 125·5° ; a hypnotic. (B., 19, 280.)

PREPARATION 407.—**Phenacetin** (*Aceto*-p-*phenetidine*).

$C_{10}H_{13}O_2N$. 179.

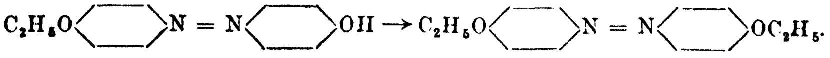
(1) 13·7 gms. *p*-phenetidine (see Preparation 368) are dissolved in 200 c.cs. water and 37·5 gms. 20% hydrochloric acid, and diazotised below 6° with 6·3 gms. sodium nitrite. The diazonium solution is then run into a solution of 9·5 gms. phenol in 350 c.cs. of 2% sodium carbonate solution. The azo compound separates out in about 1 hour, and is filtered off and dried.



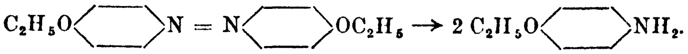
Yield.—Theoretical. M.P. 104·5°.

(2) 24 gms. of the azo compound are dissolved in 100 c.cs. alcohol and 4 gms. caustic soda. The solution is then placed in an enamel-lined autoclave, 7 gms. ethyl chloride are added, and the whole is heated under

pressure for 5–6 hours at 90°–100°. On cooling, the diethoxy azo compound separates, and is filtered off (M.P. 156°).

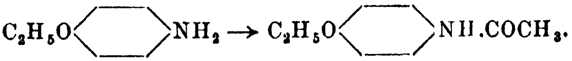


(3) 10 gms. of the diethoxy azo compound are mixed with 50 gms. 20% hydrochloric acid, and 6 gms. of granulated tin are added. When all has gone into solution, caustic soda solution is added to make alkaline, and the *p*-phenetidine distilled over by superheated steam at 160°–180°.



2 mols. of *p*-phenetidine are thus prepared from the initial 1 mol. of *p*-phenetidine. (D.R.P., 48453.) See also U.S.P., 1890430.

(4) Equal weights of distilled *p*-phenetidine and glacial acetic acid are heated under a reflux with the addition of a little fused sodium acetate until no free base remains (diazotise and test with alkaline β-naphthol). The excess acetic acid is removed by distillation *in vacuo*, and the residue dissolved in boiling water containing decolourising carbon, and after cooling and filtering, phenacetin separates out. It is filtered, washed, and recrystallised from water or 60% alcohol, a little sulphur dioxide solution being added to prevent oxidation.



White glistening scales ; M.P. 134° ; a very important analgesic and antipyretic. (D.R.P., 139568.)

For preparation of sulphanilamide, see p. 327.

CHAPTER XXVIII

ELECTROLYTIC PREPARATIONS

PREPARATION 408.—**Benzaldehyde.**

$C_6H_5.CHO. \qquad C_7H_6O. \qquad 106.$

The apparatus for this preparation consists of a narrow glass beaker, or a wide-mouthed bottle. The beaker is corked, and an efficient glass stirrer passing through the centre is attached to a small turbine or motor. Four electrodes are fixed in position so that they are clear of the stirrer. Two anodes, each of sheet platinum of about 1 sq. dcm. surface, are placed diametrically opposite one another, while the two cathodes, spirals of platinum wire and each of 2 cms. surface, are placed between them near the sides of the beaker. 50 gms. toluene, 200 c.cs. of 10% sulphuric acid and 250 c.cs. of acetone are placed in the cell, which is surrounded by cold water. The current density should be 1·5–2 amperes, the E.M.F. 5–6 volts, and the temperature 15°–20°. The stirring must be vigorous to keep the mixture well emulsified.

$$C_6H_5.CH_3 + 2O = C_6H_5.CHO + H_2O.$$

50 gms. of toluene require 58 ampere hours, but in order to ensure complete oxidation 65 ampere hours should be passed. The contents are then transferred to a flask, and made slightly alkaline with sodium carbonate. The acetone is removed by distillation, and the residue steam distilled, when benzaldehyde and unchanged toluene pass over. Benzaldehyde is separated as its bisulphite compound from which it is isolated as described in Preparation 156.

Yield.—7–8 gms. (see p. 229). The procedure for *o*- and *p*-xylene is similar. (Am. Soc., 22, 723. Faraday Soc., 1904, 31.)

PREPARATION 409.—**Iodoform** (*Triiodomethane*).

$CHI_3. \qquad 394.$

20 gms. of anhydrous sodium carbonate and 20 gms. (8 mols.) of potassium iodide are dissolved in 20 c.cs. of water, 50 c.cs. (excess) of absolute alcohol added, and the whole poured into a beaker. The anode is a sheet of platinum foil, 8 by 10 cms., the cathode of platinum wire wound into a spiral of 1 cm. diameter.

The solution is warmed to 60°–70°, and a current of 3 amperes per sq. dcm., counting both sides of the anode, is passed through the solution, while carbon dioxide is bubbled into the liquid to neutralise the caustic potash formed. After 1 hour the iodoform which has separated is filtered off and washed with cold water.

$$2KI + H_2O + CO_2 \longrightarrow K_2CO_3 + H_2 + I_2.$$

$$CH_3CH_2OH \xrightarrow{I_2} CH_3CHO \xrightarrow{3I_2} CI_3CHO \longrightarrow CHI_3.$$

Yield.—75% theoretical. Yellow crystals; insoluble in water; soluble in alcohol and ether; volatile in steam; M.P. 119°. (C., 1897, II, 695.)

PREPARATION 410.—**Methyl Alcohol.**

CH_3OH. CH_4O. 32.

A solution in 500 c.cs. water is made from 110 gms. potassium acetate, 26 gms. potassium carbonate and 28 gms. potassium bicarbonate, and poured into a lead cell or glass beaker, which need contain no anode chamber. The beaker should be placed in a basin of cold water, and the cathode should take the form of a thin lead pipe, with a copper connection soldered to it, wound in the form of a coil, and placed close to the inner walls of the beaker. Through this pipe a supply of cold water is run, so that the temperature is maintained at 25°–30° during the electrolysis. The anode is of platinum, and should be so arranged that it can be rotated. The current density is 20–25 amperes per sq. dcm., and the E.M.F. 7–8 volts.

As the electrolysis proceeds, acetic acid is dropped in at such a speed that the solution does not become acid. When 50–60 ampere hours have passed the electrolysis is stopped. The contents of the cell are then distilled to remove the methyl alcohol, and some formaldehyde, which is also produced. The alcohol is dried and redistilled in the usual way.

$$CH_3COO^+ + OH' \longrightarrow CH_3OH + CO_2.$$

Yield.—50–60% theoretical (see p. 217). (A., 323, 304.)

PREPARATION 411.—***p*-Phenylenediamine.**

$H_2N.C_6H_4.NH_2$. $C_6H_8N_2$. 108.

20 gms. *p*-nitroaniline are dissolved in 150 c.cs. of alcohol, and to this is added a solution of 5 gms. sodium acetate in 100 c.cs. hot water. This mixture is then placed in a beaker, which acts as a cathode cell. The anode cell, which is a porous pot, contains a 20% solution of sodium carbonate. The cathode and the anode are both of nickel gauze.

The mixture is first warmed to 75°, and the high current keeps it boiling. Alcohol may be added from time to time to replace that evaporated. The current density is 15 amperes, and the E.M.F. 7–8 volts. After about 20 ampere hours have passed, the current density is cut down to 2 amperes. After 24 ampere hours have passed, the current is stopped; the hot cathode liquid is then poured into a mixture of 50 c.cs. of sulphuric acid and 100 c.cs. of water, and allowed to stand. The *p*-phenylenediamine sulphate is filtered and dried on a porous plate.

Yield.—75% theoretical (10 gms.). *o*-Nitroaniline gives by same method *o*-phenylenediamine; *m*-nitroaniline gives by same method 3 : 3′-diaminoazobenzene. (B., 28, 2350.)

PREPARATION 412.—**Borneol.**

$C_{10}H_{18}O$. 154.

A 10% solution of camphor in alcohol and half its volume of 75% sulphuric acid is placed in the cathode chamber and 70% sulphuric acid placed in the anode chamber. The current density is 12 amperes, and the E.M.F. 10–15 volts. The current is allowed to pass for 5 hours, the temperature being kept below 20°. The product is then poured into water, and the solid filtered off, dried and recrystallised from petroleum ether.

Yield.—40% theoretical. M.P. 204°–205°. (Z. e., 8, 288.)

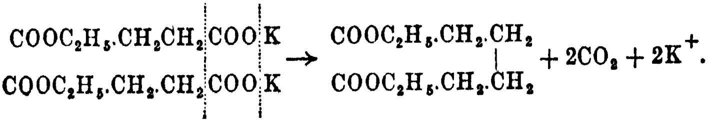
PREPARATION 413.—**Diethyl Adipate** (*Di-ethyl ester of hexan di-acid*).

$\mathrm{COOC_2H_5.(CH_2)_4.COOC_2H_5}$. $\mathrm{C_{10}H_{18}O_4}$. 202.

Ethyl Acrylate.

$\mathrm{CH_2 : CH.COOC_2H_5}$. $\mathrm{C_5H_8O_2}$. 100.

A nearly saturated solution of potassium ethyl succinate (1·5 parts of salt to 1 part of water) is placed in a tall beaker, which must not be more than half full, and which should be cooled in ice-water. An anode of stout platinum wire, made into a spiral, is introduced. The cathode consists of a piece of sheet platinum. A current of 50–75 amperes per sq. dcm. of anode surface is then passed through. Much frothing takes place. At the end of the reaction—70 c.cs. of solution require 20 ampere hours—the mixture with the adipic ester floating on the surface is diluted with water in a separating funnel, and extracted twice with ether. The ethereal extract is dried over calcium chloride and placed in a distilling flask. After removing ether, the fraction distilling up to 120° containing ethyl acetate is separately collected. The residue containing diethyl adipate is distilled under reduced pressure.



$$\begin{matrix} \mathrm{COOC_2H_5.CH_2CH_2COOK} \\ \mathrm{COOC_2H_5.CH_2.CH_2COOK} \end{matrix} \rightarrow \begin{matrix} \mathrm{COOC_2H_5.CH_2.CH_2} \\ | \\ \mathrm{COOC_2H_5.CH_2.CH_2} \end{matrix} + 2\mathrm{CO_2} + 2\mathrm{K^+}.$$

Yield of Diethyl Adipate.—30–35% theoretical; B.P. ^{760} 245°; colourless liquid with characteristic odour. Ethyl acrylate, which is a by-product, is obtained in only very low yield; B.P. ^{760} 101°–102°. (T. R. S. E., 36, 211.)

For a theoretical treatment of electrolytic oxidation and reduction, see text-book of this title by Glasstone and Hickling (1935).

CHAPTER XXIX

PRODUCTS FROM NATURAL SOURCES

PREPARATION 414.—**Quinine Sulphate.**

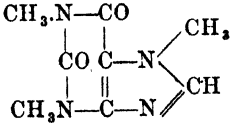
$$C_{29}H_{24}N_2O_2.H_2SO_4 + 8H_2O.$$

80–100 gms. of powdered cinchona bark are placed in a mortar and ground up with about 250 c.cs. of milk of lime. The whole is evaporated to dryness on the water bath, and the mass powdered up when cold. This residue is shaken up with about 200 c.cs. of chloroform, and allowed to stand in a flask for about 12 hours. It is then filtered and washed with chloroform. The quinine is removed from the chloroform extract by shaking up 2 or 3 times with dilute sulphuric acid and then with water, until the aqueous solution no longer exhibits a blue fluorescence. The acid and aqueous extracts are carefully neutralised with ammonia, and the whole is evaporated on the water bath until quinine sulphate begins to separate out ; it is filtered off, on cooling. Another crop of crystals may be obtained by concentrating the mother liquor. The quinine sulphate may be recrystallised from water.

Yield.—1–2 gms.

The free base may be isolated by dissolving the sulphate in water slightly acidified with dilute sulphuric acid. Excess of sodium carbonate solution is then added, when the quinine is precipitated. It is filtered off, washed and dried. M.P. 175°.

PREPARATION 415.—**Caffeine** (1 : 3 : 7-*Trimethylxanthine*).



$C_8H_{10}O_2N_4$. 194.

¼ lb. of tea is boiled up with 600 c.cs. of water for 15 minutes, and filtered through fine cotton, the leaves being washed with about 300 c.cs. of boiling water.

The filtrate is heated to boiling, and basic lead acetate (made by boiling lead acetate with litharge and water, and filtering) is added until no further precipitation of the albumins and tannins present takes place. This is filtered and the residue washed with hot water. The lead in the filtrate is precipitated by adding dilute sulphuric acid. The clear liquor is decanted from the lead sulphate and concentrated to 300 c.cs., decolourising carbon being added. After filtering and cooling, the filtrate is extracted several times with chloroform. The chloroform is removed by distillation on the water bath, and the crude product boiled with water and decolourising carbon, and filtered. The filtrate is then concentrated until crystallisation takes place.

Yield.—1–2 gms. Fine needles, containing $1H_2O$; M.P. 234°–235°. Caffeine may be synthesised from uric acid. (D.R.P., 121224.)

PREPARATION 416.—***d*-Alanine** (*d-2-Amino-propan acid*).

$CH_3.CH(NH_2)COOH.$ $C_3H_7O_2.N.$ 89.

Glycocoll-ester Hydrochloride (*Hydrochloride of ethyl ester of amino-ethan acid*).

$CH_2(NH_2.HCl.).COOC_2H_5.$ $C_4H_{10}O_2.N.Cl.$ 139·5.

The raw material employed is the cheap waste of raw Milan silk, 500 gms. of which are treated with 2 litres of fuming hydrochloric acid (D. 1·19) and frequently shaken until in the course of an hour the threads have fallen to pieces. The flask is warmed, with frequent shaking, on a steam bath; the liquid foams considerably, and a dark violet solution is produced. This is boiled under a reflux condenser for 6 hours; it is advisable to add a few gms. of decolourising carbon. When cold, the acid liquor is filtered through a coarse but strong filtering cloth, and evaporated under reduced pressure (10–15 mms.) at 40°–45° to a thick syrup. This is treated while still warm with 3 litres of absolute alcohol, and a very rapid current of dry hydrogen chloride passed in without cooling and with frequent shaking, until the liquid is saturated. In this process complete solution should occur, and the alcohol should boil. The operation is usually finished in 1½ hours. If the current of hydrogen chloride, and consequently the rise in temperature, is too small, the mixture must be boiled afterwards for ½ hour on the water bath, in order to render the esterification as complete as possible.

The very dark brown liquid is now cooled to 0°, and " inoculated " with a few small crystals of glycocoll-ester hydrochloride, and the greater part of the glycocoll-ester hydrochloride separates in the course of 12 hours at 0° in the form of a thick paste of crystals. The mass is filtered at the pump through coarse linen, well pressed, and washed with a little ice-cold alcohol. The acid alcoholic solution is evaporated as completely as possible under low pressure from a bath at 40°–45°, and the residual syrup is again esterified with 1½ litres of alcohol and hydrogen chloride, as before. The cold solution is " inoculated ", and allowed to stand for 2 days at 0°, when the remainder of the glycocoll is for the most part precipitated as ester hydrochloride. The solution, after filtration, is again evaporated under reduced pressure. The syrup left behind contains the hydrochlorides of the other amino-acid esters. In order to liberate the esters, the residue is dissolved by vigorous shaking at ordinary temperature in the smallest quantity of water (about ¼ volume). To the solution is added about twice its volume of ether, and the whole is carefully cooled in a freezing mixture. Strong caustic soda is then cautiously added until the free acid is almost neutralised, and, finally, a saturated solution of potassium carbonate. On vigorous shaking, a considerable part of the liberated esters goes into solution in the ether. The ether is now poured off and replaced by fresh ether. The whole is carefully cooled, then an excess of concentrated alkali is added, and immediately afterwards potassium carbonate in small portions, until the whole mass has become a thick paste. The ether is repeatedly renewed during the operation.

The extraction with ether is continued until the extracts are colourless. This requires 4–5 litres of ether.

The united ethereal solutions, which are brown in colour, are shaken for 5 minutes with potassium carbonate, then poured off, and dried for 12 hours over anhydrous sodium sulphate. When the greater part of the ether has been evaporated at ordinary pressure on a water bath, the distillation is continued under a pressure 10–12 mms. At ordinary temperature, ether first passes over. The distilling vessel is now warmed in warm water, when a first fraction is obtained, which still contains alcohol and ether, and also some glycocoll ester and alanine ester. When the temperature of the bath has risen to 55°, the main part of the alanine ester begins to boil. The operation is discontinued when, at a bath temperature of 80°, nothing more distils over. In this way 110–125 gms. distillate are obtained, consisting for the most part of alanine ester.

To obtain free alanine the alanine ester is heated for about 6 hours with 5 times its weight of water on a water bath, until the alkaline reaction has disappeared. The solution is evaporated on a water bath till crystallisation begins. The liquid is allowed to stand at 0°, when about 30 gms. alanine separate ; optical examination shows this to consist of almost pure *d*-compound. From the mother liquor a second crop of 20–25 gms. may be obtained, and this still consists of fairly pure active amino-acid, so that the total yields amount to 50–55 gms. The last mother liquor still contains a fair amount of active alanine, but it is mixed with so much racemic substance that it cannot be separated from it by mere recrystallisation from water. The first two crops are dissolved once more in hot water, and the liquid evaporated on the water bath till it begins to crystallise. At 0° a large quantity of the pure, active amino-acid separates out.

Glycocoll-ester hydrochloride : Colourless needles ; soluble in hot alcohol ; very soluble in water ; M.P. 144°. *D-alanine* : Needles ; soluble in water ; decomposes on heating ; $[\alpha]^{20}_{D}$ (hydrochloride) = $+9{\cdot}55°$. (J. pr., [2], 37, 160 ; B., 27, 60 ; 32, 2459 ; O. S., IX, 4 ; C. r., 186, 1844.)

PREPARATION 417.—**Cystine** {*Di-(2-amino-2-carboxy-ethanyl-*(1))- *disulphide*}.

$$\left.\begin{array}{l}HOOC.CH(NH_2).CH_2S\\ HOOC.CH(NH_2).CH_2S\end{array}\right> \qquad C_6H_{12}O_4N_2S_2. \qquad 240.$$

500 gms. of horsehair are boiled in a flask of 3 litres capacity with 1½ litres of conc. hydrochloric acid (about 30% strength) for 6 hours under a reflux condenser. The dark-coloured liquid is diluted with 4 litres of water, and, while kept fairly cool, is treated with conc. potassium hydroxide solution (33%) until the reaction is only faintly acid. To clarify the liquid it is warmed and vigorously stirred for some time with about 40 gms. decolourising carbon, and filtered. The filtrate is exactly neutralised with potassium hydroxide, and set aside to crystallise at low temperature, preferably in the ice chest, for 5–6 days. The cystine which separates is filtered at the pump, washed with cold water, then dissolved in the minimum quantity of warm 10% ammonia, again treated with decolourising carbon in the warm, and finally precipitated from the filtrate by the

addition of acetic acid. This operation is repeated once more; the final product is quite colourless and free from tyrosine.

Yield.—15 gms. Colourless crystals. (E. Fischer, *Organic Preparations*, 1908; O. S., V, 39.)

PREPARATION 418.—**Glucosamine Hydrochloride** (*Hydrochloride of* 2-*Amino*-3 : 4 : 5 : 6-*tetrol-hexanal*-(1)).

$CH_2OH.(CHOH)_3CH(NH_2HCl).CHO.$ $C_6H_{14}O_5Cl.$ 191·5.

The carapaces and claws of lobsters, which have been cleaned, as far as possible mechanically, are digested for 24 hours with cold dilute hydrochloric acid. They may then be cut up easily, and freed from adherent fibres and flesh. 100 gms. of the material thus prepared are covered in a porcelain dish with fuming hydrochloric acid, and heated to gentle boiling on a sand bath. The chitin quickly goes into solution, and the liquid becomes dark in colour. The liquid is evaporated until a considerable crystallisation of glucosamine hydrochloride has taken place, then allowed to cool, filtered at the pump, through linen or hardened paper, and washed with a little cold hydrochloric acid. The mother liquor, on further evaporation, yields a second crop of crystals. To purify the salt it is dissolved in warm water, and the solution concentrated till crystallisation begins.

Colourless crystals; soluble in hot water. (B., 17, 213.)

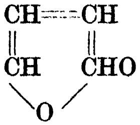
PREPARATION 419.—**Tyrosine** {2-*Amino*-3-(*p-hydroxyphenyl*)-*propan acid*}.

$HO.C_6H_4.CH_2.CH(NH_2).COOH.$ $C_9H_{11}O_3.$ 167.

100 gms. of silk waste are boiled for 6 hours under a reflux condenser with 300 c.cs. of fuming hydrochloric acid (D. 1·19). The greater part of the hydrochloric acid is removed by evaporating the brown coloured solution under reduced pressure; the residue is dissolved in water, filtered, and made up to a known volume. The percentage of hydrochloric acid is determined by titration of an aliquot part of the liquid, and the amount of sodium hydroxide calculated for the whole solution is then added, with ice cooling and constant stirring. A brownish-black precipitate is at once produced. After it has stood for an hour in ice-water, it is filtered off at the pump, dissolved again in hot water, and boiled vigorously with about 10 gms. decolourising carbon. The filtered liquid is now colourless, and deposits pure tyrosine on cooling. By concentrating the mother liquor a second crop of crystals may be obtained.

Yield.—5–6 gms. Colourless crystals; soluble in hot water. (Z. ph., 48, 528.)

PREPARATION 420.—**Furfuraldehyde** (*Furfurol*).



$C_5H_4O_2.$ 96.

A mixture of 200 gms. of bran, 200 gms. of conc. sulphuric acid, and 600 gms. of water is distilled from a large flask till the distillate measures about 600 c.cs. The latter is neutralised with caustic soda, mixed with

150 gms. of common salt and again distilled, till about 200 c.cs. have passed over. The distillate is again saturated with common salt, extracted with ether, the extract dried over anhydrous sodium sulphate, the ether removed on the water bath, and the residue distilled, the fraction 160°–165° being collected separately.

Yield.—6 gms. Colourless liquid ; characteristic smell ; darkens on standing ; B.P. 162° (A., 74, 280 ; 116, 258 ; O. S., I, 49.)

PREPARATION 421.—**Oleic Acid** (9-*Octadecen Acid*).

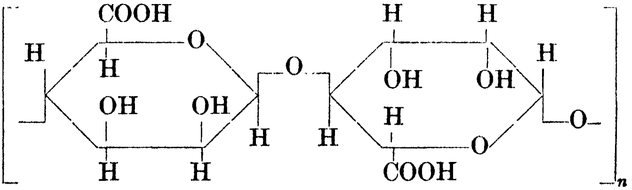
$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$. $C_{18}H_{34}O_2$. 282.

10 gms. of potassium hydroxide in 100 c.cs. of alcohol are heated with 30 gms. olive oil for 1–2 hours under a reflux. The alcohol is removed on a water bath, and dilute acetic acid is added to the residue until it is neutral to phenolphthalein. 30 gms. of conc. lead acetate solution are then added ; this precipitates a mixture of the lead salts of oleic, palmitic, and stearic acids. The mixture is filtered and washed with alcohol to remove unchanged oil. It is then extracted in a Soxhlet apparatus with ether, which dissolves lead oleate. When the ether is evaporated lead oleate remains. Pure dilute nitric acid is added, and oleic acid separates as an oil. The oil is removed by means of a separating funnel, dried over calcium chloride, and distilled under reduced pressure.

$$C_3H_5(O.COC_{17}H_{33})_3 + 3KOH \longrightarrow 3C_{17}H_{33}COOK + C_3H_5(OH)_3.$$

Colourless oil ; M.P. 14° ; B.P. ^{10} 223° ; decomposes on heating at ordinary pressure ; D. $^{15}_{4}$ 0·895. (B., 27, 172.)

PREPARATION 421A.—**Alginic Acid.**



Fresh seaweed, containing 70–90% water, is dried in a current of air at laboratory temperature for 2 days, the moisture content then being 20–30%. 25 gms. of the material is finely-divided and covered with 0·5% hydrochloric acid in a large beaker. After keeping for 24 hours the material is placed on a Buchner funnel and washed with water, the filtrate being rejected. The product is then digested at room temperature for 24 hours with 5% aqueous sodium carbonate, this process being repeated a second time with fresh carbonate solution. The combined extracts are separated from the pulp on a wire sieve. The brown viscous filtrate is vigorously shaken with decolourising carbon and filtered on a Buchner funnel. To the filtrate is added hydrochloric acid until the alginic acid is completely precipitated. The latter is washed free of chloride on the sieve with water, dehydrated by successive washings in alcohol, and finally with ether. It is finally dried in a stream of air.

Yield.—2 gms. (15–40%). White amorphous powder. Forms insoluble fibres with polyvalent metals. E.P. 541847, 545872.

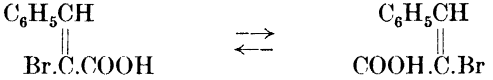
CHAPTER XXX

STEREOCHEMICAL REACTIONS

PREPARATION 422.—α-**Bromocinnamic Acid** (*3-Phenyl-2-bromo-2-propen acid*).

$C_6H_5.CH : CBr.COOH. \quad C_9H_7O_2Br. \quad 227.$

5 gms. of pure α-bromo-*allo*cinnamic acid (p. 427) are placed in a test tube with a thermometer immersed in the substance. The tube is immersed in a bath of conc. sulphuric acid heated to 200°–210°, and kept there for 10 minutes. After cooling, the product is dissolved in dilute alkali, and after neutralising the excess of alkali the solution is treated with a solution of barium chloride, which precipitates the barium salt of α-bromocinnamic acid. The free acid is obtained by treating the washed precipitate with conc. hydrochloric acid. After washing and drying it is recrystallised from benzene.

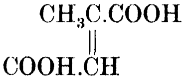


$$\begin{array}{c} C_6H_5CH \\ \| \\ Br.C.COOH \end{array} \quad \rightleftarrows \quad \begin{array}{c} C_6H_5CH \\ \| \\ COOH.C.Br \end{array}$$

α-Bromocinnamic acid. M.P. 131°. α-Bromo-*allo*cinnamic acid. M.P. 120°.

Yield.—80–85% theoretical (4–4·2 gms.). Colourless prismatic needles; soluble in hot benzene; M.P. 131°. (J. C. S., 83, 686.)

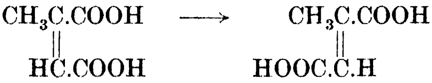
PREPARATION 423.—**Mesaconic Acid** (*trans-3-Carboxy-2-buten acid*).



$$\begin{array}{c} CH_3C.COOH \\ \| \\ COOH.CH \end{array}$$

$C_5H_6O_4. \quad 130.$

20 gms. of citraconic acid (see p. 246) are dissolved in the minimum quantity (about 25 c.cs.) of pure dry ether in a quartz flask. 5 gms. of chloroform and a few drops of a moderately strong solution of bromine in chloroform are then added. The solution is exposed to strong sunlight, or to a mercury vapour lamp. (see p. 56). Mesaconic acid soon begins to separate on the side of the flask nearest to the light. The flask is occasionally turned, and drops of bromine are added at intervals until no further separation takes place. The pasty mass is filtered, washed with ether and dried.



$$\begin{array}{c} CH_3C.COOH \\ \| \\ HC.COOH \end{array} \longrightarrow \begin{array}{c} CH_3C.COOH \\ \| \\ HOOC.C.H \end{array}$$

Yield.—73% of complete conversion (15 gms.). Colourless crystals; M.P. 202°; somewhat soluble in water; insoluble in ether and in chloroform. (A., 188, 73.) See also O. S., XI, 74.

PREPARATION 424.—**Benz*anti*aldoxime** (*β-Benzaldoxime*).

$$\begin{array}{c} C_6H_5CH \\ \| \\ HO.N \end{array}$$

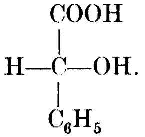
C_7H_7ON. 121.

12 gms. α-benzaldoxime (p. 294) are dissolved in 50 c.cs. pure anhydrous ether. Dry hydrogen chloride is passed into this solution, using a rather wide delivery tube, since the hydrochloride of the β-oxime, which separates quickly, is liable to block the end of the tube. The precipitate is filtered off, washed with ether, transferred to a separating funnel and mixed with 50 c.cs. of ether. Conc. sodium carbonate solution is then added, with shaking, until effervescence ceases. The ethereal layer, which contains the β-oxime, is separated from the lower aqueous sodium chloride layer, dried over anhydrous sodium sulphate, and the ether removed in a vacuum desiccator. The residue forms a mass of small needles, which are pressed out on a porous plate.

Yield.—80% theoretical (8 gms.). M.P. 128°–130° (on quick heating). (B., 23, 1684.)

$$\begin{array}{c} C_6H_5CH \\ \| \\ NOH \end{array} \longrightarrow \begin{array}{c} C_6H_5.CH \\ \| \\ HO.N \end{array}$$

PREPARATION 425.—**Resolution of Mandelic Acid.**



$$\begin{array}{c} COOH \\ | \\ H—C—OH. \\ | \\ C_6H_5 \end{array}$$

$C_8H_8O_3$. 152.

25 gms. *r*-mandelic acid in 30 c.cs. absolute alcohol are added slowly to a warm solution of 25 gms. *l*-ephedrine in 45 c.cs. absolute alcohol. The whole is gently warmed (not boiled) for 2 hours on a water bath and cooled in the ice-chest overnight. The crystals of *l*-ephedrine-*l*-mandelate are filtered, washed with 15 c.cs. absolute alcohol and then boiled with 30 c.cs. absolute alcohol. On cooling, the complex is filtered, drained, and mixed with excess hydrochloric acid until definitely acid to Congo red. The *l*-mandelic acid is extracted with ether (six times), the aqueous layer being finally acid to Congo red. The ether extract (dried over anhydrous sodium sulphate) yields about 11 gms. *l*-mandelic acid, $[\alpha]_{5461} = -177°$ in acetone. The aqueous layer is made alkaline with *excess* of strong caustic soda solution and the *l*-ephedrine extracted (4 times) with ether. The ethereal solution is dried over anhydrous sodium sulphate and the *l*-ephedrine recovered by distillation of the ether.

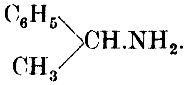
The alcoholic filtrate and washings from the above resolution can be united, split into two parts, and 20 gms. *r*-mandelic acid dissolved in one and 20 gms. of *l*-ephedrine in the other. The two solutions are slowly mixed, warmed on a water bath for an hour, cooled, when *l*-ephedrine-*l*-mandelate appears. This is treated as above and 10 gms. *l*-mandelic should be obtained ($[\alpha]_{5461} = -147°$ in acetone). With the filtrate and washings from this second crop another resolution with 20 gms. *r*-mandelic acid and 20 gms. *l*-ephedrine can be effected. This gives a third crop (12 gms.) of *l*-acid ($[\alpha]_{5461} = -78{\cdot}3^\circ$ in acetone).

Finally, the alcohol is removed from the filtrate and washings under diminished pressure on the water bath. The syrupy residue is dissolved in hydrochloric acid and *d*-acid extracted with ether when 22 gms. *d*-acid, $[\alpha]_{5461} = +160^\circ$ in acetone, are obtained.

The first crop of *l*-mandelic acid is recrystallised from benzene containing acetone, when it yields 7·5 gms. pure *l*-mandelic acid, $[\alpha]_{5461} = -190^\circ$. The second and third crops of *l*-acid can be recombined with *l*-ephedrine as described above, yielding a further 15 gms. of pure *l*-mandelic acid. The crude *d*-acid after recrystallisation from benzene-acetone gives 15 gms. *d*-acid, $[\alpha]_{5461} = +190^\circ$ in acetone. (J. C. S., 1935, 1544.) Colourless needles, M.P. 133°–134°.

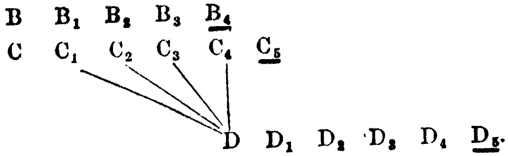
r-Mandelic gives *d*-acid by resolution with cinchonine (B., 16, 1773; 32, 2385), and the *l*-acid by resolution with morphine. (J. C. S., 1899, 753.)

PREPARATION 426.—Resolution of α-Phenylethylamine.



$$\begin{matrix} C_6H_5 \\ CH_3 \end{matrix}\Big\rangle CH.NH_2. \qquad C_8H_{11}N. \qquad 121.$$

Dextro-base.—165 gms. of dry *laevo*-malic acid are covered with 660 c.cs. of cold water in a beaker. 148 gms. of racemic α-phenylethylamine (p. 375) —necessary to form the acid salt—are then added, during a few minutes with constant stirring. Both base and acid dissolve, but before the acid has completely disappeared the solution becomes slightly syrupy, and a crystalline powder begins to separate. The mass is stirred with a glass rod until the malic acid is all dissolved, and then left to stand overnight. The crude *l*-malate of *d*-α-phenylethylamine is filtered off with suction, well pressed down, and washed with a little cold water. (The mother liquor *A*, containing chiefly the *l*-malate of *l*-α-phenylethylamine, is reserved for the preparation of the *l*-amine (see below).) The crude salt, which, when dry, is approximately equal in weight to that of the phenylethylamine used, is recrystallised 3 or 4 times from water. The following method is convenient (p. 14): the crude salt is divided into two portions, *B* and *C*. *B* is dissolved in the minimum of hot water (not above 90°), filtered hot, if necessary, and set aside to crystallise; the formation of small crystals should be induced by cooling in ice-water and scratching with a glass rod. When no more crystals separate, the crop B_1 is filtered off, and the filtrate and small quantity of washings used to recrystallise *C*, from which crop C_1 is obtained. B_1 is recrystallised in the minimum of hot water, yielding crop B_2, and a mother liquor, which is used to recrystallise C_1. The recrystallisation is continued in this manner until crops B_4 and C_4 are obtained. B_4 is pure *d*-amine-*l*-malate, M.P. 184°. The mother liquors from C_1, C_2, C_3 and C_4 are combined and evaporated to about $\frac{1}{4}$ of their volume, then cooled in ice-water, and the resulting crop of crystals *D* filtered off. C_4 is recrystallised once more from fresh hot water, and the mother liquor from C_5 is used to recrystallise D. C_5 is pure, and D_1 is recrystallised 4 more times from water, after which it is pure.



If large quantities of salt are being recrystallised, the mother liquors of D_1–D_5 should be worked up after the above manner to yield more *d*-amine-*l*-malate. The yield of pure *d*-amine-*l*-malate should be about 70% (76·5 gms.) of the crude product. The pure salt is dissolved in water, the solution placed in a separating funnel, and caustic soda solution (30%) added so long as any turbidity of the aqueous layer is produced. The upper layer of base is separated, and the lower aqueous layer extracted with ether to recover any dissolved base. The ethereal extract is united with the base and dried over anhydrous sodium sulphate. The ethereal solution is introduced, in portions at a time, to a Claisen distilling flask of appropriate size, and the ether distilled off (see p. 20). The residue is then distilled in an apparatus filled with hydrogen, the fraction 180°–190° being collected. For polarimetric observations, the amine should be distilled directly into a polarimeter tube, as it is a strong base which absorbs carbon dioxide with avidity.

Yield.—90% theoretical (calculated on pure malate), or 30% of the weight of racemic base used. B.P. 186°–187°; $[\alpha]_D^{17^\circ} = +41{\cdot}59^\circ$; $D.^{17}$ 0·9502.

In the above resolution an equivalent amount of the carbamate of the base can be used in place of the free base.

Laevo-base.—The solution A (referred to above) plus the mother liquors from the recrystallisation of the malate is treated with an excess of caustic soda (50%) to liberate the base, which is extracted with ether, the dark brown colour of the liberated amine being discharged by standing in contact with potash and ether. The base obtained gives $\alpha = 20^\circ$ in a 1 dcm. tube at 15°, which corresponds with an *l*-base content of about 75%. To purify it further, it (60 gms.) is slowly poured, with stirring, into a solution of tartaric acid (75 gms.) in warm 96% alcohol (1,000 c.cs.). After standing overnight the mixture solidifies completely, but the mass is not crystalline, having rather the nature of a gel. It is heated gently on a water bath to 60°, when it becomes liquid, containing a deposit of heavy, colourless, prismatic crystals, which are collected and washed with alcohol at 50°–60°. The mother liquors on cooling set to a firm, gel-like mass, which can easily be liquefied by heating to 40°.

The prisms are dissolved in fresh 96% alcohol by heating under reflux for a considerable time, as they are not very soluble, even at the boil. After cooling, the crystals are collected and washed with warm alcohol. 78 gms. (47% theoretical) of *l*-amine-*d*-tartrate are thus obtained. This salt forms colourless monoclinic prisms, very soluble in water (from which it may readily be recrystallised); sparingly soluble in 96% alcohol; almost insoluble in absolute alcohol. M.P. 192°–193·5°.

The *l*-base liberated (compare *d*-base for fuller details) from this salt by 30% potash, after drying and distillation in a current of hydrogen, gave $[\alpha]^{15^\circ}_{D} = -41{\cdot}48^\circ$. (J. R. T. C., 1926, 65.) See also C. V., II, 506.

Note

At the present time commercial malic acid is chiefly produced by the hydration of maleic anhydride obtained by oxidation of benzene (p. 250) and is optically inactive.

The amine can also be resolved by the use of tartaric acid (G., 1920, 50, 276; Archiv der Pharmazie and Berichte der Deutschen Pharmazeutischen Gesellschaft, 1935, 408).

The amine (121 gms.) is added slowly to a solution of tartaric acid (150 gms.) in 750 c.cs. methyl alcohol. After cooling, the complex is immediately filtered and recrystallised from boiling methyl alcohol (2 litres). The complex is decomposed in the usual manner, when pure amine, $[\alpha]^{20}_{5893} = -38{\cdot}7^\circ$, is obtained.

The methyl alcohol is removed from the filtrate and the residue recrystallised from water. In this crystallisation it may be necessary to concentrate and cool the solution in ice. Two or three recrystallisations from water may be necessary. The complex obtained yields amine of $[\alpha]^{20}_{5893} = +37^\circ$ to 38°.

CHAPTER XXXI

DECOMPOSITIONS

PREPARATION 427.—**Butyric Acid** (*Butan Acid*).

$CH_3.CH_2.CH_2.COOH. \quad C_4H_8O_2. \quad 88.$

10 gms. of ethylmalonic acid (p. 244) are introduced into a small distilling flask, which is placed in an oil bath with the side tube sloping upwards. A cork, carrying a thermometer with bulb immersed in the substance, is inserted in the neck of the flask. The substance is heated at 180° until no further carbon dioxide is evolved. The side tube of the flask is then sloped downwards, and the product (butyric acid) distilled. the fraction 160°–165° being collected.

$$CH_3.CH_2CH(COOH)_2 \longrightarrow CH_3.CH_2.CH_2.COOH + CO_2.$$

Yield.—85% theoretical (5·5 gms.). Colourless liquid; rancid odour; B.P. 162·3°; D. $^{16\cdot5^\circ}_{4}$ 0·8141. (A., 138, 218; J., 1868, 514.)

PREPARATION 428.—**Pyrogallol** (1 : 2 : 3-*Trihydroxybenzene*).

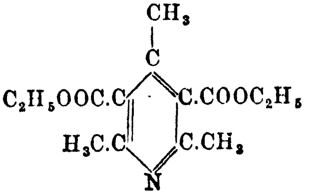
$C_6H_3(OH)_3. \quad C_6H_6O_3. \quad 126.$

10 gms. of gallic acid and 20 gms. of powdered pumice are mixed and placed in a retort. A cork, carrying a delivery tube, is inserted through the tubulus to serve for the entrance of carbon dioxide. The retort is then heated on a sand bath with a stream of carbon dioxide passing through, the stem of the retort sloping downwards into a receiver. Crystals of pyrogallol condense in the stem, which should be warmed with a small flame to cause the product to melt and flow down into the receiver.

$$C_6H_2(OH)_3.COOH \longrightarrow C_6H_3(OH)_3 + CO_2.$$

Yield.—40% theoretical (3 gms.). Colourless crystals; M.P. 133°; soluble in alcohol, ether and water. (A., 101, 48.)

PREPARATION 429.—**Diethylcollidine dicarboxylate** (2 : 4 : 6-*Trimethyl-3 : 5-dicarbethoxy-pyridine*).



$C_{14}H_{19}O_4N. \quad 265.$

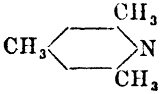
20 gms. of ethyldihydrocollidinedicarboxylate (see Preparation 93) and 20 gms. alcohol are placed in a small flask, which is immersed in a bath

of cold water. Nitrous fumes (p. 520) are led into the mixture until a test sample dissolves to a clear solution in dilute hydrochloric acid. The alcohol is then evaporated off on a water bath, the residue treated with sodium carbonate until alkaline, and the oil which separates extracted with ether. The ethereal extract is dried over potassium carbonate, the ether evaporated, and the residue distilled. The fraction 290°–310° is collected and redistilled, the pure ester distilling at 308°–310°.

$$C_5H_2N(CH_3)_3(COOC_2H_5)_2 + O \longrightarrow C_5N(CH_3)_3(COOC_2H_5)_2 + H_2O.$$

Yield.—80% theoretical (16 gms.). Yellow oil; B.P. 308°–310° (A., 215, 8.)

Preparation 430.—**Collidine** (2 : 4 : 6-*Trimethylpyridine*).



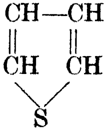
$C_8H_{11}N$. 121.

10 gms. of powdered, dry dipotassium collidine dicarboxylate (see Preparation 181) are intimately mixed with 20 gms. of slaked lime, and the mixture introduced into a 50-cm. length of combustion tubing, closed at one end. A loose plug of asbestos is placed near the mixture in the open end of the tube which is tapped horizontally on the bench to make a passage for gas and then connected by means of an adapter to a small receiver. The tube is placed in a sloping combustion furnace so that the sealed end is slightly elevated. The closed end is first heated slightly, the rest gradually, and finally the whole length is strongly heated with the tiles in position. The distillate is taken up with ether, the extract dried over solid potassium hydroxide and distilled, the fraction 169°–174° being separately collected.

$$C_5N(CH_3)_3(COOK)_2 + 2Ca(OH)_2 \longrightarrow 2CaCO_3 + 2KOH + C_5NH_2(CH_3)_3.$$

Yield.—75% theoretical (3 gms.). B.P. 172°; greenish-yellow liquid with an obnoxious odour. (A., 215, 32.)

Preparation 431.—**Thiophen.**



C_4H_4S. 84.

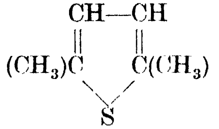
100 gms. (less than 1 mol.) of phosphorus trisulphide (p. 519) and 100 gms. (1 mol.) of thoroughly dry sodium succinate are intimately mixed and placed in a 500-c.c. retort, to which is attached a tube for passage of carbon dioxide throughout the operation. The retort is connected to a condenser, which passes through a cork to a receiver cooled in a freezing mixture. A wash-bottle containing dilute caustic soda and fitted with a cork carrying two delivery tubes is connected on one side to the receiver, and on the other to a draught chamber (or a slight suction from a pump).

On heating the retort with a small flame a reaction soon commences, and the mass swells up with the evolution of much sulphuretted hydrogen. At this stage the flame is withdrawn and the reaction allowed to proceed spontaneously until completion (e.g. till gas ceases to bubble through the wash-bottle). The contents of the receiver are distilled from a water bath, washed with dilute caustic soda, dried over metallic sodium and redistilled.

$$(CH_2.COONa)_2 + 4H_2S \longrightarrow C_4H_4S + Na_2S + 2S + 4H_2O.$$

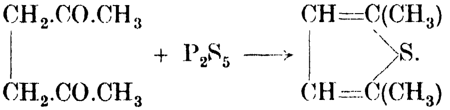
Yield.—30% theoretical (15 gms.). Colourless liquid; faint smell resembling that of benzene; B.P. 84°. Gives blue colour (indophenine) with isatin and conc. sulphuric acid. (B., 18, 454; O. S., XII, 72.)

PREPARATION 432.—**Thioxene** (2 : 5-*Dimethylthiophen*).



C_6H_8S. 112.

6 gms. (1 mol.) of acetonyl-acetone (see p. 199) are heated with 4 gms. (excess) of finely-powdered phosphorus pentasulphide in a sealed tube at 140°–150° for an hour. On cooling, a colourless liquid and a solid are obtained; the former is poured off and fractionally distilled. The distillation is repeated over metallic sodium, the fraction 132°–136° being retained.



Yield.—50% theoretical (3 gms.). Colourless, mobile liquid; characteristic odour; B.P. 135°; D. $^{17\cdot5}_{4}$ 0·9755; gives a cherry-red colour with a solution of isatin in conc. sulphuric acid. (B., 18, 2251; 20, 1747.)

PREPARATION 433.—**Phenyl*iso*thiocyanate** (*Phenyl mustard oil*).

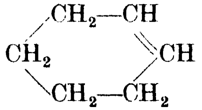
C_6H_5NCS. C_7H_5NS. 135.

64 c.cs. conc. hydrochloric acid and 20 gms. thiocarbanilide (p. 446) are boiled for 30 minutes in a flask attached to a reflux, when the phenyl isothiocyanate separates as an oil. 40 c.cs. water are added and the whole distilled until about 15 c.cs. remain in the flask. The distillate is extracted with ether, which is then dried with calcium chloride. The ether is removed by distillation, and the fraction boiling at 197°–222° collected. This is redistilled, and the fraction 218°–222° retained.

$$(C_6H_5NH)_2CS \xrightarrow{HCl} C_6H_5NCS + C_6H_5NH_2(HCl).$$

Yield.—55% theoretical (7 gms.). Colourless liquid with pungent odour; B.P. 222°; D. $^{15\cdot5}$ 1·135. (Z. Ch., 1869, 589; O. S., VI, 72.)

PREPARATION 434.—**Cyclohexene** (*Tetrahydrobenzene*).



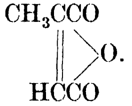
C_6H_{10}. 82.

20 gms. cyclohexanol are placed in a 200-c.c. flask fitted with a column, thermometer, and long condenser dipping via an adapter into an ice-cooled receiver. 2 c.cs. conc. sulphuric acid and a few pieces of porous tile are added to the flask which is gently shaken. The flask is gently heated and the temperature at top of the column is not allowed to exceed 100°. The distillate is collected until only a small residue remains, and solid sodium chloride and a few c.cs. sodium carbonate solution added. The bottom aqueous layer is discarded and the top layer treated with anhydrous calcium chloride, decanted, and distilled, the fraction B.P. 80°–85° being collected.

$$C_7H_{12}O - H_2O \longrightarrow C_6H_{10}.$$

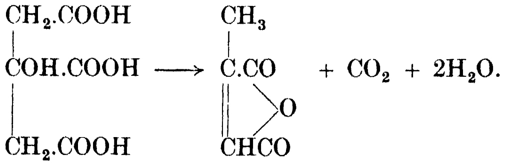
Yield.—75% theoretical (12 gms.). Colourless liquid ; B.P. 83° ; D. 0·809. O. S., 5, 33.

PREPARATION 435.—**Citraconic Anhydride** (*Anhydride of cis-3-carboxy-2-buten acid*).



$C_5H_4O_3$. 112.

250 gms. of crystallised citric acid are dehydrated by heating in a porcelain basin to a temperature not exceeding 150°. When the acid has become fluid the whole is allowed to cool, removed from the basin and coarsely powdered. The anhydrous acid is then placed in a retort and rapidly distilled. The distillate separates into two layers, the upper layer consisting of water and citraconic acid and the lower layer of impure citraconic anhydride. The layers are separated and the upper layer fractionated, the fraction 190°–210° being collected and added to the anhydride layer. This mixture is distilled under 30 mms. pressure, the fraction 110°–114° being retained.



Yield.—22–25% theoretical (30–35 gms). Colourless liquid ; B.P.^{30} 110°–114° ; B.P.^{760} 213°–214°. (A., 188, 73.) See also O. S., XI, 28.

PREPARATION 436.—**Ethylene** (*Ethen*).

$$CH_2 : CH_2. \quad C_2H_4. \quad 28.$$

50 c.cs. syrupy *ortho*-phosphoric acid (D. 1·75) are heated in a flask until

the temperature reaches 210°, and alcohol run in very slowly by means of a dropping funnel drawn out to a point and reaching to the bottom of the flask. During the addition the temperature must be kept between 200° and 220°. The gas is dried by bubbling through conc. sulphuric acid.

$$C_2H_5OH - H_2O = C_2H_4.$$

Colourless gas with sweet smell; sparingly soluble in water, more readily in alcohol and ether; liquefies at 10° and 60 atms. (P. C. S., 17, 147.) See also Preparations 9 and 326.

PREPARATION 437.—**Acetonitrile** (*Methyl cyanide*).

CH_3CN. C_2H_3N. 41.

15 gms. of phosphorus pentoxide are introduced into a 200-c.c. distilling flask attached to a short condenser. As the pentoxide absorbs moisture rapidly and becomes sticky, it is convenient to push the neck of the distilling flask through a cork, which fits the phosphorus pentoxide bottle, and then to shake the oxide until the required weight is introduced 10 gms. of powdered acetamide are immediately introduced, the mixture shaken up, and distilled over a small flame, which is constantly moved about. To the distillate is added about half its volume of water, and then solid potassium carbonate, until no more dissolves. The upper layer of liquid, which consists of methyl cyanide, is separated and distilled over a little fresh phosphorus pentoxide.

$$CH_3.CO.NH_2 - H_2O = CH_3CN.$$

Yield.—70% theoretical (5 gms.). Colourless liquid; characteristic odour; B.P. 82°. (A., 64, 333; 65, 297.) See Reaction CXXVII.

PREPARATION 438.—**Acrolein** (*Propenal*).

$CH_2 : CH.CHO$. C_3H_4O. 56.

200 gms. of glycerol previously dehydrated by heating in an open basin to 170° are mixed with 400 gms. of potassium bisulphate broken to the size of small shot in a glass tube, or better, a metallic retort of at least 4 litres capacity. The delivery tube of the retort is connected to a long condenser to the lower end of which a distillation flask is fastened on tightly (e.g. by means of an adapter).

This latter is surrounded by a freezing mixture, and its side tube connected to a draught pipe. The whole apparatus is fitted up in a fume cupboard.

The mixture is allowed to stand in the closed retort for several days, and then slowly heated and distilled, a gas-ring being used to heat the retort. Water first distils, then the contents of the retort swell considerably, and acrolein mixed with water and sulphurous acid passes over. The distillation is continued till, after several hours, practically no more liquid distils.

The distillate consists of two layers, the upper one being acrolein, the lower an aqueous solution of sulphur dioxide. The SO_2 is removed by shaking with powdered litharge till no more white lead sulphite is formed. The whole mass is again distilled on a water bath, the receiver being cooled, as before, and the same precautions taken to prevent the escape of uncondensed vapours.

The distillate is dried over calcium chloride and again distilled on a water bath. All these operations *must* be carried out in a good fume cupboard, and, to prevent loss by polymerisation, as quickly as possible.

$$CH_2OH.CHOH.CH_2OH \longrightarrow CH_2{=}CH.CHO + 2H_2O.$$

Yield.—30% theoretical (35 gms.). Colourless mobile liquid; penetrating odour; attacks the eyes; polymerises on keeping to a white translucent solid (*disacryl*) resembling porcelain; a small quantity of akali or a solution of potassium cyanide brings about the change in a few minutes; B.P. 52°. (B., 36, 550; A. Ch., [6], 26, 367; O. S., VIII, 120.)

PREPARATION 439.—**Pyruvic Acid** (*Propanon Acid*).

$CH_3.CO.CO.OH$. $C_3H_4O_3$. 88.

200 gms. of potassium hydrogen sulphate and 100 gms. of tartaric acid are finely-powdered and *intimately* mixed. The mixture is distilled in a short-necked, 2-litre, round-bottomed flask, attached to a moderately long condenser, from a paraffin bath heated to 220°. The apparatus is fitted up in a fume cupboard. The mass froths a great deal at first, and it is necessary to interrupt the heating when the flask is half full of froth, as otherwise it may boil over. When the temperature of the bath has fallen to about 120° the heating is recommenced. The distillation is continued until no more liquid distils. The distillate is at once fractionated under reduced pressure, the fraction 68°–70° at 20 mms. being separately collected. It may also be fractionated at ordinary pressures, the fraction 130°–180° being redistilled and collected at 165°–170°, but it is difficult to obtain it colourless in this way.

$$COOH.CH(OH).CH(OH).COOH = CH_3.CO.COOH + H_2O + CO_2.$$

Yield.—50% theoretical (30 gms.). Colourless liquid; polymerises on keeping; has a characteristic odour somewhat resembling that of acetic acid; M.P. 10°; B.P. ^{20} 68°–70°; B.P. ^{760} 165°; (A., 242, 268; O. S., IV, 63.)

PREPARATION 440.—**Acetaldehyde Ammonia.**

$CH_3CH(OH)NH_2$. C_2H_7ON. 61.

The apparatus is set up as shown in sketch (Fig. 57). To the 1½-litre round-bottomed flask is attached a slanting condenser with a long delivery tube dipping into 50 c.cs. dry ether in a flask surrounded by a freezing mixture of ice and conc. hydrochloric acid, a further delivery tube passing into a second flask containing dry ether. A tap funnel is also attached to the flask. A side tube leading below the surface of the liquid in the flask is used for the passage of a moderately strong current of carbon dioxide throughout the oxidation. 30 c.cs. ethyl alcohol are brought to the boil in the flask over a small flame. 140 c.cs. conc. nitric acid (D. 1·42) are added to a mixture of 70 gms. sodium dichromate, 265 c.cs. water, and 14 c.cs. conc. sulphuric acid, and the whole added from the funnel at such a rate that the thermometer suspended inside the condenser by a wire attached to the upper cork of this apparatus reads 20°–25°. The funnel should be emptied in about 30 minutes and a further 10 minutes is sufficient to remove the aldehyde. The aldehyde passes over into the ether. Anhydrous sodium sulphate is added to the ethereal solution, which is still kept in the freezing mixture. After a time the solution is decanted and the residue washed with a little dry ether. The solutions are combined, replaced in the freezing mixture, and dry ammonia gas (for preparation, see p. 514) passed through until the solution is saturated. After standing for an hour, the solution deposits crystals, which are filtered off and washed with a little dry ether.

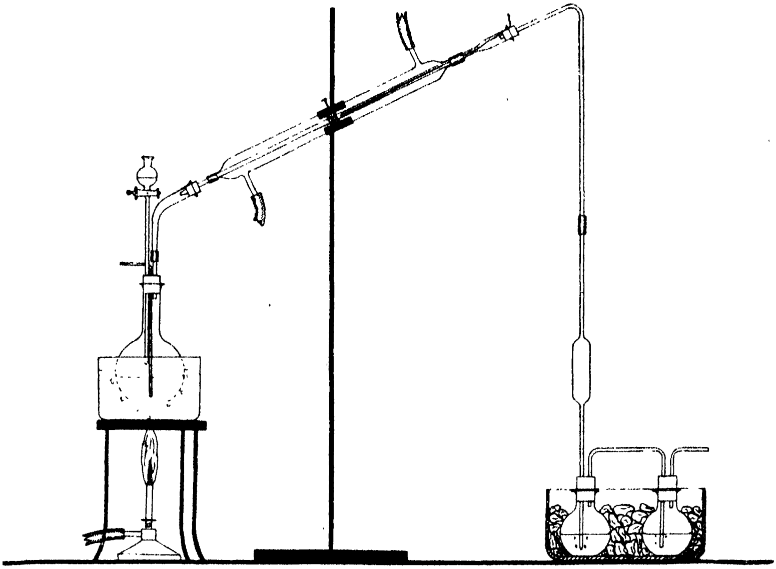


FIG. 57.

$$C_2H_5OH \longrightarrow CH_3.CHO \longrightarrow CH_3.CH(OH).NH_2.$$

Yield.—70% theoretical (22 gms.). The compound actually isolated is the trimeride, $(CH_3CHOHNH_2)_3$. (A., 14, 133 ; J. pr., [1], 76, 54.)

For modifications of the above method, see Am. Soc., 44, 2658 ; Z. a., 36, 546.

Dehydrogenation of Primary Alcohols to yield Aldehydes

When ethyl alcohol is passed over reduced copper at 300°–400°, decomposition takes place into acetaldehyde and hydrogen, the reaction being reversible.

$$CH_3.CH_2OH \rightleftarrows CH_3.CHO + H_2.$$

Methyl alcohol as well as the higher aliphatic and the aromatic alcohols behave similarly. The copper acts catalytically, and while cobalt, nickel, iron, zinc, platinum also serve, copper is the most suitable.

At high temperatures two side reactions accompany the main reaction.

1. The aldehyde formed is split up into hydrocarbon and carbon monoxide.

$$R.CHO \longrightarrow RH + CO.$$

2. Dehydration of the alcohol takes place.

$$R.CH_2.CH_2OH \longrightarrow RCH : CH_2 + H_2O.$$

The operation should, therefore, be conducted at less than 20° above the lowest temperature at which dehydrogenation proceeds.

Dehydration can be effected catalytically. (E.P., 425,550.)

PREPARATION 441.—Acetaldehyde.

$$CH_3CHO. \qquad C_2H_4O. \qquad 44.$$

A combustion tube 1 metre long is loosely packed for three-quarters of its length with copper oxide (either small lumps or wire form), the layer being held in position with loose asbestos plugs. The tube is placed in a cylindrical air bath 75 cm. long fitted with 2 thermometers, preferably nitrogen filled. The oxide is reduced to metal by heating to 180°–200° in a current of specially purified hydrogen. The reduction occupies about 6 days. The hydrogen (from a Kipp) should be passed first through caustic soda solution, then through conc. sulphuric acid, then over heated copper gauze or turnings (previously washed with alcohol to remove grease) to remove arsenic, and finally through a tower containing sticks of caustic soda. On no account must any part of the apparatus be heated until all air has been expelled from the apparatus.

When the reduction is finished, the side tube of a silica distilling flask is connected to the combustion tube, while a dropping funnel is inserted through a cork in the neck of the flask. The other end of the combustion tube is connected first to an empty flask, and then to a worm condenser, which in turn is connected to two suction flasks, cooled in ice and salt. The silica flask is heated in an air bath to 300° while alcohol is dropped in at moderate rate from the tap funnel. At the same time the combustion tube is heated to 300° or even as high as 340°. The vapours from the tube, after condensation, yield unchanged alcohol, a little water, and up to 40% of acetaldehyde ; the escaping hydrogen is led to a draught pipe. After a time, when the catalyst begins to lose its activity, the temperature of the air bath is raised to near 400°.

The aldehyde is separated from the condensed liquid by fractional distillation ; with an efficient column two distillations should give a pure product. The recovered alcohol, after treatment with alkali (to remove traces of acid which always develop) and redistillation, can be again passed over the catalyst.

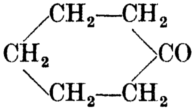
The highest conversion obtainable with one passage over the catalyst is about 40%, since an equilibrium results at this stage.

The copper loses its activity after some time, but is easily regenerated by oxidation in a current of air at 300°, and subsequent reduction with hydrogen.

$$CH_3CH_2OH \rightleftarrows CH_3CHO + H_2.$$

For use of Cu-carbon catalyst, see C. r., 193, 1189.

PREPARATION 442.—**Cyclohexanone.**



$C_6H_{10}O$. 98.

20 gms. cyclohexanol are placed in a flask and to it is added in one portion at 30° a mixture of 41 gms. potassium dichromate, 200 c.cs. water, and 19 c.cs. conc. sulphuric acid. The mixture is shaken and the rising temperature checked at 60° by immersion in cold water, and maintained at 55°. When temperature remains steady the contents are heated to 60° and then cooled to ordinary temperature for one hour. The mixture is placed in a distilling flask with 200 c.cs. water and distilled until 100 c.cs. are collected. To the distillate are added 20–25 gms. sodium chloride and after shaking the lower layer separated and extracted with 20 c.cs. ether. The extract is added to the cyclohexanone upper layer, dried over anhydrous sodium sulphate, decanted or filtered, and distilled, the fraction B.P. 150°–155° being collected.

$$>CHOH + O \longrightarrow >CO + H_2O.$$

Yield.—60% theoretical (12 gms.). Colourless liquid ; B.P. 155° ; D. 0·947. C., 1930, I, 3297.

PREPARATION 443.—**Benzil.**

$$C_6H_5.COCO.C_6H_5. \qquad C_{14}H_{10}O_2. \qquad 210.$$

20 gms. benzoin (p. 110) and 50 c.cs. conc. nitric acid (D. 1·42) are placed in a large flask, which is then heated on an actively boiling water bath. A vigorous reaction soon commences, and torrents of nitrous fumes are evolved at first ; for this reason the operation should be conducted in a fume cupboard. After 2 hours' heating, the product is poured into vigorously stirred cold water, the crystalline deposit filtered off, washed with cold water, pressed out on filter paper and recrystallised from alcohol.

$$C_6H_5.CO.CH(OH).C_6H_5 + O \longrightarrow C_6H_5CO.CO.C_6H_5 + H_2O.$$

Yield.—80% theoretical (16 gms.). Yellow prisms ; insoluble in water ; M.P. 95°. (A., 34, 188 ; Am. Soc., 51, 2822 ; O. S., I, 25 ; VI, 6.)

For use of copper sulphate as oxidant, see C. V., I, 87.

PREPARATION 444.—**α-Bromocinnamic** (*cis*) **and α-Bromo*allo*cinnamic** (*trans*) **Acids.**

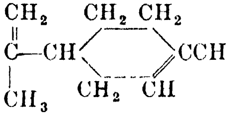
$$C_6H_5CH : CBrCOOH. \qquad C_9H_7O_2Br. \qquad 227.$$

20 gms. (1 mol.) of cinnamic acid dibromide (p. 346) are covered with alcohol and the theoretical amount (2 mols.) of alcoholic potash (say, 70 gms. of a 10% solution) added. After heating for about 15 minutes in a small flask, the mixture is evaporated to dryness in a dish on a water bath. The residue is digested with an amount of water sufficient to dissolve about 75% of the potassium salts, and an excess of a 10% solution of barium chloride added. Barium α-bromocinnamate is precipi-

tated, while barium α-bromo*allo*cinnamate remains in solution. The former is filtered off, washed with dilute barium chloride solution, and the free acid precipitated by treatment with hydrochloric acid; it is filtered off, washed with water and dried on a porous plate. It is recrystallised from benzene as colourless prismatic needles; M.P. 131°; yield 11 gms. The bromo*allo*-acid is recovered in a similar manner by acidifying the solution containing its barium salt. It is recrystallised from petroleum ether as prisms with a yellow tinge; M.P. 120°.

$C_6H_5CHBr.CHBr.COOH + 2KOH \rightarrow C_6H_5CH : CBr.COOK + KBr + 2H_2O$. (J. C. S., 83, 673.)

PREPARATION 445.—**Dipentene** ($\Delta^{1 \cdot 8}$-*Menthadiene*).



$C_{10}H_{16}$. 136.

10 gms. (1 mol.) of pure dipentene hydrochloride (see p. 347) are carefully heated with 20 gms. (excess) of aniline until the reaction commences, and heating is continued for 2–3 minutes. To the mixture are added 20 c.cs. (excess) of glacial acetic acid, and the excess of aniline removed by steam distillation. Oxalic acid is added to the distillate and steam distillation again effected. The aqueous distillate is separated, the hydrocarbon being dried over solid caustic potash. It is then twice distilled over metallic sodium.

$$C_{10}H_{18}Cl_2 \xrightarrow{-2HCl} C_{10}H_{16}.$$

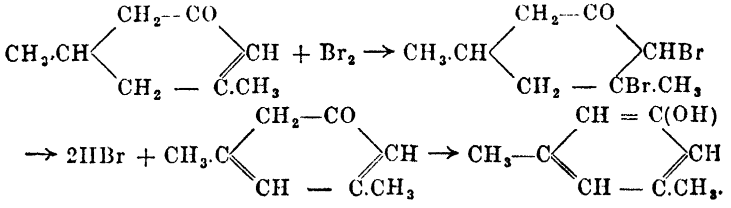
Colourless liquid; B.P. 178°–180°. (B., 40, 603; A., 245, 196; 350, 150.)

PREPARATION 446.—*s*-**Xylenol** (3 : 5-*Dimethyl*-1-*hydroxybenzene*).

$(CH_3)_2C_6H_3(OH)$. $C_8H_{10}O$. 122.

10 gms. of dimethylcyclohexenone (p. 89) are dissolved in 20 gms. of glacial acetic acid, and the solution cooled by ice-water, care being taken that the acid does not solidify. A solution of 13 gms. of bromine in 10 gms. of glacial acetic acid is added slowly from a dropping funnel with stirring, and the whole allowed to stand overnight in a draught cupboard; hydrobromic acid is evolved. Next day the solution is heated on a water bath to about 50° with frequent shaking; after being a short time at this temperature the bath is raised to boiling, and heating continued until there is but slight evolution of hydrobromic acid. A reflux air condenser is then attached and heating continued over a wire gauze until the acetic acid commences to boil, and until the evolution of hydrobromic acid almost ceases. The solution is cooled and poured into a cold solution of 75 gms. of caustic potash in 150 c.cs. of water. The by-products insoluble in the potash solution are extracted with ether and the alkaline solution saturated with carbon dioxide to liberate the xylenol, which is distilled off in steam in presence of carbon dioxide. The distillation is stopped when a test portion of the distillate gives no precipitate of tribromo-xylenol (see

p. 360) on the addition of a few drops of bromine. The distillate is left in the ice chest overnight, when the greater part of the xylenol crystallises out; this is filtered off. The xylenol in the filtrate is recovered by saturating with common salt and extracting with ether.



Yield.—60% theoretical (6 gms.). Crystalline substance; M.P. 64°; B.P.^{760} 220°–221°. (Bl., [3], 11, 702; B., 18, 362, 2672; 20, 410.)

PREPARATION 447.—**Glutaric Acid** (*Pentan di-acid*).

$$COOH.CH_2.CH_2.CH_2.COOH. \qquad C_5H_8O_4. \qquad 132.$$

A mixture of 20 gms. methylenedimalonic ester (p. 150), 20 gms. conc. hydrochloric acid and 20 c.cs. of water is heated for 6 hours in a flask under reflux. At the end of this time the product is evaporated to dryness, and the residue (glutaric acid) distilled under reduced pressure; it distils at 185°–195° under 10 mms. pressure. The small quantity of anhydride formed is eliminated by warming with a little water. After drying, the product is recrystallised from benzene.

$$CH_2\{CH(COOC_2H_5)_2\}_2 \rightarrow COOH.CH_2.CH_2.CH_2.COOH + 4C_2H_5OH + 2CO_2.$$

Yield.—75% theoretical (6 gms.). Soluble in hot benzene; M.P. 97°. (B., 27, 2346; O. S., V, 69; X, 58.)

PREPARATION 448.—**2 : 6-Dibromoaniline** (2 : 6-*Dibromo*-1-*aminobenzene*).

$$C_6H_3(NH_2)Br_2. \qquad C_6H_5NBr_2. \qquad 251.$$

45 gms. of conc. sulphuric acid, 13 c.cs. of water and 10 gms. of dry dibromosulphanilic acid are placed in a flask, which is fitted with a cork bored with three holes. Through one hole a glass tube, sealed at the lower end and passing down into the mixture, is inserted; inside this tube a thermometer is placed. The other holes hold glass tubes to convey superheated steam through the flask. The mixture is heated to 170° in an oil bath, and superheated steam is blown through. The temperature rises gradually, but must not be allowed to exceed 180°. Some of the dibromoaniline formed is carried over by the steam, but most of it remains in the flask. After about 90 minutes, steam is shut off and the contents of the flask poured into a large volume of cold water. The precipitate is filtered off, dried on filter paper, and recrystallised from petroleum ether.

$$NH_2.C_6H_2Br_2SO_3H + H_2O \longrightarrow NH_2C_6H_3Br_2 + H_2SO_4.$$

Yield.—83% theoretical (6 gms.). Colourless needles; M.P. 83°–84°. (A., 253, 275; O. S., 24, 47.)

PREPARATION 449.—**Benzenesulphinic Acid.**

$C_6H_5.SO_2H$. $C_6H_6O_2S$. 142.

40 c.cs. water are placed in a 300-c.c. flask provided with a reflux condenser and dropping funnel and heated to boiling. 10 gms. of good quality zinc dust are added, the source of heat is withdrawn, and 10 gms. of benzenesulphonic chloride (p. 432) in small portions are added from the funnel. A vigorous reaction follows each addition, and this is allowed to subside before more is added. When all is in, the flask is heated for a short time over a small flame, then cooled, and the excess of zinc and zinc benzenesulphinate filtered off. The precipitate is then mixed with a solution of 10 gms. anhydrous sodium carbonate in 50 c.cs. of water, and the whole heated for 10 minutes on a boiling water bath ; by this means sodium benzenesulphinate is formed and goes into solution. The precipitate is filtered off. The filtrate is evaporated to half its volume, then cooled and acidified with dilute sulphuric acid. Scratching the sides of the containing vessel with a glass rod induces colourless crystals of benzenesulphinic acid to separate after a time. These are filtered off and recrystallised from a little water.

$$C_6H_5SO_2.Cl \longrightarrow (C_6H_5SO_2)_2Zn \longrightarrow C_6H_5SO.OH.$$

Colourless crystals ; insoluble in water ; M.P. 83°–84°. (B., 9, 1585 ; O. S., II, 89.)

PREPARATION 450.—**Allyl Alcohol.**

$CH_2 : CH.CH_2OH$. C_3H_6O. 58.

This preparation must be conducted in a fume cupboard.

400 gms. of glycerol (excess), 100 gms. oxalic acid, and 0·5 gms. ammonium chloride are heated in a retort with condenser and receiver attached. The heating is carried out on a wire gauze, and a thermometer is inserted in the liquid. Carbon dioxide is rapidly evolved at first, and the temperature remains about 130°. The evolution of gas slackens as the temperature gradually increases to about 180° and then ceases. At 195° the receiver containing aqueous formic acid is changed, and at 200°–210° carbon dioxide is again evolved, and oil condenses in neck of retort. The temperature is raised to 220°–230° and maintained there for some time, being finally raised to 260°, at which temperature distillation is stopped. The residue in the flask consists of glycerol to which more oxalic acid may be added and the process repeated. The distillate containing allyl alcohol is again distilled until no oil separates from a sample of the distillate on treating with solid potassium carbonate, which takes place when the temperature reaches about 105°. The allyl alcohol is separated from the distillate, by adding solid potassium carbonate, and distilled, the fraction boiling at 93°–97° being collected.

$$C_3H_5(OH)_3 \longrightarrow C_3H_5(OH)_2O.CO.COOH \longrightarrow C_3H_5(OH)_2O.COH \longrightarrow$$
$$CH_2 : CHCH_2OH + CO_2 + H_2O.$$

Yield—30 gms. ; B.P. 96° ; D^0 0·87. (A., 156, 129 ; O. S., I, 15.)

CHAPTER XXXII

MISCELLANEOUS PREPARATIONS

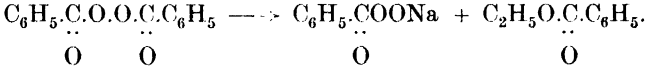
PREPARATION 451.—**Benzoyl Peroxide.**

$C_6H_5CO.O.O.CO.C_6H_5$. $C_{14}H_{10}O_4$.   242.

50 c.cs. of 10% hydrogen peroxide are placed in a glass-stoppered flask surrounded by a good cooling mixture. 4N-caustic soda solution and benzoyl chloride are dropped in alternately, with continual shaking, so that the solution remains weakly alkaline. The hydrogen peroxide is decomposed when 30 c.cs. of caustic soda solution and 15 gms. of benzoyl chloride have been added. The benzoyl peroxide separates in crystalline flocks, is filtered, washed with water, and crystallised from a small quantity of boiling alcohol.

Yield.—80–95% theoretical (10–12 gms.); colourless prisms; M.P. 106°–108°, with decomposition. Important polymerising agent. See *Free Radicles*, Waters.

By the action of sodum ethoxide in absolute ether, it is decomposed into sodium perbenzoate and benzoic ester. C. V., I, 431.



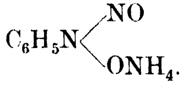
$$C_6H_5.\underset{O}{C}.O.O.\underset{O}{C}.C_6H_5 \longrightarrow C_6H_5.\underset{O}{C}ONa + C_2H_5O.\underset{O}{C}.C_6H_5.$$

Perbenzoic acid (M.P. 41°–43°) can be obtained by extracting with chloroform after acidification. (B., 27, 1510; 33, 1575.)

The peroxide is used as an oxidising and a benzoylating agent. (G., 60, 859; J. pr., 128, (ii), 171.)

Many aliphatic and aromatic acids yield similar derivatives.

PREPARATION 452.—**Cupferron (NH$_4$ salt of nitrosophenylhydroxylamine).**

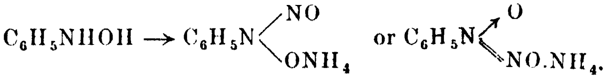


$$C_6H_5N\begin{cases}NO\\ONH_4.\end{cases}$$

$C_6H_9O_2N_3$.   155.

725 gms. phenylhydroxylamine, obtained from the reduction of nitrobenzene (see Preparation 376), are treated with 3 litres ether. The ether insoluble material (sodium chloride) is filtered off and weighed, this weight being deducted from the weight of crude phenylhydroxylamine. The filtrate is placed in a 5-litre round-bottomed flask, cooled to 0°, and stirred with an efficient mechanical stirrer, while a rapid stream of ammonia gas is passed into the solution. After about 15 minutes the theoretical quantity of freshly-distilled amyl nitrite (107 gms. for each 100 gms. phenylhydroxylamine) is added through a dropping funnel. The addition of amyl nitrite requires about 30 minutes, during which time the stream of ammonia is continued, so that ammonia will remain in excess (otherwise

a coloured product results). The temperature should not exceed 10° during this addition. After the addition of the nitrite the mixture is stirred for 10 minutes to ensure complete reaction. The cupferron is then filtered off, washed several times with ether, and dried by exposure on sheets of filter paper. It is stored in a bottle, where it is exposed to the vapours of ammonia: this is effected by placing a small tube containing solid ammonium carbonate, and which is drawn out to a fine capillary, inside the bottle of cupferron.



$$C_6H_5NHOH \rightarrow C_6H_5N\left\langle\begin{matrix}NO\\ONH_4\end{matrix}\right. \quad \text{or} \quad C_6H_5N\left\langle\begin{matrix}\nearrow O\\ \searrow NO.NH_4\end{matrix}\right..$$

Yield.—80–90% theoretical (800 gms.). (O. S., IV, 19.)

This reagent is much used for the estimation of copper and iron (hence its name). See text-books on inorganic analysis. (Am. Soc., 41, 276.)

PREPARATION 453.—Benzenesulphonyl Chloride.

$C_6H_5SO_2Cl$. 176·5.

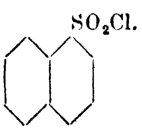
150 gms. of sodium benzene sulphonate (p. 317), dried for 3 hours at 140°, are mixed with 85 gms. of finely-divided phosphorus pentachloride in a round-bottomed flask provided with a reflux condenser. The mixture is heated at 170°–180° in an oil bath. The flask should be removed every 4 hours, stoppered, and vigorously shaken until the mass becomes pasty. The mass is poured into a mixture of ice and water, when the benzene sulphonyl chloride sinks to the bottom; it is separated, washed with water, and distilled *in vacuo*, the fraction 113°–115° at 10 mms. being collected. The phosphorus pentachloride may be replaced by 100 gms. phosphorus oxychloride.

$$3C_6H_5SO_2.ONa + PCl_5 = 3C_6H_5SO_2Cl + 2NaCl + NaPO_3.$$

$$2C_6H_5SO_2.ONa + POCl_3 = 2C_6H_5SO_2Cl + NaCl + NaPO_3.$$

Yield.—75–80% theoretical (110–120 gms.). Colourless oil; M.P. 14·5°; B.P. ^{760} 246° (decomposition). (B., 42, 1802, 2057; O. S., I, 21; X, 6.)

PREPARATION 454.—α-Naphthalenesulphonyl Chloride.



$C_{10}H_7O_2ClS$ 226·5.

30 gms. (1 mol.) of sodium α-naphthalene sulphonate previously dried at 150° are gradually added while warm to 30 gms. (slight excess) of phosphorus pentachloride contained in a basin or beaker. The reaction commences on the addition of the first portions, and further addition is regulated so that the reaction does not become too vigorous. After the final addition, the whole is heated on a water bath until homogeneous. Afterwards it is transferred to a flask and distilled under reduced pressure until the distillate—which consists at first of phosphorus oxychloride—

weighs 15–20 gms. The residue in the flask is poured into a mortar and stirred as it solidifies; when solid it is mixed with ice-water, ground up and filtered. It is then well pressed for a short time on a porous plate, and after complete drying, *in vacuo*, over sulphuric acid, is recrystallised from a mixture of benzene and petroleum ether.

$$C_{10}H_7SO_2OH + PCl_5 \longrightarrow C_{10}H_7SO_2Cl + HCl + POCl_3.$$

Yield.—60% theoretical (17·5 gms.). M.P. 66°.

β-Naphthalenesulphonyl chloride is prepared in a similar manner from sodium β-naphthalene sulphonate. (A., 275, 233.)

Preparation 455.—**Ethyl Potassium Sulphate.**

$C_2H_5O.SO_3K$. $C_2H_5O_4SK$. 164.

To 100 c.cs. ethyl alcohol in a ½-litre round-bottomed flask are carefully added with cooling 40 c.cs. conc. sulphuric acid. A reflux condenser is attached and the mixture heated for an hour on the water bath, and then allowed to cool. The liquid is poured into ½ litre of water in a porcelain basin, and to this is added chalk, with stirring, until effervescence ceases. The calcium sulphate is filtered off, and washed with a little warm water. To the filtrate, which contains ethyl calcium sulphate, is added saturated potassium carbonate solution until the liquid gives a faint alkaline reaction to phenolphthalein. The calcium carbonate is filtered off and washed with a little hot water. The filtrate is then evaporated until crystallisation begins, when it is set aside to cool. The crystals of ethyl potassium sulphate are filtered off and dried, and a further crop obtained by concentrating the mother liquor.

$$C_2H_5OH + H_2SO_4 \rightarrow C_2H_5O.SO_3H \rightarrow (C_2H_5O.SO_3)_2Ca \rightarrow C_2H_5O.SO_3K.$$

Yield.—15% theoretical (45 gms.). Deliquescent, monoclinic plates; soluble in water; insoluble in alcohol or ether. (B., 19, 295.)

Preparation 456.—**Aminoazobenzene.**

$C_6H_5N : N.C_6H_4NH_2$. $C_{12}H_{11}N_3$. 197.

10 gms. finely-ground diazoaminobenzene (p. 382), 5 gms. aniline hydrochloride, and 20 gms. of aniline are heated in a beaker at 40° for an hour. After standing overnight at ordinary temperature, the mixture is treated with an excess of dilute acetic acid to dissolve the aniline; aminoazobenzene remains undissolved. It is filtered off, washed with water, and recrystallised from dilute alcohol containing ammonia.

$$C_6H_5N : N.NH.C_6H_5 \longrightarrow C_6H_5N : N.C_6H_4NH_2.$$

Yield.—80% theoretical (8 gms.). Yellow needles; M.P. 126°; weak base. (B., 19, 1953; 20, 372.)

Preparation 457.—**Nitrosobenzene.**

C_6H_5NO. 107.

4·6 gms. potassium dichromate (or an equivalent quantity of sodium dichromate) are dissolved in 200 c.cs. water and the solution cooled to 0°

in a freezing mixture. A mixture containing 4 gms. finely-powdered phenylhydroxylamine, 30 gms. conc. sulphuric acid, and 270 c.cs. of water is also cooled in ice-water, and to it the dichromate solution is added quickly. The nitrosobenzene which separates is removed by steam distillation, and if any solidifies in the condenser the water should be run out of the latter until the solid melts and flows down into the receiver. The nitrosobenzene is filtered off from the distillate, pressed on a porous plate until dry, and washed with a little petroleum ether.

$$C_6H_5NH.OH + O \longrightarrow C_6H_5NO + H_2O.$$

M.P. 68° ; colourless or yellow crystals. (O. S., 25, 80.)

PREPARATION 458.—**Aniline Nitrate** (*Phenylammonium nitrate*).

$C_6H_5NH_3.NO_3$. $C_6H_8O_3N_2$. 156.

Aniline Hydrochloride (*Phenylammonium chloride*).

$C_6H_5NH_3.Cl$. C_6H_8NCl. 129·5.

The preparation of aniline nitrate is fully described on p. 383 under the preparation of diazobenzene nitrate. The crude product therein obtained is recrystallised by dissolving in a little absolute alcohol and precipitating therefrom with ether. The preparation and purification of aniline hydrochloride are exactly similar:

$$C_6H_5NH_2 + HNO_3 = C_6H_5NH_3.NO_3.$$
$$C_6H_5NH_2 + HCl = C_6H_5NH_3.Cl.$$

Yield.—Aniline Nitrate.—80% theoretical (13 gms. from 10 gms. of aniline). *Aniline Hydrochloride.*—80% theoretical (10 gms. from 10 gms. of aniline). Colourless crystals ; soluble in water and alcohol ; insoluble in ether ; aniline hydrochloride melts at 198° ; aniline nitrate transforms to nitroaniline at 190°. (A., Ch., [6], 21, 355 ; J., 1861, 495 ; B., 14, 1083.)

Aniline Sulphate.

$(C_6H_5NH_3)_2SO_4$. $C_{12}H_{16}O_4N_2S$. 284.

To 10 gms. (2 mols.) of aniline 15 c.cs. (an excess) of dilute (5N) sulphuric acid are added. The precipitate is recrystallised from a little water.

$$2C_6H_5NH_2 + H_2SO_4 = (C_6H_5NH_3)_2SO_4.$$

Yield.—90% theoretical (13·5 gms.). Colourless crystals ; soluble in water ; slightly soluble in absolute alcohol ; insoluble in ether. (A., Ch., [6], 21, 355 ; B., 18, 3313.)

PREPARATION 459.—**Aniline Hydroferrocyanide** (*Phenylammonium ferrocyanide*).

Aniline is dissolved in conc. hydrochloric acid until only slightly acid. Water is then added until the whole is a saturated solution of aniline hydrochloride at ordinary temperature. A saturated solution of sodium ferrocyanide is then added until precipitation is complete. The solution should be slightly acid after this stage has been reached. The white precipitate is filtered off, washed first with a little alcohol, and then ether and dried by suction.

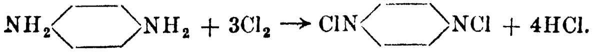
$$2C_6H_5NH_2 + H_4Fe(CN)_6 \longrightarrow 2C_6H_5NH_2.H_4Fe(CN)_6[.2H_2O].$$

Yield.—Theoretical. White rhombohedral crystals with greenish tinge; infusible; almost insoluble in water, solution being decomposed on boiling with evolution of hydrocyanic acid; insoluble in alcohol or in ether. Many other aromatic organic bases yield similar compounds. (J. C. S., 121, 1293.)

PREPARATION 460.—*p*-**Benzoquinone Dichlorimide.**

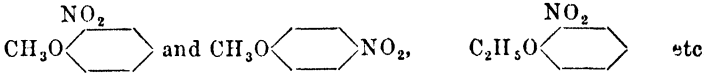
$C_6H_4N_2Cl_2$. 175.

Chlorine is passed into 250 c.cs. water containing 45 gms. caustic soda until the total weight is 332 gms. 750 c.cs. of ice-water are then added. A solution prepared from commercial sodium hydrochlorite (p. 519) may be employed. Into the cold solution are slowly run 27 gms. *p*-phenylenediamine hydrochloride (p. 367) in 300 c.cs. water and 60 c.cs. conc. hydrochloric acid. After the blue colour disappears the dichlorimide separates, is filtered and washed with water until the filtrate is free from chlorine; it is then recrystallised from 70% alcohol or petroleum ether (40°–60°).



Colourless needles, which explode at 126° (*caution!*). (B., 12, 47.)

PREPARATION 461.—**Alkyl Nitrophenols** (1-*Methoxy-2-nitrobenzene, etc.*).

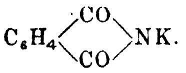


o-Nitro-anisole. *o*-Nitro-phenetole.

70 gms. *o*- or *p*-nitrophenol (pp. 281, 284), 20 gms. caustic soda, and 40 gms. sodium carbonate are dissolved in 200 c.cs. water. To this solution are added 250 c.cs. methyl (or ethyl) alcohol, and the whole cooled to 10° and placed in an autoclave. 1·75 mols. of methyl or ethyl chloride (both are gases at ordinary temperature) are then added, the autoclave closed (p. 50) and the temperature raised to 100° for 8 hours—pressure 4–5 atms. The product is poured into water and the alkyl ether separated. The alcohol is then recovered. The alkyl compound is washed with a little caustic soda solution to remove free nitrophenol. It is purified by distillation.

Yield.—75-80% theoretical. *o*-Nitroanisole: M.P. 9°; B.P. 265°; *p*-nitroanisole: M.P. 54°; B.P. 258°. *o*-Nitrophenetole: M.P. 78°; B.P. 268°; *p*-nitrophenetole: M.P. 60°; B.P. 283°.

PREPARATION 462.—**Potassium Phthalimide.**



$C_6H_4\langle (CO)_2 \rangle NK$. $C_8H_4O_2NK$.   185.

2·4 gms. phthalimide are dissolved under reflux in 50 c.cs. absolute alcohol. 1 gm. caustic potash is dissolved in 1 c.c. of water and diluted with 3 c.cs. of absolute alcohol. While still hot the first solution is added to the second. When cold, the white precipitate is filtered off, washed with dry ether, and dried in an oven.

Yield.—68% theoretical (2 gms.).

Sodium phthalimide may be prepared in a similar manner, the yield being 50% theoretical.

By using amyl alcohol in place of ethyl alcohol the yields may be improved to above 90% theoretical. (J. C. S., 121, 2362 ; A., 215, 181.)

PREPARATION 463.—**Phenylhydrazone of *d*-Mannose** (+ + + + *Pentolhexanal*).

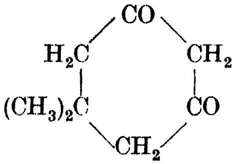
$CH_2(OH)(CH(OH))_4CH : NNH.C_6H_5$. $C_{12}H_{18}O_5N_2$.   270.

To 4 gms. (1 mol.) of mannitol dissolved in 20 c.cs. of water, a solution of 1 gm. of ferrous sulphate in cold water is added, and then gradually 12 c.cs. (1 atom of O) of hydrogen peroxide solution (20 vols.), or more if solution is weaker, are dropped in. The solution must be well cooled throughout. Sodium carbonate solution is added till just alkaline, and the whole filtered. To the bulk of the filtrate 1 c.c. (excess) of phenylhydrazine dissolved in a slight excess of dilute acetic acid is added, the solution allowed to stand, and the precipitate of mannose phenylhydrazone filtered off. It is recrystallised from dilute alcohol.

$$CH_2OH(CHOH)_4CH_2OH + O = CH_2OH(CHOH)_4CHO + H_2O.$$

Yellow crystals ; M.P. 198°.

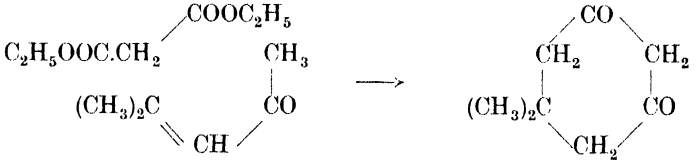
PREPARATION 464.—**5 : 5-Dimethylcyclohexane-1 : 3-dione** (*Dimedone*).



$C_8H_{12}O_2$.   140.

40 c.cs. absolute alcohol previously dried over sodium and distilled (p. 217) are placed in a 300-c.c. flask fitted with an addition tube (Fig. 45) and reflux condenser provided with a calcium chloride tube. 2·5 gms. bright sodium is added through the other limb of the addition tube which is then corked. When the sodium is dissolved 17 gms. diethylmalonate is added, followed by 10 gms. mesityl oxide dropwise with shaking. After two hours refluxing on the steam bath with occasional shaking a solution of 12·5 gms. caustic potash in 55 c.cs. water is added and the mixture refluxed with shaking for six hours. The mixture while hot is then made just acid to litmus with about 55 c.cs. dil. hydrochloric acid (1 vol. conc. to

2 vol. water) and distilled on a steam bath to remove as much as possible of the alcohol. The residue after cooling and adding decolourising carbon (1–2 gms.) is boiled, filtered, neutralised to litmus with about 15 c.cs. dil. hydrochloric acid (1 vol. conc. to 2 vols. water). After further boiling with carbon and filtering, the hot solution is made acid to methyl orange with 5–10 c.cs. dil. hydrochloric acid, boiled for ten minutes, and allowed to cool. The product which crystallises is filtered, washed with ice-water, dried in air, and recrystallised from acetone.



Yield.—65% theoretical (9 gms.). Colourless crystals; M.P. 147°. Used for detection and identification of aldehydes. (A., 294, 314.)

Iodobenzene and some Related Compounds

Aromatic iodo-compounds containing iodine in the nucleus unite with two atoms of chlorine to form iodochlorides (Preparation 469), the iodine becoming trivalent. Caustic soda converts the latter into iodoso-compounds, oxygen replacing the two chlorine atoms (Preparation 465).

$$C_6H_5I \longrightarrow C_6H_5ICl_2 \longrightarrow C_6H_5IO.$$

Iodoso-compounds behave as diacid bases, e.g. $C_6H_5I(OH)_2$, which combine with acids to form salts (Preparation 466). Reducing agents or the action of heat convert them into iodo-compounds, while oxidising agents yield iodoxy-compounds (Preparation 467).

For review of polyvalent iodine compounds, see Chem. Rev., 1943, 249.

PREPARATION 465.—**Iodosobenzene.**

$C_6H_5I:O$. C_6H_5OI. 220.

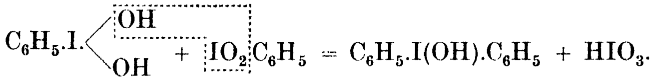
By-product.—**Diphenyliodonium Iodide.**

$(C_6H_5)_2:I.I$. $C_{12}H_{10}I_2$. 408.

10 gms. of phenyliodide dichloride (p. 439) are carefully rubbed with a solution of 5 gms. of sodium hydroxide in 40 gms. of water in a mortar and allowed to stand overnight. The iodosobenzene is filtered off, washed with water, and pressed on a porous plate. The alkaline filtrate is saturated with sulphur dioxide, and the precipitated diphenyliodonium iodide crystallised from a small quantity of hot water, or from alcohol.

$$\begin{aligned}C_6H_5I:Cl_2 + 2H_2O &= C_6H_5I(OH)_2 + 2HCl\\ &= C_6H_5.I:O + H_2O + 2HCl.\end{aligned}$$

A small portion of the iodosobenzene is probably oxidised to iodoxybenzene, $C_6H_5IO_2$, which reacts with the hypothetical hydroxide, $C_6H_5.I(OH)_2$ to give diphenyl iodonium hydroxide and iodic acid. This base is present in the alkaline filtrate from the iodosobenzene. The sulphur dioxide reduces the iodic acid to hydriodic acid, which, combining with the iodonium base, forms an iodide insoluble in cold water.



$$C_6H_5.I{<}^{OH}_{OH} + IO_2C_6H_5 = C_6H_5.I(OH).C_6H_5 + HIO_3.$$

$$HIO_3 + 3SO_2 + 3H_2O = HI + 3H_2SO_4.$$

$$(C_6H_5)_2I.OH + HI = (C_6H_5)_2I.I + H_2O.$$

Yields.—Iodosobenzene.—75% theoretical (6 gms.). White amorphous substance; soluble in water, yielding a neutral solution; decomposes when heated to above 240°. (O. S., 22, 70.)

Diphenyliodonium Iodide.—Crystallises from alcohol in long, yellow needles: M.P. 175°–176°; on melting decomposes completely into iodobenzene. (B., 25, 3495; 26, 1307, 1354; 27, 506; O. S., 22, 52.)

PREPARATION 466.—**Iodosobenzene Acetate.**

$C_6H_5I : (O.CO.CH_3)_2.$ $C_{10}H_{11}O_4I.$ 322.

5 gms. (1 mol.) of iodosobenzene are dissolved with heat in the smallest possible quantity of glacial acetic acid, the solution evaporated to dryness on a water bath, and the powdered residue recrystallised from a little benzene.

$$C_6H_5I : O + 2CH_3COOH = C_6H_5I : (O.CO.CH_3)_2 + H_2O.$$

Yield.—Theoretical (7 gms.). Colourless prisms; M.P. 156°–157°.

PREPARATION 467.—**Iodoxybenzene** (*Phenyl iodite*).

$C_6H_5.IO_2.$ $C_6H_5O_2I.$ 236.

10 gms. (1 mol.) of iodosobenzene are mixed in a flask with sufficient water to form a thin paste, and steam distilled until no more iodobenzene comes over, and until all the iodosobenzene has completely reacted. If the iodoxybenzene formed does not dissolve completely, water is added until solution takes place. The residue is then filtered and concentrated on a water bath until a test portion, on cooling, gives a copious precipitate.

$$2C_6H_5I : O = C_6H_5IO_2 + C_6H_5I.$$

Snow-white powder; decomposes suddenly at 210°–230°. (O. S., 22, 72.)

PREPARATION 468.—**Diphenyliodonium Iodide.**

$(C_6H_5)_2I.I.$ $C_{12}H_{10}I_2.$ 408.

10 gms. (1 mol.) of iodosobenzene and 11 gms. (1 mol.) of iodoxybenzene are treated with water and with 20 gms. (excess) of freshly-precipitated silver oxide in a stout, well-stoppered bottle, shaken mechanically for 4 hours, and filtered. The filtrate, which contains free diphenyliodonium hydroxide, has a strongly alkaline reaction.* The base has not been obtained in a pure form, but its salts are readily prepared from the solution.

---

* Test solution for an iodate.

The solution contains part of the base in the form of its iodate, and is therefore first treated with sulphur dioxide, and then with excess of potassium iodide solution, when the iodide separates out completely. It is recrystallised from alcohol.

$$C_6H_5I:O + C_6H_5IO_2 + AgOH \longrightarrow (C_6H_5)_2I.OH + AgIO_3.$$

$$(C_6H_5)_2I.OH + KI \longrightarrow (C_6H_5)_2I.I.$$

Yield.—93% theoretical (17 gms.). Yellow needles from alcohol; M.P. 175°–176°; on melting decomposes completely into iodobenzene. (B., 27, 426; 502, 1592; O. S., 22, 52.)

PREPARATION 469.—**Phenyliodide Dichloride.**

$C_6H_5.I:Cl_2$. $C_6H_5Cl_2I$. 275

10 gms. (1 mol.) of iodobenzene are dissolved in 20 c.cs. of dry chloroform, and a current of chlorine, dried by bubbling through two concentrated sulphuric acid wash-bottles, is led into the solution through a *very wide* delivery tube. During the passage of the gas the solution is cooled by ice-water; when no more gas is absorbed the yellow crystals are filtered off, washed with chloroform, spread out in a thin layer on a pad of filter paper, and allowed to dry in the air.

$$C_6H_5I + Cl_2 = C_6H_5I:Cl_2.$$

Yield.—Almost theoretical (13 gms.). Very unstable yellow crystals; decompose on heating. (B., 26, 357; A., 369, 119; O. S., 22, 69.)

PREPARATION 470.—**α-Naphthalenesulphonylglycine.**

$C_{10}H_7.SO_2.NH.CH_2.COOH$. $C_{12}H_{11}O_4NS$. 265.

2 gms. (1 mol.) of glycocoll are dissolved in 27 c.cs. (1 mol.) of normal sodium hydroxide, and to this an ethereal solution of 12 gms. (2 mols.) of β-naphthalene-sulphonyl chloride is added. The mixture is shaken in a stoppered bottle in a shaking machine at ordinary temperature. Three times, at intervals of about an hour, the same amount of normal alkali is again added. After about 4 hours the aqueous liquid, which still reacts alkaline, is separated from the ethereal layer in a funnel, filtered, and acidified with hydrochloric acid. The oil which is precipitated soon crystallises. For complete purification it is recrystallised from hot water.

$$C_{10}H_7.SO_2Cl + NH_2.CH_2.COOH = C_{10}H_7SO_2.NHCH_2.COOH + HCl.$$

Colourless laminae, M.P. 156° (159° corr.). (B., 35, 3780.)

PREPARATION 471.—**Thiophenol.**

C_6H_5SH. C_6H_6S. 110.

This experiment should be performed in a good draught chamber. 240 gms. conc. sulphuric acid and 720 gms. crushed ice are placed in a litre round-bottomed flask. The mixture is cooled by placing the flask in a freezing mixture; the temperature should be kept below 0°. Stirring is commenced, and 60 gms. benzene sulphonyl chloride (see p. 432) are gradually run in during ½ hour. 120 gms. of zinc dust are then added as quickly as possible without allowing the temperature to rise above 0° ; this requires about ½ hour. The stirring is continued for 1–1½ hours, the temperature being kept below 0°. A reflux condenser is now attached, the freezing bath is removed, and the temperature allowed to rise spontaneously or by the application of a little heat, the agitation being maintained. A vigorous action ensues after a time, and much hydrogen is evolved, at which stage cooling should be applied. The mixture is then heated to boiling until the solution becomes clear (about 4–7 hours). The thiophenol is steam distilled, separated from the water, and dried with calcium chloride. It is distilled, the fraction boiling at 166°–175° (71° at 15 mms.) being collected.

$$C_6H_5SO_2Cl + 6H \longrightarrow C_6H_5SH + 2H_2O + HCl.$$

Yield.—90% theoretical (34 gms.). Colourless liquid ; B.P. 173° ; characteristic unpleasant odour ; produces burns on the skin ; vapour irritates the eyes. (A., 119, 142 ; B., 28, 2319 ; 51, 751 ; O. S., 1, 71.)

PREPARATION 472.—**Lead and Mercury Salts of Thiophenol.**

$(C_6H_5S)_2Pb$. $(C_6H_5S)_2Hg$.

$C_{12}H_{10}S_2Pb$. 425. $C_{12}H_{10}S_2Hg$. 418.

1 gm. (excess) of lead acetate or mercuric chloride is dissolved in alcohol by the application of heat, and the solution cooled and filtered. 0·5 c.c. (2 mols.) of thiophenol is then added drop by drop when a precipitate of the required salt is obtained. It is washed with a little alcohol.

$$2C_6H_5SH + (CH_3COO)_2Pb = (C_6H_5S)_2Pb + 2CH_3.COOH.$$

$$2C_6H_5SH + HgCl_2 = (C_6H_5S)_2Hg + 2HCl.$$

Yield.—Theoretical (1 gm.). Crystalline substances ; insoluble in alcohol.

PREPARATION 473.—**Lead and Calcium Salts of Glyceric Acid.**

$$(Pb\ or\ Ca)[O.CO.CH(OH)CH_2OH]_2.$$

Pb Salt.—A dilute aqueous solution of glyceric acid (p. 252) is neutralised with lead carbonate containing a small quantity of lead oxide. The mixture is heated to boiling and filtered hot. The filtrate, on concentrating and cooling, yields the required salt in crusts, which adhere to the sides of the vessel. A further crop may be obtained by concentrating and cooling the mother liquors. The product may be recrystallised from hot water.

Yield.—Theoretical (twice the weight of acid taken).

Ca Salt.—A dilute aqueous solution of glyceric acid is boiled with excess of calcium carbonate and filtered hot. The filtrate, on concentrating and cooling, yields colourless crystals of the required salt, which may be recrystallised from hot water. (A., 120, 226.)

PREPARATION 474.—**Triphenylchloromethane** (*Triphenylmethyl chloride*).

$(C_6H_5)_3CCl$. $C_{19}H_{15}Cl$. 278·5.

12·5 gms. of freshly-prepared, finely-divided anhydrous aluminium chloride (see p. 514) are added in 4 equal portions to a mixture of 10 gms.

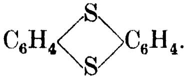
(1 mol.) of redistilled carbon tetrachloride, which has stood for 48 hours over calcium chloride, and 35 gms. (excess) of pure similarly treated benzene, in a flask fitted with a long reflux condenser. When the reaction moderates, it is completed by heating on a water bath for 1 hour. On cooling, the contents of the flask are very slowly poured with mechanical stirring on to ice surrounded by a freezing mixture. Three times during the addition benzene is added, sufficient to dissolve the triphenylchloromethane as it separates. The benzene solution is separated, washed with dilute hydrochloric acid, then with water, dried over calcium chloride, and evaporated on a water bath until triphenylchloromethane crystallises on cooling a sample. After filtration, a further yield may be obtained by removing the benzene under reduced pressure at 40°, and washing the residue with ether. The whole is purified by retreatment with benzene, as above.

$$3C_6H_6 + CCl_4 \longrightarrow ClC(C_6H_5)_3 + 3HCl.$$

Yield.—80% theoretical (14 gms.). Colourless crystals; somewhat soluble in benzene; M.P. 111°; converted by zinc or silver into hexaphenylethane which by dissociation yields triphenylmethyl (See below). (A., 194, 253; O. S., XXIII, 100.)

Triphenylmethyl.—3 gms. triphenylchloromethane (Preparation 474) are dissolved in 30 c.cs. anhydrous benzene in a glass-stoppered bottle. 8 gms. good quality zinc dust are added and the mixture shaken for 5 minutes. A yellow solution is formed. A portion withdrawn and diluted with an equal volume of benzene in a test-tube becomes colourless on shaking, the colour reappearing on standing. The effect may be repeated several times. Another portion is filtered and divided into two lots. Air is bubbled through one causing precipitation of triphenylmethyl peroxide. A solution of iodine in benzene is decolourised on addition to the other.

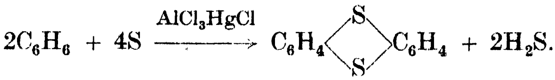
PREPARATION 475.—**Thianthren** (*Diphenylene disulphide*).



$$C_6H_4{<}\genfrac{}{}{0pt}{}{S}{S}{>}C_6H_4.$$

$C_{12}H_8S_2$. 216.

To the catalyst prepared as described on p. 67, from 25 gms. of aluminium powder, 45 gms. of mercuric chloride and 25 gms. (excess) of pure dry benzene, 10 gms. (4 atoms) of flowers of sulphur are added under good mechanical stirring, and the mixture heated on a water bath until hydrogen sulphide is no longer evolved. The product, on cooling, is decomposed by adding ice, filtered, and the residue repeatedly extracted with chloroform from which the thianthren is obtained on concentration. It is recrystallised from acetone.



$$2C_6H_6 + 4S \xrightarrow{AlCl_3HgCl} C_6H_4{<}\genfrac{}{}{0pt}{}{S}{S}{>}C_6H_4 + 2H_2S.$$

Yield.—80% theoretical (14 gms.). Colourless crystals; soluble in chloroform; insoluble in cold acetone; M.P. 160°. (J. C. S., 117, 1335.)

This is an extension of the Friedel-Crafts Reaction (see p. 65).

Reactions of Unsaturated Hydrocarbons to yield Oxy and other Compounds

Developments within the last ten years have shown the importance of acetylene as a primary material. Its use for the manufacture of acetaldehyde, acetone, acrylic acid, vinyl chloride and acetate are now well-known. Alcohols may also be formed from olefines. Sulphuric acid (20–45%), phosphoric acid (30–35%), or acetic acid (96%), in presence of a mercury salt may be employed. Selenium dioxide has been used for a similar purpose (J. C. S., 1932, 2342 ; A. C. R., 1934, 123 ; Chem. Rev., 1945, 235).

With sulphuric acid (55–76%) on alcohol secondary reactions involving dehydration and polymerisation may take place :

$$3C_4H_9OH - 3H_2O \longrightarrow (C_4H_8)_3.$$

The polymerisation of *iso*-butylene to liquid hydrocarbons is an important technical process. Di- and tri-*iso*butylenes are formed, the relative proportion depending on the concentration of sulphuric acid used. By catalytic reduction they yield *iso*-octane (see p. 75).

PREPARATION 476.—**Acetaldehyde.**

$CH_3.CHO$. C_2H_4O. 44.

Acetylene prepared from calcium carbide and purified by passing (1) through copper sulphate solution, and (2) through a tower packed with bleaching powder, is led into a flask containing 300 c.cs. of 96% acetic acid and 9·5 gms. mercuric sulphate in solution, the temperature of which is kept at 30° (see Fig. 58). The exit tube from the flask is connected (1) to a cold water condenser, and (2) to two wash-bottles containing ether and cooled in ice. The gas should be passed at a very moderate rate for 1 or 2 days, and a little water (1–2 c.cs.) added at intervals to replace that taken up in the reaction. When it is decided

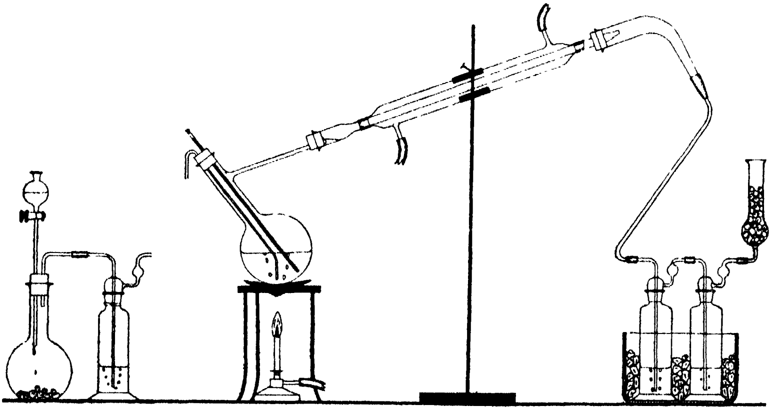


FIG. 58.

to discontinue the reaction the flask is warmed to 60°–70° to drive all the aldehyde over into the ether. The ethereal solution is dried over anhydrous sodium sulphate, then decanted, and saturated with dry ammonia. A very good yield of aldehyde-ammonia results.

$$CH \vdots CH + H_2O \longrightarrow CH_3.CHO.$$

$$CH_3.CHO + NH_3 \longrightarrow CH_3CHOH.NH_2.$$

Recycling the escaping acetylene repeatedly through the catalyst gives improved yields. (See Preparation 440.) See also E.P., 373893.

For isomerisation of ethylene oxide to acetaldehyde, see P.R.S., 1946, Dec. 92.

PREPARATION 477.—Paracetaldehyde.

$$(CH_3CHO)_3. \qquad C_6H_{12}O_3. \qquad 132.$$

A paste, consisting of 10 gms. mercuric sulphate, and 40 gms. of ammonium hydrogen sulphate with 20 c.cs. of water is introduced into a strong glass bottle of 1,500 c.cs. capacity. The bottle is three-fourths filled with glass beads, and thoroughly shaken; it is then fitted with a one-holed cork, carrying a delivery tube, which passes down through the beads. A current of acetylene, prepared from calcium carbide and water, and purified by passing first through copper sulphate solution, and then through a tower packed with bleaching powder, is led into the bottle, which has no outlet and which is periodically shaken.

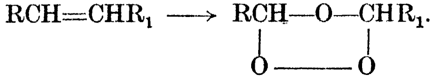
In about 2 hours the beads adhere together somewhat; then paracetaldehyde begins to collect at the bottom of the bottle. Water is added, 2–3 c.cs. at a time, at intervals during the formation. The yield is good, and there is practically no escape of acetylene or acetaldehyde from the apparatus. The action consists in the formation of a mercuric sulphate acetylene compound and its subsequent decomposition giving paracetaldehyde. The passage of acetylene should be continued for about 2 days. The contents of the bottle are finally shaken up with ether, the ethereal solution separated, dried over anhydrous sodium sulphate, and distilled. Paracetaldehyde passes over as a colourless liquid, boiling point 124°.

$$3C_2H_2 + 3H_2O \longrightarrow (CH_3CHO)_3.$$

(Am. Soc., 43, 2071.)

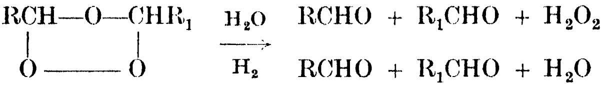
Action of Ozonised Oxygen on Unsaturated Compounds

When ozonised oxygen (containing usually 3–5% ozone) is passed at low temperature into unsaturated compounds, e.g. hydrocarbons, primary, or secondary alcohols, in a solvent such as chloroform, carbon tetrachloride, ethyl acetate, ozonolysis takes place, three oxygen atoms combining at the double bond.



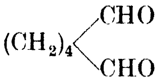
$$RCH{=}CHR_1 \longrightarrow \begin{array}{ccccc} RCH & — & O & — & CHR_1. \\ | & & & & | \\ O & & — & & O \end{array}$$

The reaction is not accompanied by secondary oxidation products, such as when chromic acid or permanganate is used. The ozonides, usually viscid oils, are readily decomposed by water or by catalytic reduction.



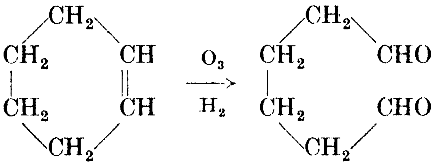
The reaction can be used to determine the position of a double bond. (Am. Soc., 1934, 176.) For review, see Chem. Rev., 1940, 437.

PREPARATION 477A.—**Adipic Dialdehyde** (*Hexan dialdehyde*).



$(CH_2)_4 < \begin{smallmatrix} CHO \\ CHO \end{smallmatrix}$ $C_6H_{10}O_2$. 114.

10 gms. cyclohexene (see Prep. 422) are dissolved in 250 c.cs. *dry* ethyl acetate and the solution cooled to −20° to −30° in solid carbon dioxide and alcohol. To the flask is attached a delivery tube for admitting ozone from the ozoniser (see p. 57), and also a calcium chloride tube leading to a flask containing acidified potassium iodide solution. When iodine is freely liberated the reaction is complete. 0·5 gm. Adams catalyst (C.V., I, 463) is added and the product hydrogenated as described on p. 197. The catalyst is filtered and the solvent evaporated. The residue is distilled and the fraction B.P. 92°–94° at 9 mm. collected. The dialdehyde is stored in a sealed tube under nitrogen or carbon dioxide.



Yield.—60% theoretical (8 gms.). Dioxime, M.P. 172°. (B., 1933, 666).

PREPARATION 478.—**Chloroform** (*Trichloromethane*).

$CHCl_3$. 119·5.

From Acetone.—200 gms. bleaching powder (available chlorine: 30–35%) are made into a paste with 300 c.cs. water, and placed in a litre flask. A small piece of paraffin wax is added to minimise loss of chlorine and check frothing. Through the two-holed stopper are placed a condenser attached to a receiver immersed in a freezing mixture, and a dropping funnel containing 32 c.cs. acetone and 32 c.cs. water. To ensure regular boiling a tube sealed at one end is placed in the flask with the open end under the surface, and the sealed end resting on the neck of the flask. 5 c.cs. of the acetone-water mixture are led from the dropping funnel below the surface and heat applied until gentle frothing takes place. Heat is withdrawn until frothing ceases after which the remainder of the acetone-water is added at such a rate as to maintain the reaction.

The mixture is then distilled until all the chloroform has passed over. The distillate is placed in a separating funnel, and the bottom layer of chloroform run off. This is washed with dilute sodium hydroxide, dried over granular calcium chloride and distilled.

Yield.—(20 gms.).

$$CH_3.CO.CH_3 + 3Cl_2 \longrightarrow CH_3COCCl_3 + 3HCl.$$

$$2CH_3.CO.CCl_3 + Ca(OH)_2 \longrightarrow (CH_3COO)_2Ca + 2CHCl_3.$$

From Alcohol.—46 gms. of alcohol are treated with chlorine, first below 10° and, when absorption slackens, at 60° until the gas is no longer absorbed. For further details see Preparation 355. The product which contains chiefly chloral alcoholate is washed out with water into a large flask which is connected to a long condenser having an attached adapter dipping just under the surface of water in a receiver. 115 gms. of fresh 35% bleaching powder and 20 gms. lime ground up into a paste with water in a mortar are washed into the flask with water, 450 c.cs. of water being used altogether. The method thereafter is the same as described above.

$$CH_3CH_2OH \longrightarrow CCl_3CHO \longrightarrow CHCl_3 + Ca(OOCH)_2.$$

Colourless liquid ; B.P. 61° ; D. $^{12}_{4}$ 1·504.

(A., 23, 244 ; J. Eng., 4, 345, 406 ; J. C. Ed., 1940, 565.)

PREPARATION 479.—**Iodoform** (*Triiodomethane*).

CHI_3. 934.

From Alcohol.—To 32 gms. potassium carbonate dissolved in 80 gms. water 16 gms. 95% alcohol are added, and the solution heated to 70°. 32 gms. powdered iodine are added gradually with stirring. Iodoform gradually separates out, and when the solution has become completely decolourised, is filtered off, washed with water, and dried at ordinary temperature. A further yield is obtained by adding 2–3 gms. potassium bichromate and 16–24 gms. conc. hydrochloric acid, neutralising and adding 32 gms. potassium carbonate, 16 gms. 95% alcohol and 6 gms. iodine, and carrying out as before.

The iodoform is then recrystallised from alcohol.

$$C_2H_5OH \longrightarrow CI_3CHO \longrightarrow CHI_3.$$

(J., 1874, 317.) See also B., [3], 1, 4.

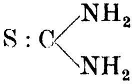
From Acetone.—10 gms. iodine are dissolved in 32 gms. warm 10% caustic soda solution, and after cooling, 2 gms. of acetone added. 10 gms. powdered iodine are added with stirring and then caustic soda solution gradually, until the iodine disappears. The iodoform separates and is filtered off. 2 gms. acetone are added to the filtrate, which has been acidified with hydrochloric acid, and then made alkaline with caustic soda and a further yield of iodoform is obtained.

$$CH_3COCH_3 \longrightarrow CH_3COCI_3 \longrightarrow CHI_3.$$

Lemon yellow hexagonal crystals ; M.P. 115° ; characteristic odour ; sparingly soluble in water.

(A. Spl., 7, 218, 377.)

PREPARATION 480.—**Thiourea** (*Thiocarbamide*).



$$S : C\begin{cases}NH_2\\NH_2\end{cases} \qquad CH_4N_2S. \qquad 76.$$

50 gms. of ammonium thiocyanate are melted in a round-bottomed flask in a paraffin bath and kept at a temperature at which the mass remains just liquid (140°–150°) for 5–6 hours, or at 170° for 1 hour. The former method gives the better yield. The cooled melt is powdered and ground up with half its weight of cold water, which dissolves unchanged ammonium thiocyanate, but little of the thiourea. The residue is recrystallised from hot water.

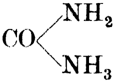
$$CNS.(NH_4) \rightleftarrows CS(NH_2)_2.$$

Yield.—14–16% of complete conversion (7–8 gms.); slightly soluble in cold water (1 in 11); soluble in hot water and alcohol; almost insoluble in ether or benzene; M.P. 172°. (J. C. S., 22, 1; 83, 1; J. pr., [2], 9, 10.)

Prepared industrially from cyanamide and ammonium sulphide.

$$NH_2CN + H_2S \longrightarrow NH_2C(SH) : NH \longrightarrow CS(NH_2)_2.$$

PREPARATION 481.—**Urea** (*Carbamide*).



$$CO\begin{cases}NH_2\\NH_3\end{cases} \qquad CH_4ON_2. \qquad 60.$$

50 gms. of potassium cyanide are heated in a large iron crucible over a large burner or blowpipe flame until it begins to fuse. 140 gms. of red lead, in small portions at a time, are added while the mixture is stirred with a rod. When the addition is complete and frothing has ceased the fused mass is poured on to an iron tray. When cold, the mass is separated from metallic lead, ground in a mortar and digested with 200 c.cs. of cold water for an hour. The filtrate from this mixture is treated with 25 gms. of ammonium sulphate and evaporated in a basin to dryness on a water bath. The residue, ground finely and transferred to a flask, is boiled with three instalments of alcohol under reflux to dissolve the urea from the potassium sulphate. Each extract is decanted or filtered, and the combined extracts are evaporated to small bulk until crystals of urea separate on cooling and standing.

$$KCN \longrightarrow KOCN \longrightarrow NH_4CNO \longrightarrow CO(NH_2)_2.$$

Prisms; M.P. 132°; very soluble in water. (J., 1880, 393.) (For views on structure, see Werner, *The Chemistry of Urea.*) For preparation of methylurea, see O. S., XV, 48.

Prepared industrially from cyanamide by hydrolysis, or from ammonium carbamate by heating under pressure.

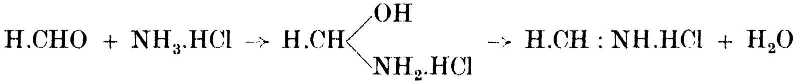
$$CaCN_2 \longrightarrow H_2NC \vdots N \xrightarrow{H_2O} CO(NH_2)_2.$$

$$NH_2COONH_4 - H_2O \longrightarrow CO(NH_2)_2.$$

PREPARATION 482.—Methylamine Hydrochloride.

$CH_3.NH_2.HCl$. CH_6NCl. 67·5.

125 gms. ammonium chloride and 250 gms. 40% aqueous formaldehyde solution are placed in a distilling flask with thermometer well below surface of liquor. The flask is attached to a water condenser, and slowly heated until the thermometer registers 104°, at which it is maintained constant until no further liquid distils over. Weight of distillate = 54 gms. The product in the flask is cooled and filtered from ammonium chloride which separates. The filtrate is evaporated on a water bath to half its original volume, cooled and a second crop of ammonium chloride filtered off. The liquid is then concentrated at 100° until a crystalline scum forms on the surface. On cooling, methylamine hydrochloride separates, and is filtered off. After further evaporation and cooling, a second crop of methylamine hydrochloride is similarly obtained. The filtrate is again concentrated, and left for 24 hours over solid caustic soda in a vacuum desiccator ; the semi-solid residue is extracted with warm chloroform which dissolves out any dimethylamine hydrochloride, and a further quantity of methylamine hydrochloride is filtered off. The total yield is treated with boiling chloroform, filtered hot, washed with warm chloroform and dried in a desiccator.



$$H.CHO + NH_3.HCl \rightarrow H.CH\begin{cases} OH \\ NH_2.HCl \end{cases} \rightarrow H.CH : NH.HCl + H_2O$$

$$CH_2 : NH.HCl + H_2O + H.CHO \rightarrow CH_3.NH_2.HCl + HCOOH.$$

Yield.—50% theoretical (45 gms.). Large deliquescent plates; insoluble in chloroform. (J. C. S., 111, 844 ; Am. Soc., 50, 1786 ; O. S., 111, 67.)

PREPARATION 483.—ββ-Dinaphthylamine.

$(C_{10}H_7)_2NH$. $C_{20}H_{15}N$. 269.

100 gms. of β-naphthylamine and 0·5 gm. of iodine are heated to 230° for 4 hours. The melt is then cooled and recrystallised from benzene.

$$2C_{10}H_7NH_2 \longrightarrow (C_{10}H_7)_2NH + NH_3.$$

Yield.—Almost theoretical (92 gms.). Silver glistening plates ; M.P. 170·5° ; sparingly soluble in hot alcohol ; easily soluble in hot glacial acetic acid. (J. pr., [2], 89, 23, 35.)

PREPARATION 484.—Phenyl-β-naphthylamine.

$C_{10}H_7NH.C_6H_5$. $C_{16}H_{13}N$. 219.

90 gms. of β-naphthol and 112·5 gms. of aniline are heated for 7 hours to 100°–190° with 1 gm. of iodine. The melt is boiled out first with dilute hydrochloric acid and then with dilute caustic soda. The residue is dried and distilled *in vacuo*. The phenylnaphthylamine passes over at 237° (15 mms.). It is recrystallised from methyl alcohol.

$$C_{10}H_7OH + H_2N.C_6H_5 \longrightarrow C_{10}H_7NH.C_6H_5 + H_2O.$$

Yield.—Almost theoretical (130 gms.). Needles ; M.P. 108°. (B., 13, 1850.)

PREPARATION 485.—**Thiocarbanilide** (*s-Diphenylthiocarbamide*).

$CS(NHC_6H_5)_2$. $C_{13}H_{12}N_2S$. 228.

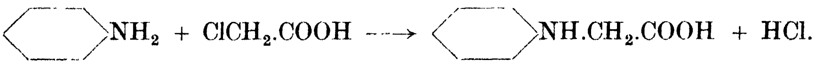
50 gms. carbon disulphide and 40 gms. aniline are dissolved in 60 c.cs. alcohol and 10 gms. powdered caustic potash are added. The whole is heated to boiling (*caution!*) on a water bath for 3–4 hours under a long reflux condenser. (Carbon disulphide boils at 46°.) The carbon disulphide and alcohol are then distilled off, and the residue is washed with water and with dilute hydrochloric acid to remove unchanged aniline. It is then filtered, washed with water, and recrystallised from alcohol.

Yield.—70% theoretical (35 gms.). Colourless plates; M.P. 151°; sparingly soluble in water. (A., 70, 142; B., 33, 2726.)

PREPARATION 486.—**Phenylglycine.**

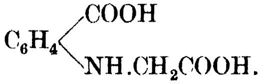
$C_6H_5NH.CH_2COOH$. $C_8H_9O_2N$. 151.

20 gms. of chloroacetic acid are dissolved in 20 c.cs. of water, and 16 gms. of calcium hydroxide added, the whole being kept cool; a mixture of 20 c.cs. of methyl or ethyl alcohol and 60 gms. of aniline is next added, and the whole stirred and warmed until the reaction is complete. The alcohol and aniline are distilled off with steam; the calcium salt is filtered off and is converted into the sodium salt when cold (see p. 317). The calculated amount of a mineral acid is added to the concentrated solution of the sodium salt, and the phenylglycine thus obtained.



Small crystals. M.P. 126°–127°. (D.R.P., 167698.)

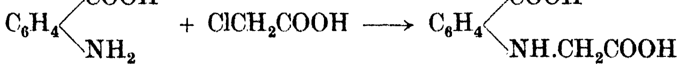
PREPARATION 487.—**Phenylglycine-*o*-carboxylic Acid.**



$$C_6H_4\begin{cases}COOH\\NH.CH_2COOH.\end{cases}$$

$C_9H_9O_4N$. 195.

11·2 gms. caustic potash are dissolved in 100 c.cs. water, and to this are added 9·4 gms. chloroacetic acid and 13·6 gms. anthranilic acid. The solution is warmed on a water bath under a reflux for 2 hours at 60°–80°. Hydrochloric acid is then added to neutralise. The phenylglycine-*o*-carboxylic acid separates out after standing and is filtered off and recrystallised from water. A further yield can be obtained by evaporating the filtrate.



$$C_6H_4\begin{cases}COOH\\NH_2\end{cases} + ClCH_2COOH \longrightarrow C_6H_4\begin{cases}COOH\\NH.CH_2COOH\end{cases}$$

Colourless crystals. M.P. 200° (with decomposition). Sparingly soluble in water. Solution in alcohol shows a blue fluorescence. (B., 23, 3432.) For use in preparation of indigo, see p. 397.

Preparation 488.—**Glycine** (*Glycocoll, Aminoacetic acid*).

CH_2NH_2COOH. $C_2H_5O_2N$. 75.

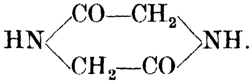
104 gms. of chloroacetic acid are dissolved in an equal weight of water, and this solution slowly run into 1,248 c.cs. of 25% ammonia, the whole being stirred well. When all the acid has been added the solution is set aside for 24 hours and then boiled until no more ammonia is evolved. It is made neutral while hot with a slight excess of copper carbonate, filtered, and the filtrate evaporated until it begins to crystallise. On allowing to cool the copper salt of glycocoll separates as blue needles, is filtered, and washed first with dilute, and then with more concentrated alcohol. The salt is dissolved in water, and the copper precipitated by sulphuretted hydrogen from the boiling solution. The sulphide is filtered off and washed well and the filtrate concentrated to small bulk. On cooling, the glycocoll separates.

$$CH_2ClCOOH + NH_3 \longrightarrow CH_2NH_2COOH + HCl.$$

Monoclinic crystals; M.P. 232°–236° with decomposition; soluble in water, almost insoluble in alcohol and ether. (A., 266, 295; O. S., IV, 31.) See also O. S., XIV, 46.

Preparation 489.—**Glycocoll Ester and Glycine Anhydride** (*Ethyl ester of amino-ethan acid*) and (2 : 5-*diketopiperazine*).

$NH_2.CH_2.COOC_2H_5$ and



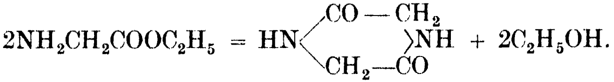
$C_4H_9O_2N$ and $C_4H_6N_2O_2$. 103 and 114.

Glycocoll Ester.—50 gms. (1 mol.) glycocoll-ester hydrochloride (see p. 410) are treated with 25 c.cs. of water, which only suffice for partial solution. 100 c.cs. ether are then added, and the whole well cooled in a freezing mixture and treated with 40 c.cs. (excess) of sodium hydroxide (33%). Finally, such an amount of dry, granulated potassium carbonate is added with cooling and shaking as to form a thick paste. After vigorous shaking, the ethereal solution is poured off, the residue is shaken two or three times with ether, and the united extracts, after filtration, are allowed to stand, with frequent shaking, first for 10 minutes with dry potassium carbonate and then for several hours with anhydrous sodium sulphate. The ether is evaporated and the residue is distilled under reduced pressure. At 10 mms. it boils at 51·5°–52·5°, and so the receiver must be well cooled.

$$NH_3Cl.CH_2COOC_2H_5 + NaOH = NH_2.CH_2COOC_2H_5 + NaCl + H_2O.$$

Yield.—65% theoretical (25 gms.). B.P. ^{748} 148°–149°, with decomposition. (A., 127, 97; J. pr., [2], 37, 166.)

Glycine Anhydride.—20 gms. (2 mols.) of glycine-ester are cooled and treated with 12 gms. of water, and the mixture is then allowed to stand at room temperature for some days. The anhydride separates out during this time in well-defined crystals. It is filtered, washed with a little cold water, and dried under reduced pressure over sulphuric acid.



$$\mathrm{2NH_2CH_2COOC_2H_5 = HN\left\langle\begin{matrix}CO-CH_2\\CH_2-CO\end{matrix}\right\rangle NH + 2C_2H_5OH.}$$

Yield.—60% theoretical (7 gms.). Colourless plates ; turns brown at 245° ; melts with blackening at 275°. Sublimes on rapid heating. (J. pr., [2], 37, 173.)

For the direct preparation of glycine-anhydride from glycocoll ester hydrochloride, see B., 39, 2930.

Preparation 490.—**Racemic Phenylalanine** (3-*Phenyl-2-amino-propan-acid*).

$\mathrm{C_6H_5.CH_2.CH(NH_2).COOH.}$ $\mathrm{C_9H_{11}O_2N.}$ 165.

50 gms. (1 mol.) of benzylmalonic acid (see p. 142) are dissolved in 250 gms. of dry ether, and 50 gms. ($1\frac{1}{5}$ mols.) bromine are gradually added in daylight. At first the halogen rapidly disappears, and clouds of hydrobromic acid are evolved. At the end the liquid is coloured reddish-brown by the excess of bromine. When it has stood for half an hour the ethereal solution is shaken with a little water, sulphuric acid being gradually added until the red colour of the bromine disappears. The ethereal layer is then separated, again washed with a little water, and carefully evaporated. The solid residue is recrystallised from about 250 c.cs. of hot benzene. Yield 95% theoretical (65 gms.). The benzyl-bromomalonic acid when dried under reduced pressure at 80° melts at 137° (corr.).

The benzylbromomalonic acid containing water is now heated in an oil bath to 125°–130°, and the fused mass evolves carbon dioxide and a certain amount of hydrobromic acid. The reaction is complete in the course of 30–45 minutes. The residue is a yellow oil, which even at a low temperature does not crystallise, and which in the main consists of phenyl-α-bromopropionic acid. For the purpose of purification it is washed with water, taken up in ether, and dried with anhydrous sodium sulphate ; the ether is then distilled off. The mobile, almost colourless oil remaining is dissolved in 5 times its volume (excess) of 25% aqueous ammonia, and either heated for 3 hours to 100° in a sealed tube or allowed to stand for 3 to 4 days at ordinary temperature. On evaporation of the ammoniacal solution an almost colourless residue is left, and this chiefly consists of ammonium bromide and phenylalanine. On boiling with absolute alcohol the amino-acid is undissolved and is recrystallised from water.

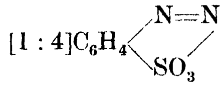
$$\mathrm{C_6H_5.CH_2CH(COOH)_2 + Br_2 = C_6H_5CH_2CBr(COOH)_2 + HBr.}$$

$$\mathrm{C_6H_5CH_2CBr(COOH)_2 \longrightarrow C_6H_5CH_2.CHBrCOOH + CO_2.}$$

$$\mathrm{C_6H_5.CH_2CHBr.COOH + 2NH_3 = C_6H_5CH_2.CH(NH_2)COOH + NH_4Br.}$$

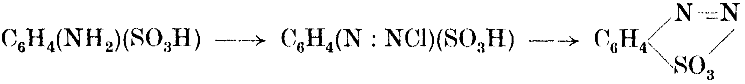
Yield.—55% theoretical (24 gms.). Colourless crystals ; soluble in hot water. M.P. 263°–265° with decomposition. (B., 37, 3064 ; O. S., 21, 99.) See also C. V., II, 489.

PREPARATION 491.—Diazobenzenesulphonic Acid Anhydride (*Inner salt of benzenediazonium-hydroxide-4-sulphonic Acid*).



$$[1:4]C_6H_4\left\langle\begin{matrix}N{=}N\\SO_3\end{matrix}\right/ \qquad C_6H_4O_3N_2S. \qquad 184.$$

20 gms. (1 mol.) of sulphanilic acid, previously dried on a water bath and finely powdered, are dissolved, in the heat, in 58 c.cs. (1 mol.) of 2N sodium hydrate ; and the solution is diluted until, on cooling to 50°, no crystallisation occurs. This solution is cooled and treated (p. 380) with 10 gms. (more than calculated amount) of sodium nitrite, and the mixture is poured, with constant stirring, into an excess of *cold*, dilute sulphuric acid. In a short time, the diazonium compound separates as a white, crystalline mass. To favour crystallisation the liquid is cooled, and after it has stood for some time the substance is filtered off. This compound can be kept in the dry state, but must not be dried at 100°. In dealing with the dry product *care is, however, always necessary, for it sometimes explodes violently when rubbed.*



$$C_6H_4(NH_2)(SO_3H) \longrightarrow C_6H_4(N:NCl)(SO_3H) \longrightarrow C_6H_4\left\langle\begin{matrix}N{=}N\\SO_3\end{matrix}\right/$$

Yield.—80% theoretical (16 gms.). Colourless crystals ; stable enough to be recrystallised from water at 60°. (A., 190, 76.)

PREPARATION 492.—Diazomethane.

CH_2N_2. 42.

Nitrosomethylurea.—20 gms. methylamine hydrochloride (Prep. 482) and 30 gms. potassium cyanate are dissolved in 120 c.cs. water, heated to 70° for 15 minutes, and then to boiling for a short time. The solution is cooled to 0° and 40 c.cs. water containing 20 gms. sodium nitrite, also cooled to 0°, added. 100 c.cs. 25% sulphuric acid are added with stirring, when nitrosomethylurea separates, is filtered, washed with ice-water, pressed, and dried in a vacuum desiccator. The product is then crystallised from methyl alcohol (light yellow needles, M.P. 124°).

Diazomethane.—When diazomethane is required for immediate utilisation, 10 gms. nitrosomethylurea are added with continued shaking in small portions to 100 c.cs. ether and 30 c.cs. 40% caustic potash placed in a wide-mouthed flask and cooled to 0°, the operation being conducted with caution in a fume cupboard. After 10 minutes the yellow ethereal extract is separated, and dried for 3 hours with a little solid caustic potash. The solution can be kept for several days in a flask fitted with a calcium chloride tube drawn out to a fine capillary. For preparative work it is used in solutions only.

$$CH_3NH_3Cl \xrightarrow{KCNO} CH_3NHCONH_2 \xrightarrow{HNO_2}$$

$$CH_3N(NO)CONH_2 \xrightarrow{KOH} CH_2N_2 + KCNO + 2H_2O.$$

Yellow explosive, toxic gas; B.P. −24°. (B., 45, 505; O. S., 25, 28.) Important methylating agent. (See J. C. S., 1946, 746; Chem, Rev., 1938, 193.)

Methylation by means of diazomethane.—The ethereal solution prepared as above is added to a solution or suspension in ether of the product to be methylated. Reaction is indicated by the disappearance of the yellow colour, and is complete when the colour persists on warming. Nitrogen is evolved and the final product is recovered from ethereal solution.

Diazomethane may also be prepared from hydrazin hydrate and chloroform. (B., 45, 505.)

$$NH_2.NH_2 + CHCl_3 \longrightarrow N_2CH_2 + 3HCl.$$

For syntheses with diazomethane, see *Preparative Organic Chemistry*, Eistart, p. 513.

The original method of preparing diazomethane is as follows. Methylurethane, formed by the interaction of methylamine and chloroformic ester, is converted into the nitroso compound by the action of nitrous acid, the latter yielding diazomethane on treatment with alcoholic potash.

$$ClCOOC_2H_5 + NH_2CH_3 \longrightarrow CH_3NHCOOC_2H_5$$

$$CH_3NHCOOC_2H_5 + HNO_2 \longrightarrow CH_3N(NO)COOC_2H_5$$

$$CH_3N(NO)COOC_2H_5 + KOH \longrightarrow CH_2N_2 + KHCO_3 + C_2H_5OH.$$

(B., 27, 1888; 28, 855; 35, 897.)

PREPARATION 493.—**Benzylthiourea Hydrochloride** (*S-Benzyl-iso-thiouronium Chloride.*)

$$[C_6H_5CH_2SC(:NH_2)NH_3]^+Cl^-. \qquad C_8H_{11}N_2ClS. \qquad 202{\cdot}5.$$

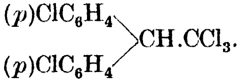
Approximately theoretical quantities (63·3 gms. and 38·0 gms., respectively) of benzyl chloride and thiourea along with 75 c.cs. of alcohol are warmed in a flask under reflux on a steam bath for 30 minutes. The white crystalline product, which separates on cooling the flask in ice-water, is collected, washed with three 25-c.c. portions of cold ethyl acetate, and dried. The low-melting (140°–145°) and the high-melting (172°–174°) forms of the product are obtained. On recrystallisation from water the former is changed to the latter.

$$[C_6H_5CH_2Cl + HSC(:NH)NH_2 \longrightarrow [C_6H_5CH_2SC(:NH_2)NH_3]^+Cl^-.$$

Yield.—50% theoretical (50 gms.). M.P. 174°. (J. of Org. Chem., 1941, 376.)

Identification of Organic Acids.—Salts, which in many instances have sharp melting-points and are easily isolated, are usually prepared by mixing the theoretical quantities of ice-cold, concentrated aqueous solutions of benzylthiourea hydrochloride and a neutral solution of an organic carboxylic or sulphonic acid. The product separates on "scratching" the vessel. See also p. 527.

Preparation 494.—D.D.T. (2 : 2-*di*(*p-chloro-phenyl*)-1 : 1 : 1-*trichloro-ethane*).



$$\begin{matrix}(p)\mathrm{ClC_6H_4}\\(p)\mathrm{ClC_6H_4}\end{matrix}\!\!>\mathrm{CH.CCl_3}.$$

$C_{14}H_9Cl_5$. 354·5.

A mixture of 22·5 gms. chlorobenzene, 17 gms. chloral hydrate and 170 gms. conc. sulphuric is vigorously stirred mechanically in a round-bottomed flask. 25 gms. of 20% oleum are added (*Care*). The temperature rises to 45°–60° ; and if the product does not separate in lumps in about an hour further small quantities of oleum are added until solidification takes place, stirring being maintained throughout the experiment.

The mixture is then poured with care on to crushed ice, the product collected when cool, washed with water and recrystallised from alcohol.

$$CCl_3CHO + 2C_6H_5Cl \longrightarrow Cl_3CCH(C_6H_4Cl)_2 + H_2O.$$

Yield.—70% theoretical (25 gms.). Colourless needles ; M.P. 103°–106°. (J. C. Ed., 1945, 170.)

PART III

CHAPTER XXXIII

ORGANIC ANALYSIS

DETECTION OF ELEMENTS PRESENT IN CARBON COMPOUNDS

Carbon and Hydrogen.—Some fine copper oxide is heated in a porcelain crucible for a few minutes to drive off all moisture, and afterwards left to cool in a desiccator. A small amount—0·1–0·2 gm.—of the compound is mixed with about 10 times its weight of the dry copper oxide and placed in a dry clean test tube 10–12 cms. long, 4–6 cms. of dry copper oxide are then added, and the tube closed with a cork carrying a delivery tube bent at a right angle. The tube is supported in a horizontal position and gradually heated, beginning first at the unmixed copper oxide and raising it to a high temperature before the compound is appreciably heated. The oxygen of the copper oxide acts as oxidising agent, and if the compound contains hydrogen, water collects on the cooler portions of the tube; if it also contains carbon, the issuing gas, when passed into lime or baryta water, causes turbidity.

Nitrogens, Halogens, Sulphur and Phosphorus.—A piece, about 0·5 c.c., of bright sodium or potassium is placed in a small hard glass test tube about 8 cms. long and 1 cm. in diameter. (In testing easily volatile compounds, a longer tube, to act as a condenser, should be used.) The end of the tube is gradually heated at some distance above a small flame until the sodium (or potassium) just melts. The tube is withdrawn from the flame, and a small quantity of the compound dropped on to the surface of the molten metal. Generally a brisk reaction, often accompanied by detonations, takes place, and when this subsides the end of the tube is gradually heated to bright redness, at which it is maintained until decomposition is complete, and any excess of sodium is oxidised. By this treatment there is formed: sodium cyanide if nitrogen is present; sodium halide if halogen is present; sodium sulphide if sulphur is present; perhaps, sodium sulphocyanide if both nitrogen and sulphur are present, but when sulphur is present, an excess of sodium should be used in order to prevent the formation of sulphocyanide. While still hot, the tube is plunged into 10 c.cs. of distilled water contained in a small beaker or dish —care should be exercised as the operation is very vigorous; by this the tube is shattered, any alkali metal remaining reacts briskly, a quantity of carbon remains suspended in the liquid, and any cyanide, halide, sulphide or sulphocyanide formed, passes into solution. The mixture is boiled for a minute, then cooled and filtered through a previously wetted filter paper. The filtrate should be water clear; if not the fusion must be repeated and more care taken to ensure the complete decomposition of the organic compound by longer heating. The filtrate is divided into portions which are tested as follows :

(*a*) *For Nitrogen.*—To one portion, about 1 c.c. of ferrous sulphate solution and a few drops of ferric chloride solution are added. Hydroxides of iron are precipitated. (If no precipitation occurs, a little caustic soda solution must be added.) The mixture is boiled for 1–2 minutes, and if alkali cyanide—equivalent to nitrogen in the original compound—is present, sodium ferrocyanide is formed. After cooling under the tap, the alkaline mixture is acidified with hydrochloric acid, which dissolves the precipitated ferrous and ferric hydroxides, and the resulting ferric salt reacting on the sodium ferrocyanide forms Prussian Blue. Accordingly, a blue or bluish-green precipitate indicates the presence of nitrogen. At times a blue or bluish-green solution is obtained, which only gives a blue precipitate after standing a few hours, or perhaps overnight. (The addition of a little potassium fluoride is often very helpful in bringing down the blue precipitate.) When the test is doubtful, it should be repeated, using more of the alkaline solution, or if the compound contains only a small percentage of nitrogen, it may be necessary to repeat the fusion, using a larger quantity of the compound. Compounds (e.g. diazo-compounds) which evolve nitrogen at moderate temperature generally fail to give a positive reaction by this method, and in such cases nitrogen can be detected by heating the compound with cupric oxide in an atmosphere of carbon dioxide after the manner of a Dumas determination of nitrogen and finding amongst the products a gas which is not absorbed by caustic potash.

For volatile or unstable nitrogen compounds a mixture consisting of 138 parts of ignited potassium carbonate and 72 parts of magnesium powder may be used in place of sodium (or potassium). Small quantities of this mixture and of the compound are intimately mixed and heated in a glass tube. The mass is extracted with water, filtered, the filtrate made alkaline and tested for cyanide.

Thorpe and Whiteley recommend the following modification of Castellana's method. A mixture of sodium carbonate (1 mol.) potassium carbonate (1 mol.), and magnesium powder (2 atoms) forms a highly active substitute for sodium. A small quantity of the organic compound is intimately mixed with about five times its bulk of this reducing mixture. The crucible containing the mixture is heated, gently at first, then more strongly, until the reaction is over. The residual mixture after cooling is boiled with water and filtered. The filtrate is tested for cyanide as before.

Middleton replaces sodium by an intimate mixture of zinc dust with ten times its weight of anhydrous sodium carbonate (or, in certain cases, with an intimate mixture of sucrose and ten times its weight of anhydrous sodium carbonate).

(*b*) *For Halogens.*—If nitrogen has been proved absent by (*a*) a portion of the solution is acidified with nitric acid, and silver nitrate added. A curdy white or yellow precipitate indicates the presence of halogen. If nitrogen is present, the solution, after acidification with nitric acid, must be boiled until all hydrocyanic acid is expelled before silver nitrate is added. In the absence of sulphur mercurous nitrate solution may be used to distinguish silver cyanide from halide, the former only being soluble.

Halogens may also be detected by Beilstein's test—a piece of pure copper oxide, held by means of a platinum wire around it, is heated in a Bunsen flame until it ceases to colour the flame green. It is then allowed to cool, and a little of the compound is placed on it. If, on heating again, there appears a bright green flame accompanied by a blue zone round the oxide (due to the volatilisation of copper halide), the presence of a halogen is indicated.

Certain nitrogenous compounds (ureas, amides, nitriles, etc.) give cuprous cyanide in this test which produces a green flame coloration. The presence of halogen must therefore be confirmed by other tests.

A third test for the presence of halogens consists in heating the compound along with an excess of pure lime in a glass tube. The mass is afterwards extracted with water, and tested with silver nitrate.

(*c*) *For Sulphur.*—To a portion of the alkaline filtrate a few drops of a freshly-prepared solution of sodium nitroprusside are added. A violet or purple coloration indicates the presence of sulphur. A dark coloration or precipitate on the addition of sodium plumbite solution (p. 515) also indicates presence of sulphur.

Other methods—in all of which the resultant sulphate is precipitated with barium chloride—for the detection of sulphur in compounds, are: (*a*) oxidation with sodium peroxide; (*b*) oxidation with sodium carbonate and potassium nitrate; (*c*) oxidation with fuming nitric acid in sealed tubes.

(*d*) *For Phosphorus.*—About 1 c.c. of the alkaline filtrate is heated with 3 c.cs. of conc. nitric acid for a few minutes. To this solution after cooling, ammonium molybdate solution is added, and the whole warmed. A crystalline yellow precipitate of ammonium phosphomolybdate on standing indicates the presence of phosphorus.

Other methods for the detection of phosphorus involve oxidation to phosphoric acid by means of (*a*) sodium peroxide; (*b*) sodium carbonate and potassium nitrate; (*c*) fuming nitric acid in sealed tubes.

The presence of phosphorus may also be ascertained by heating the compound with magnesium powder, and moistening the cold product with water, whereby phosphine (recognised by its smell) is liberated from the magnesium phosphide.

For a critical review of methods of detection of elements, see Tucker, J. C. Ed., 1945, 212.

Metallic Radicles.—The organic matter in the compound is destroyed either (*a*) by heating to redness for some time in contact with air in a quartz or porcelain crucible, or (*b*) by oxidising with a mixture of conc. nitric and sulphuric acids. After decomposition is complete, the residue is examined by the usual tests for inorganic radicles. In (*a*) volatile radicles such as mercury, arsenic and ammonium will be lost.

CHAPTER XXXIV

QUANTITATIVE ANALYSIS

MICRO METHODS

THIS chapter, which deals with the microchemical determination of carbon, hydrogen, nitrogen, halogen, sulphur and alkoxyl, is intended to serve as an introduction to organic microchemical methods. Sufficient detail has been given for the determination of any of the above. Further information regarding apparatus and procedure is given in the standard monographs on the subject which include :

Die quantitative organische Mikroanalyse, Pregl.

Die Praxis der quantitativen organischen Mikroanalyse, Friedrich.

Quantitative Organic Microanalysis of Pregl, Roth and Daw.

Quantitative Organic Microanalysis, Pregl, Fyleman.

Quantitative Organic Microanalysis, Pregl, Grant.

Organic Quantitative Microanalysis, Niederl and Niederl.

Methods of Quantitative Micro-Analysis, Milton and Waters.

Recommended specifications for microchemical apparatus are given in Royer *et al.*, J. Eng., *Anal. Ed.*, 1941, 574 ; 1943, 230, 476. The apparatus and procedures described are those used and followed for the most part in the microchemical analytical laboratory of the Royal Technical College, Glasgow.

Until recent years quantitative organic analysis was performed almost entirely by macro methods. These have now been largely superseded by micro methods the technique for which is readily acquired. Thorough cleanliness, care in all manipulations, strict adherence to routine and to time schedules are the main essentials. Micro analytical reagents (M.A.R. quality) are used throughout. The temperature of combustion in the furnaces is controlled by chrome-alumel thermocouples.

Micro Balance.—The micro balance should be housed separate from, but adjoining, the combustion room in an apartment which is air-conditioned or thermostatically controlled. A suitable mounting consists of a wooden shelf securely bracketed to a wall, this shelf carrying in upward sequence five or six large sheets of filter paper, a slate slab 2–3 in. thick, a rubber sheet approximately 2 mms. thick and finally the balance.

Weighing is performed whenever possible with the aid of counterpoises. These should be prepared in advance for the various pieces of apparatus—platinum boats, weighing tubes, absorption tubes, etc.—which are in constant use. For the lighter pieces, aluminium foil is excellent, and small flasks containing lead shot (size 15) and aluminium foil for the heavier. Counterpoises should be prepared to within 10 mgms. on a good ordinary balance and the operation completed on a microbalance. In any determination the increase in weight is seldom more than a few milligrams; hence only one 20 mgm.- and one 10 mgm.-weight are required, but these must be accurate and tested periodically.

Determination of Carbon and Hydrogen

Pressure Regulator (Fig. 59A).—This consists essentially of two bell-type gas holders mounted on a wooden stand and held in position by metal springs. The inlet of each gas holder is connected by means of artificially-aged rubber tubing (see p. 463) carrying a precision screw clip (also mounted on the stand) to the source of oxygen and air. Each exit is joined by the same kind of rubber tubing to the limbs of a three-way capillary stop cock (*b*) which is attached to the bubbler (*c*) or flowmeter. If oxygen only is used, one pressure regulator is required, and the T-piece may be replaced by a single stop cock. The gas holders are two-thirds filled with 5% caustic soda solution. By raising or lowering the sleeve (210–220 mms. long, 20–25 mms. diameter) the pressure in the system can be adjusted. A head of 50–70 mms. is required to give a flow of 4 mls. of gas per minute.

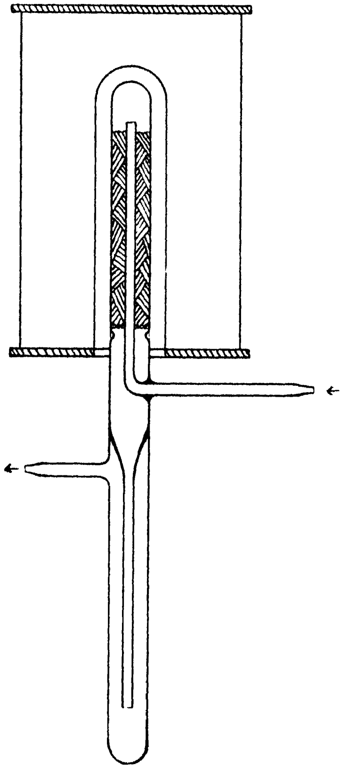


FIG. 59A.

Preheater (Fig. 59A).—This is inserted between the pressure regulator and the bubbler. It is constructed from heat resisting glass tubing 12–13 mms. internal diam. and is 310–320 mms. long, 80-90 mms. length of which, filled with platinised asbestos resting on a perforated asbestos disc, is heated in an electric furnace to 600°. Oxygen (and air, if used) enters preheater by upper side arm, then passes into lower chamber which is cooled by immersion in a cylinder of water.

Bubbler (*c*) *and U-tube* (*d*).—Though many analysts use a flowmeter of the White-Wright or similar type (Can. J. Research, 1936, 427; Metallurgia, 1944, 332), the bubbler described by Pregl, and recommended by the American Chemical Society (Royer *et al.*, J. Eng., *Anal. Ed.*, 1941, 374) is more satisfactory for the control of the rate of flow of oxygen. This bubbler consists of a cylindrical glass tube 50–55 mms. long and 14–15 mms. diameter at the end and 20–22 mms. diameter in the middle, closed at both ends, but carrying two side arms 1·5–2 mms. bore fused into the tube directly opposite one another approximately 5 mms. from the top.

The inlet side arm is extended and bent at right angles to form an internal tube 1·2–1·5 mms. in diameter at the tip. The centre of this tube is blown out to form a bulb (9–10 mms. diameter); the tube which extends from this dips below the surface of 50% caustic potash solution. This same arm is attached by impregnated rubber tubing or preferably by a ground glass joint to the delivery end of the T-piece (*b*), while the other arm may be joined, either by fusion of the arms or by a ground glass joint, to the scavenging train which consists of a U-tube (*d*) 120–140 mms. long and 12 mms. internal diameter. A ground glass stopper is fixed in the limb of the U-tube attached to the bubbler. The other end is closed but has a side arm attached by a capillary 40 mms. long to the side arm of the combustion tube. The bore of all glass tubing and joints from the pressure regulator to the combustion tube is 1·5–2 mms. and all glass joints and stoppers are fixed with Krönig cement, made by melting 1 part white paraffin wax with 4 parts colophony. The U-tube is separately charged in the reverse order with the same absorbents as are used in the absorption train in the ratio of one third water absorbent to two thirds carbon dioxide absorbent. Small plugs of cotton wool are inserted into the side arms to prevent pieces of absorbent from falling into the bubbler or combustion tube.

The Combustion Tube (Fig. 59 (*e*)).—This tube, of Supremax glass, Monax combustion glass or clear silica, is 520–530 mms. long, exclusive of neck, has external diameter of 9·5–10·5 mms. and a side arm bent at right angles attached about 15 mms. from the mouth. That part of the side arm attached to the tube is 40–45 mms. long and is bent at right angles forming an arm 25–30 mms. in length. This arm has external diameter of 5 mms. and internal diameter of 1·5–2 mms. At the other end of the combustion tube there is a neck, 30–35 mms. in length, with external and internal diameters of 3·3–3·5 mms. and 1·5–2·0 mms. respectively.

Pregl Filling.—A choking plug (A) 6–7 mms. in length of specially-purified asbestos, so packed that it allows 3–4 mls. of oxygen per minute to pass through the tube with 40–60 mms. depth of water in the pressure regulator, is first inserted in the tube. This adjustment is a matter of experiment and is more quickly accomplished if the number of bubbles per minute is measured against the volume of water collected. Next is placed in position 20–25 mms. length of black lead dioxide (B) (see note, p. 461) distributed evenly by careful tapping, followed by a plug (A), 2 mms. thick, of loosely-packed asbestos. This prevents the silver which is next inserted from being contaminated by the lead dioxide. This silver packing (C) is about 40 mms. long and can be made readily from pure, clean, reduced silver gauze or wool. Another loosely-packed plug (A) of asbestos 2 mms. thick follows the silver, and then a column (D) about 140 mms. long of copper oxide impregnated with lead chromate. The length of this column is determined by the length of the electrically- or gas-heated furnace and should be of such length that 5 mms. project beyond the furnace. A plug of silver gauze (C) 15–20 mms. in length keeps the filling in place.

Notes.—(1) Silica tubing is not suitable for the lead chromate-copper oxide filling as the chromate attacks silica. An alternative procedure is to increase the length of the lead dioxide by 5–10 mms. and replace the filling with copper oxide-cerium oxide or thorium oxide.

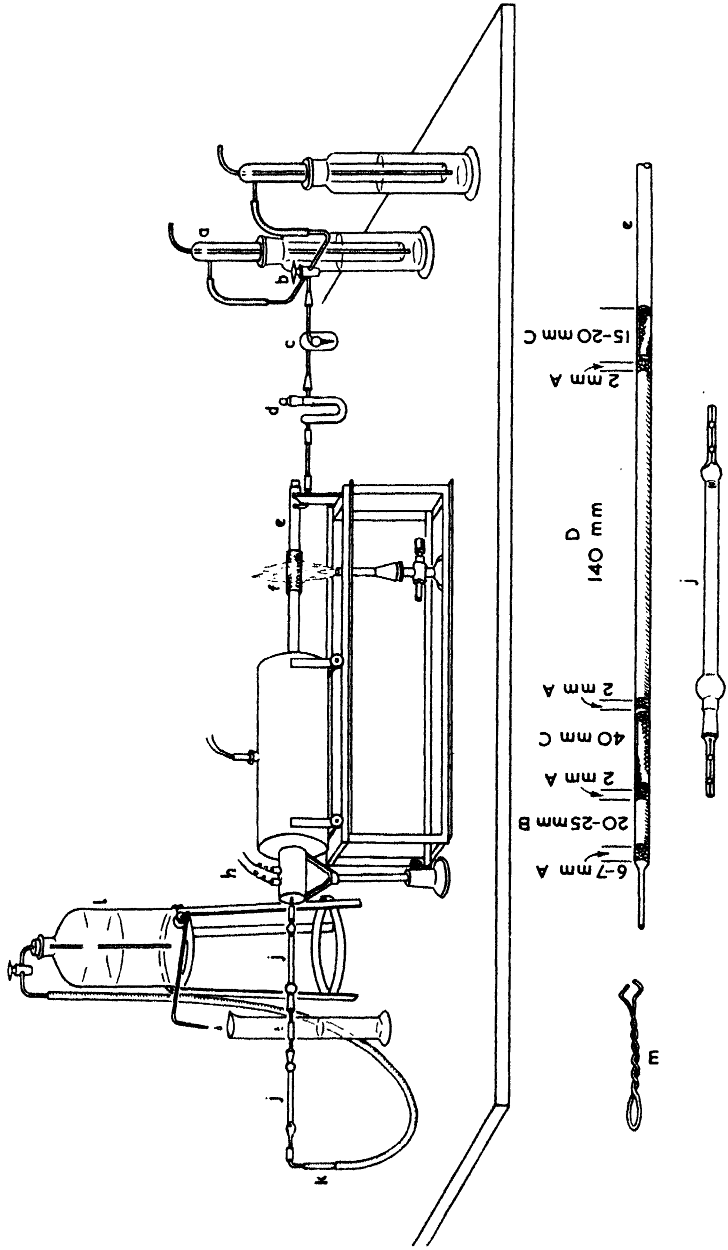

a
b
c
d
e
f
h
i
j
k
l
m
6-7 mm A
20-25 mm B
2 mm A
40 mm C
2 mm A
D
140 mm
2 mm A
15-20 mm C
e
j

FIG. 59.

(2) Lead dioxide pellets made as follows are satisfactory. Black M.A.R. lead dioxide is digested with fuming nitric acid in a porcelain basin on the water bath for about two hours, adding small amounts of acid to keep moist. It is then evaporated to dryness, transferred to a bottle, and shaken with distilled water, allowed to stand, and the water decanted off, more distilled water added, the contents shaken, and the lead dioxide filtered off on a suction filter. It is washed until nitric acid free as shown by diphenylamine-sulphuric acid indicator, pressed firmly to form a cake, washed with a little hydrogen peroxide, then with 1% sodium silicate solution, dried in an oven at 120° and cut into 1–1·5 mm. cubes. It is then transferred to a bottle and rotated slowly to remove the sharp edges (see also Pregl, Grant, p. 44).

Friedrich Filling.—The choking plug is as described for the Pregl filling. Next comes the lead dioxide placed in a boat, followed by the platinum contacts consisting of two specially-designed platinum cylinders, each about 70 mms. long and fitting closely into the tube. Sometimes the lead dioxide is preferred as in the Pregl filling. Though the advantage of ease of replacement is lost, this is largely compensated by the longer activity of the lead dioxide.

If the substance for combustion is rich in nitrogen, it is advantageous to increase the length of the lead dioxide, and/or to introduce a bubbler of the spiral type containing chromic acid (potassium dichromate + conc. sulphuric acid) between the two absorption tubes.

If the substance is nitrogen-free lead dioxide may be omitted aud the tube filled with a plug of asbestos as before, a silver spiral (10–15 mms. long), four equal sections (50–60 mms. long) filled with platinised asbestos and copper oxide in sequence (sections being separated by asbestos plugs) and a platinum or silver spiral (10–15 mms. long). (See also Niederl and Niederl, p. 108).

Heating Mortar (Fig. 59 (*h*)).—Lead dioxide introduces serious errors since it absorbs varying amounts of water depending on the partial pressure and the gas temperature. Consequently errors are minimised by keeping the dioxide at the same temperature throughout all estimations. Originally this was done by means of the heating mortar, a specially-designed piece of apparatus, which surrounds that part of the tube containing the lead dioxide, and which consists of a hollow mortar filled with a liquid such as dekalin (B.P. 189°) or *p*-cymene (B.P. 175–178°), kept refluxing (see Mikrochemie, 1931, 123; 1934, 263). This mortar is now replaced by an electrically-heated unit thermostatically controlled to within 1° C. and operated at 189°. Inserted in an opening in the mortar is a copper rod about 60 mms. long and 3 mms. diameter, to the end of which is soldered a copper bar in the form of a hook, 3 mms. wide. This hook is placed over the capillaries during combustion and the heat conducted assists in preventing condensation of water. See also J. S. C. I., 1939, 117, for a mortar filled with mercury and heated electrically.

Absorption Tubes (Fig. 59 (*j*)).—The carbon dioxide tube consists of a cylindrical thin-walled glass tube, 130–140 mms. in length and 8–9 mms. internal diameter. One end of the tube is constricted to a double capillary, each capillary 4–5 mms. long and 0·25 ± 0·05 mm. internal diameter, the total length of the constriction being 30–32 mms. and external diameters

3·25 ± 0·25 mms. About 10 mms. from the end there is a fused-in diaphragm in the centre of which is a hole 0·25 ± 0·05 mm. wide. A chamber is thus formed and the water produced during combustion slowly diffuses to the absorbent. At the other end there is a ground-in glass stopper carrying a doubly-constricted capillary similar to that described. The water-absorption tube is similar or may be 10 mms. shorter. For designs of absorption tubes, see Z. a., 1926, 720 ; Mikrochemie, 1932, 329 ; 1935–36, 23 ; 1937–38, 285 ; 1938, 65.

Anhydrous magnesium perchlorate is preferred to calcium chloride for the absorption of water. The filling of the tube is similar to that for the absorption of carbon dioxide, except that either of the above desiccants replaces the soda-asbestos. If calcium chloride is used, it is advisable to pass carbon dioxide through it until all the air in the tube is displaced, and. by closing the open end, to allow to stand under presssure for ten minutes, The carbon dioxide is displaced by air or oxygen before weighing.

For the absorption of carbon dioxide, soda-asbestos (ascarite, carbosorb) or soda lime is used. First, a loose pad of cotton wool, 3–5 mms. thick is placed on the diaphragm. Two or three larger pieces of anhydrous magnesium perchlorate (anhydrone) or calcium chloride are introduced, then a loose pad of cotton wool 3–5 mms. thick, the rest of the tube being filled with carbon dioxide absorbent. A small pad of cotton wool keeps the filling in place.

The stoppers of both absorption tubes are fixed with Krönig cement,the surplus of which is scraped away with a pointed stiff wire, and the last traces removed by cotton wool moistened with benzene. When not in use, the ends of the tubes are closed with rubber tubing and glass rods.

Cleaning and Weighing of Absorption Tubes.—In the Pregl method, the tubes are held in a clean, damp cloth, and the constriction rubbed with cotton wool affixed to the end of a roughened wire. The tubes are then rubbed with moist flannel, and wiped similarly with clean, damp chamois. Each is placed on a metal stand for 10 minutes, then removed to the hooks of the balance by means of the fork (*m*), and weighed accurately, using a counterpoise, on the 15th minute after completing the wiping. The same procedure is adopted with the tube before and after combustion. In order to obtain the weight of the tube at the 15th minute, the interval from the 11th to the 14th minute is spent ascertaining the weight within 1 division on the rider scale, and the balance set swinging at the end of the 14th minute. Readings of the swings are taken some seconds before and after the 15th minute.

Alternatively, the use of cotton or chamois gloves, chamois fingers, or special forceps for handling the tubes eliminates the wiping procedure once the initial wiping and cleaning have been done. The cleaning of the ends covered by the rubber tubing, and light brushing of the whole tube with a marten hairbrush are all that are now necessary. This covering of the fingers avoids the use of the special fork (*m*) otherwise necessary for transferring the tubes from the stand to the balance.

Note.—These special forceps (Fig. 59B) are made from ordinary weighing forceps by soldering on to each limb a half section of a brass tube 15 mm. long and 10–12 mms. diameter. Each section is lined with chamois, affixed with Krönig Cement.

Mariotte Bottle (Fig. 59 (*l*)).—This is not absolutely necessary but its use is strongly recommended as it serves the following purposes; calibration of tube and bubbler or flowmeter, detection of leaks, slow aspiration of gas through freshly-filled tubes, estimation of gas velocity, measurement of the 100 mls. gas used during the combustion. Furthermore, it allows a small suction to be applied during the combustion and obviates back-flow of material or gas beyond the gas burner.

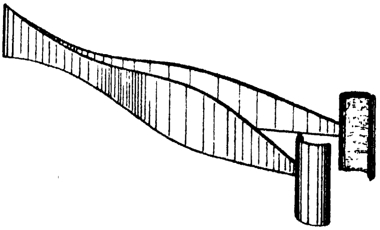


FIG. 59B.

The Mariotte bottle is attached by about 200 mms. artificially-aged rubber tubing (see below) to a thin-walled calcium chloride tube (*k*), 110–120 mms. long, and 11–12 mms. external diameter, one end of which is drawn out to a tube 5 mms. external diameter, and bent at right angles to form a limb 30–35 mms. long. About 10 mms. from this end of the tube there is a diaphragm with a hole at its centre and fused in to form a small chamber. The other end of the calcium chloride tube contains a one-holed impregnated rubber stopper through which passes a tube similar to that at the other end. It is attached to the carbon dioxide absorption tube by a 25 mm. length of wax-impregnated rubber tubing.

Rubber Tubing.—The treatment of rubber tubing is of the utmost importance (Mikrochemie, 1928, 133; Pregl, Grant (p. 39)). Artificial ageing (Z. a., 1923, 481) is done as follows: new rubber tubing (wall thickness 1·0–1·2 mm. and bore 3·4–4·0 mms.) is immersed in 40–50% caustic potash solution at 60° for 2 hours, and steam passed through the tubing thereafter for 2 hours.

The aged rubber used to connect the water absorption tube to the combustion and the carbon dioxide absorption tubes is thick-walled (external diameter 8 mms., bore 2·0–2·5 mms.). Lengths of 20 mms. and 25 mms. are cut, placed in white molten paraffin wax in a flask which is then evacuated on a good pump. When foaming ceases, air is allowed to enter slowly. The molten wax is thus forced into the interstices of the rubber. Evacuation and readmission of air are repeated until no more bubbles appear under vacuum. The tubing while warm is drained from wax, surplus of which is removed (*a*) from the outside by wiping with cotton wool and (*b*) from the inside just before use by wiping first with benzene-damped cotton wool attached to a roughened wire and then with undamped cotton wool similarly attached.

Weighing of Substance.—This is done directly into a platinum boat whenever possible. A volatile solid or liquid is weighed in a capillary tube; a solid in a capillary tube into which fits a thin glass rod. The substance to be weighed, if solid, is pressed into the capillary either by a spatula or by pressing down the tube on to the powdered solid. The outside is wiped and the capillary inserted into another capillary closed at one end, to which is attached a glass rod to serve as a handle. At this closed end a bead of fused potassium chlorate is placed. The thin glass rod then serves as a ramrod, and the substance is ejected into the second capillary. The rod is partially withdrawn and the first capillary and rod removed carefully. The tube containing the substance is gently heated at the open end and drawn out. For liquids the procedure is as above but the thin rod is unnecessary. Glass capillaries are completely surrounded with a protective roll of copper gauze or platinum foil before insertion into the combustion tube. (See also *Quantitative Organic Micro Analysis*, Pregl; Mikrochemie, 1938, 47, 167.)

Course of Analysis.—The balance door is opened for half an hour before weighing in order to attain atmospheric equilibrium. During this period the large furnace is switched on, if electric, or lit, if gas is used. The bubbler or flowmeter is adjusted and oxygen turned on. The small gas burner is lit and that portion of the tube from the side-arm to the filling carefully heated, making use of the short wire gauze (*f*) to remove any moisture. This gas is turned off, and while that portion is cooling, the absorption tubes are carefully cleaned and wiped with damp flannel and chamois, and placed on a stand near the balance case for 10 minutes. At the end of the 9th minute, the water absorption tube is placed on the balance hooks and weighed on the 15th minute (see p. 462). The same procedure is followed in the case of the carbon dioxide tube. While the tubes are on the stand the substance for analysis is weighed. Each tube, after weighing, is placed on the stand, and carried to the combustion apparatus. The absorption tubes are joined head to head and glass to glass, by the 15 mms. length of waxed rubber tubing, and attached to the snout of the combustion tube by the 20 mms. length of rubber tubing. Waxed rubber tubing prior to use should be moistened on the inside with a little glycerine carried on cotton wool round a roughened wire, the excess being removed by cotton on a wire. The oxygen is turned off by rotating stop cock (*b*), the cork removed from the mouth of the combustion tube, and the platinum boat containing the substance carefully transferred by platinum-tipped forceps to the combustion tube, gently pushed with a clean glass rod to a position 30 mms. from the filling, the cork replaced and the oxygen turned on. The apparatus is now tested for air-tightness, by raising the side arm of the Mariotte bottle to the perpendicular or by turning the stop cock on top of Mariotte bottle. Any leak is indicated in the bubbler or flowmeter. When the apparatus is leakproof, the combustion is carried out as follows.

The Mariotte bottle is disconnected and the levels of its arm and internal tubes adjusted to give a slight suction. The apparatus is then reconnected to the bottle and the oxygen flow adjusted to give 4 mls. per minute. The movable gauze (*f*) heated by a full but barely luminous flame is brought up to the end of the boat. The heat, transferred slowly from the wire gauze, gently vaporises the substance. The gauze and the burner are slowly moved towards the snout end of the combustion tube about 2 mms. at a time, and the substance thus vaporised into the heated portion of the tube. This initial combustion should take 10–15 minutes, and when completed combustion is continued until a further 100 mls. of air or oxygen, as measured in the measuring cylinder, have passed through. Carbonaceous residues which are deposited from certain substances on the cooler parts of the tube are readily removed by moving the furnace to the right about 1–2 cms. This brings the deposit into the hot part of the furnace. During the passage of the first 40 mls. of the additional air or oxygen those parts of the tube, behind, under, and in front of the boat, are heated to ensure complete volatilisation of the substance, and the movable burner then removed.

Meanwhile care is taken to ensure that no moisture condenses in the capillaries of the tube or water absorption tube. This is done either by placing the hot copper hook (p. 461) attached to the heating mortar on the capillaries, or by heating the tips of tongs and applying them to the capillaries. A length of platinum or silver wire introduced into the end capillary seems to prevent condensation of water.

When 100 mls. of water have collected, the combustion is stopped by raising the arm of the Mariotte bottle to the perpendicular or by closing stop cock on top of Mariotte bottle, detaching the absorption tubes and placing them on the stand. They are then wiped and weighed as before.

Calculation.

$$\%\ \text{Hydrogen} = \frac{\text{Wt. of } H_2O \times 2{\cdot}016 \times 100}{\text{Wt. of sample} \times 18{\cdot}016}.$$

$$\%\ \text{Carbon} = \frac{\text{Wt. of } CO_2 \times 12 \times 100}{\text{Wt. of sample} \times 44}.$$

In a later development (Chem. Fabrik, 1934, 7, 63; Mikrochemie 1943, 31, 149) the principal features are the automatic moveable heater and the automatic wiper for cleaning the absorption tubes before weighing.

Determination of Nitrogen

Micro Dumas Method.—The principle of the method is that the substance containing nitrogen is oxidised in an atmosphere of nitrogen-free carbon dioxide, by means of copper oxide, with metallic copper present to reduce any oxides of nitrogen. The nitrogen produced is collected in a graduated precision micro-azotometer.

Various forms of apparatus and procedures have been suggested to eliminate sources of error which arise mainly from impurities in the carbon dioxide. See J. Eng., *Anal. Ed.*, 1931, 202; 1931, 151; 1932, 440; 1944, 344; *Semi-micro Quantitative Organic Analysis*, Clark, 45–47; *Semi-micro Quantitative Organic Analysis*, Belcher and Godbert; Tucker, The Analyst, 1939, 610; J. C. Ed., 1942, 320; H. Acta., 1939, 1088. A recent development is the use of solid carbon dioxide, J. Eng., *Anal. Ed.*, 1937, 303; 1941, 574; 1943, 476.

Potassium Hydroxide Solution.—50% potassium hydroxide solution is used and it is absolutely essential that the surface of this solution in the azotometer should be free from foam. This can be achieved by dissolving 100 gms. potassium hydroxide in 100 mls. water, adding 1 gm. barium hydroxide, shaking for a few minutes, and passing carbon dioxide for 30 seconds. After a few days, the potassium hydroxide may be decanted from the barium carbonate and used or suitably stored.

The Precision Micro-Azotometer (Fig. 60 (*g*)).—This is a micro modification of the usual type with necessary refinements, the most important of

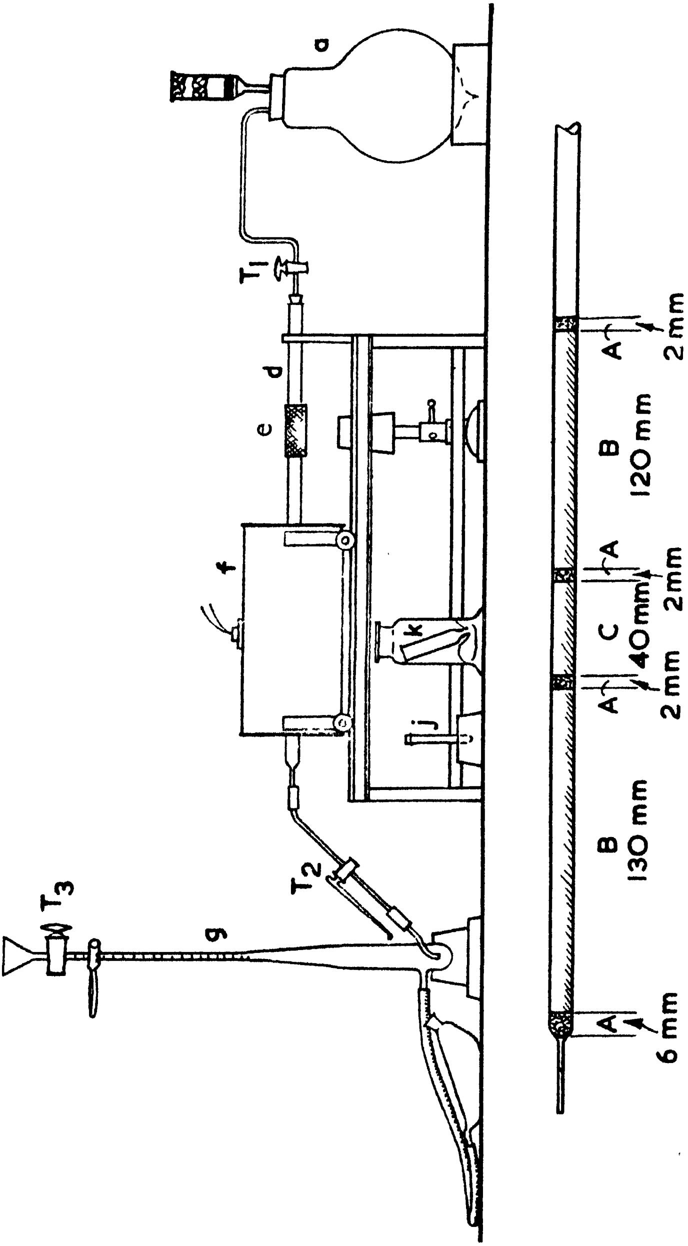


FIG. 60.

which is the long-handled stop cock with groove, which connects the azotometer to the combustion tube. For standard design, see J. Eng., 1941, 574; 1943, 476. Few alterations or improvements have been suggested on the azotometer as described by Pregl, a detailed description of which is given in his and other text-books (p. 457), but a decided improvement in design which prevents the collection of nitrogen bubbles on the surface of the mercury consists in extending the side arm capillary below the surface of the metal.

An azotometer in which the caustic potash does not come in contact with the rubber tubing is described in Chem. Fabrik 1943, 154.

The scale is generally 1·3–1·5 ml. and is graduated in hundredths, the marking round the stem making it possible to estimate the third decimal place. Readings are taken with the aid of a movable lens.

Combustion Tube Fig. 60 (*d*).—This is made of Supremax glass, Monax combustion glass or clear silica. It is 520–530 mms. long, 11·25 ± 0·5 mms. external diameter, and 8 ± 0·25 mms. internal diameter, and is provided with a snout 30–35 mms. long, 3·25 ± 0·25 mms. external diameter, 1·5–2·0 mms. internal diameter.

A wad of freshly-ignited purified asbestos (A) is pushed up to the neck with a glass rod and compressed to about 6 mms. Some analysts prefer this pad to be so packed that it allows only 2–4 bubbles to pass per second. This assists adjustment of the carbon dioxide flow later in the combustion and avoids a sudden rush of gas. Freshly-ignited wire-form copper oxide (B) (size 4–5 mms.) to a length of 130–140 mms. is introduced, carefully packed by rotating the tube when inclined slightly from the horizontal, and kept in place by a loose pad of freshly-ignited asbestos. There follows a 40 mms. length of wire-form copper (C), prepared by reducing the oxide in a separate loosely-packed tube, with hydrogen, purified by passage through aqueous potassium permanganate. When cold, the metallic copper is transferred to the combustion tube, and any slight superficial oxidation which takes place during the transference is removed by heating in a current of purified hydrogen for a short time. An alternative method reduces a 40 mms. length of the copper oxide *in situ* in the combustion tube with hydrogen similarly purified but passed in the opposite direction in order to prevent choking of the snout with water. This metallic copper is kept in place by another pad of loosely-packed asbestos. A 120 mms. column (B) of medium-sized copper oxide follows. This completes the permanent filling which is renewed only when necessary.

It is advisable before using the tube to heat and cool this filling three times in a current of carbon dioxide and finally to store it in an atmosphere of this gas.

This permanent filling is followed by a temporary removable filling (length approx. 30 mms.) of coarse copper oxide wire, and by copper oxide containing the substance (see later).

Apparatus (Fig. 60).—A convenient arrangement is shown. Solid carbon dioxide is powdered and packed very tightly into an ordinary thermos flask or insulated Dewar flask (*a*) fitted with a mercury valve (Fig. 61) which is built into a sintered glass funnel 60 mms. long and 10 mms. wide, and consists in sequence, of the sintered filter disc, a layer of mercury, an air space 20–30 mms. high, a plug of cotton wool, an intimately mixed layer of iodine and charcoal, and finally a plug of cotton wool. After a few hours micro bubbles to fulfil the requirements (*Quantitative Organic Micro Analysis*, Pregl, p. 67) are obtained in the azotometer (*g*). Excess carbon dioxide escapes into the atmosphere through the valve. Using an ordinary thermos flask, the solid carbon dioxide normally requires renewal daily but a Dewar flask holds sufficient to last a week or more. The furnace (*f*) is electrically-heated and the temperature of the copper oxide filling is ascertained by a previously calibrated thermo-couple. A temperature of 650°–700° is best.

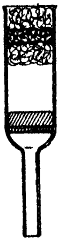


FIG. 61.

Weighing of Substance.—About 2–5 mgms. of substance, generally sufficient to give 0·3–0·5 ml. nitrogen in the azotometer, are used. Adjustments in the amount taken are made depending on the percentage of nitrogen.

If solid, the substance is weighed in a weighing tube with a long or short handle. These tubes are easily made from a thin soft glass tube, 20–25 mms. long, and 2–3 mms. internal diameter, closed at one end, fused to which is a solid glass handle 50 or 130 mms. long and 1·5 mms. diameter. The substance is introduced into the tube, carefully tapped to the bottom, the outside cleaned with chamois, the tube placed on the hooks of the balance pan, and weighed using a counterpoise. The tube is then removed from the balance using gloves or chamois fingers, its mouth carefully introduced into a cleaned mixing tube (*j*) (a sodium fusion tube serves the purpose), and by careful tapping, sufficient substance is transferred, and the tube reweighed. The mixing tube is now half-filled with dry copper oxide by scooping the oxide from a metal tray on which it has been ignited and cooled, fitted with a clean non-porous cork, and shaken vigorously to obtain intimate mixing. A layer (10–20 mms.) of copper oxide is now introduced into the combustion tube, again by scooping from the tray, the contents of the mixing tube transferred to the combustion tube through a filling funnel, and the mixing tube and funnel washed out three times with copper oxide. The copper oxide scooped from the tray and used in washing the funnel is prepared from the copper oxide wire previously mentioned by breaking in a mortar.

If the substance is a non-volatile liquid or adheres to the sides of the mixing tube it may be weighed directly into a platinum or porcelain boat, covered with very fine copper oxide, and the whole transferred to the combustion tube, into which a layer (10–20 mms.) of fine copper oxide has been previously introduced. 20–30 mms. fine copper oxide followed by 20 mms. coarse copper oxide complete the filling.

Liquids are weighed in a capillary by the method described on p. 463.

Course of Analysis.—The combustion tube is slipped through a loosely-fitting cylindrical wire gauze (*e*) 40 mms. long, and into the furnace (*f*), so that the neck protrudes 40 mms. It is attached to the carbon dioxide apparatus through a rubber stopper impregnated with wax.

Tap T_1 (Fig. 60) is opened full, and carbon dioxide passed for three to four minutes to displace all air from the tube. The furnace is then switched on, and when the required temperature is attained, as shown by the thermocouple, the combustion tube is attached to the long-handled connection of the azotometer by a 25 mms. length of thick wax-impregnated rubber tubing. Taps T_1, T_2 and T_3 are all opened for a few seconds to expel air in the azotometer side arm, after which tap T_2 is closed and the azotometer filled with the potash solution by gently raising the reservoir slightly above the level of the top of the tap T_3, closing tap T_3, and placing the reservoir on the bench. Tap T_2 is then opened carefully and adjusted to allow a speed of 2 to 4 bubbles per second. By this time the tube should be at a red heat. As soon as micro bubbles are obtained (a bubble may be considered sufficiently small when it takes more than 30 seconds to ascend the height of the azotometer), tap T_1 is closed, tap T_2 is fully opened and the short length of wire gauze (*e*) placed so that its end is just over the copper oxide layer behind the substance while the gas burner with flame just non-luminous is placed under the middle of the gauze. An increase in bubble frequency is soon apparent, but when this slackens, the reservoir is raised as before, tap T_3 opened, any foam expelled, tap T_3 closed, and the reservoir replaced on the bench. The small roll of gauze and burner are now pushed forward slightly and this movement continued, care being taken that the bubble frequency at no time exceeds 2 bubbles every 3 seconds, until the gauze and burner reach the furnace. At this stage the bubble frequency falls and the mercury in the well of the azotometer may suck back slightly. Tap T_2 is then closed, T_1 opened, and T_2 carefully opened and adjusted to allow a frequency of 2 bubbles every 3 seconds. Great care is necessary in opening the long-handled stop cock T_2 as any sudden rush of gas leads to high results. During this sweeping-out process, the tube is similarly heated again in front of, under, and behind the fine copper oxide. As soon as the bubbles begin to decrease in size, the electric furnace is switched off and the bubble frequency increased. When the bubbles are again micro in size tap T_2 is closed and the azotometer removed to a suitable place. After 15 minutes tap T_2 is opened and the volume of nitrogen at atmospheric pressure read in the usual way, the temperature registered by a thermometer suspended from tap T_1 being also noted.

It has been confirmed that the volume of nitrogen collected is about 2% in excess of the theoretical, arising mainly from air retained by copper oxide in the removable or temporary filling (1·2%) adherence of caustic potash solution to the wall of the azotometer (0·5%) and vapour tension of caustic potash solution (0·3%). This 2% deduction is made before calculating the results and is accurate so long as the volume of nitrogen collected is between 0·3 and 0·5 ml.

$$\%\ \text{Nitrogen} = \frac{V \times W \times 100}{\text{Wt. of substance in mgm.}}$$

where V = corrected vol. of nitrogen, W = wt. of 1 ml. nitrogen at $t°$ and p mm. pressure. (See Table, p. 524).

Micro-Kjeldahl Method (Fig. 62).—The principle of the method is the decomposition by conc. sulphuric acid, generally with the aid of a catalyst, of the nitrogen-containing substance, whereby the nitrogen is quantitatively converted into ammonia. The ammonia is then liberated by alkali, steam-distilled, absorbed in standard acid and back-titrated with standard alkali. Standard boric acid may be used for the absorption of the ammonia. Instead of methyl red as indicator a mixture of bromcresol green (10 pts.) and methyl red (1 pt.) is recommended (J. Eng., 1942, 280). With substances of low nitrogen content the titration of the excess acid may be done iodometrically using potassium iodide/iodate.

Mercury, selenium, copper, various mixtures of these and their salts and perchloric acid have been recommended as catalysts. (Mikrochemie, 1938, 145 ; 1942, 760, 914.)

The scope of the method has been widened by Friedrich (Z. Physiol. Chem., 1933, 88) who introduced the now standard procedure of reducing with hydriodic acid and red phosphorus before combustion.

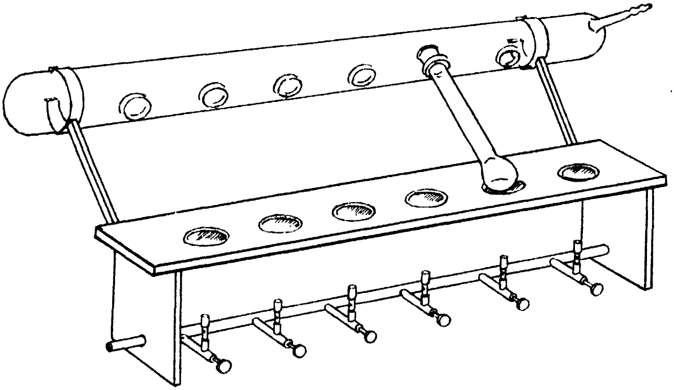


FIG. 62.

Generally a battery of six digestors (Fig. 62) is used, enabling several digestions to be carried out at the same time. After digestion (see later), steam is generated in the glass vessel (Fig. 63, (*A*)), passed through the trap (*B*), into the distilling flask (*C*) (originally the digestor), driving the ammonia through the silvered condenser (*D*) into the flask (*E*) which contains the standard acid.

Course of Analysis.—About 2–4 mgms. of the substance are weighed directly into the digestion flask by means of a long-handled weighing tube, 1 ml. iodine-free hydriodic acid (D. 1·7) is run down the walls and a few mgms. red phosphorus added. The flask is heated on the digestor stand (Fig. 62) and gently boiled for 30 minutes, after which the neck of the flask is washed down with distilled water until the bulb is half-full. 2 mls. conc. sulphuric acid are carefully added, the mixture shaken gently, the flask placed on the stand and boiled vigorously until the hydriodic acid, and iodine are completely boiled off. This takes about 30 minutes. A little mercuric acetate (about 10 mgms.) or other selected catalyst and 30–40 mgms. potassium sulphate are added and the contents boiled for 30 minutes, cooled and diluted with 2–3 mls. water.

Meanwhile the distillation apparatus and silvered condenser have been steamed out. A quartz flask (*E*) containing 8 mls. (or a suitable volume) standard N/100 acid and a drop of methyl red indicator is so placed that the condenser tube is well immersed in the acid. The digestion flask is now connected, the attaching springs (*G*) fixed, and 15 mls. 30% sodium hydroxide solution added to the flask through the funnel (*F*) to make the contents alkaline. Both spring clips are closed, and steam is admitted to the solution at once. Distillation is continued for 7–10 minutes after which the receiver stand is lowered until the condenser tube is 2 cms. above the surface of the acid and the tube washed with 2 mls. water. The flask is then removed, the contents boiled for one minute, and titrated, using a micro burette, see Pregl, Grant, p. 29.

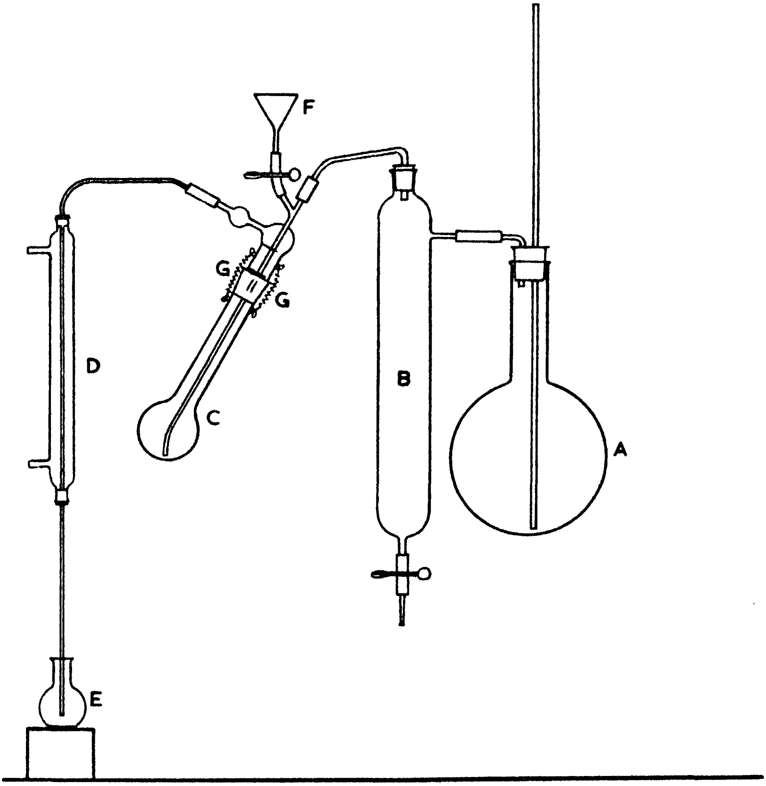


FIG. 63.

Micro-Kjeldahl apparatus with ground glass joints throughout is now available.

Calculation.

1 ml. N/100 acid = 0·14 mg. nitrogen.

Hence,
$$\% \text{ Nitrogen} = \frac{(\text{ml. N/100 acid used} \times 0{\cdot}14 \times 100)}{\text{Wt. of substance in mgm.}}.$$

Determination of Halogens

Chlorine and bromine are usually determined by Pregl's catalytic combustion in a spiral or bead tube, by a micro adaptation of the Carius method, or by the alkalimetric method of Zacherl and Krainick (Mikrochemie, 1932, 61) when the substance is decomposed in a current of hydrogen, with conc. sulphuric acid in the presence of potassium dichromate and silver dichromate. Iodine, though capable of determination by these methods, is usually done by Liepert's titrimetric method (Michrochimica Acta., 1938, 147). See also *Organic Quantitative Micro Analysis*, Niederl and Niederl, p. 118, for various improvements in technique; Rauscher, J. Eng., *Anal. Ed.*, 1937, 296, for a description of a micro-Stephanow method and Beazley (ibid, 1939, 229) for the use of a two-piece tube with a ground glass joint between the heated and unheated spiral portions, and Burger, Ang. Chem. 1941, 479 ; Die Chemie 1942, 245, for a method by fusing with potassium in a sealed tube.

For titrimetric methods for chlorine and bromine, see Z. Anorg. Allgem. Chem., 1924, 221 ; Am. Soc., 1930, 3273 ; J. Eng. *Anal. Ed.*, 1935, 178 ; 1946, 719.

Pregl's Catalytic Combustion Method (Fig. 64).—The principle is one of combustion in a slow current of oxygen over red-hot platinum contacts, and absorption of halogen by passage over a glass spiral or glass beads moistened with sodium carbonate solution containing sodium bisulphite. The halogen is estimated gravimetrically as silver halide.

The combustion tube is of Supremax glass or clear silica, 730 ± 10 mms. long, 1·5 mms. wall, and 7·75–8·25 mms. internal diam. One end of the tube is drawn out to a thick-walled snout 20 mms. long and 5–7 mms. diameter with the orifice 0·5–0·6 mm. diameter. This fine opening is necessary to allow the washings to drain out slowly, thereby facilitating complete removal of the products of combustion. A glass spiral (B) (or column of glass beads) fills the tube for 200 mms. and is kept in position by an indentation therein. This part of the tube is not heated, and is about 40 mms. distant from the furnace. Two platinum contacts (A) follow, 20 mms. apart, the nearer being 60 mms. from spiral. These contacts are specially designed perforated cylinders about 70 mms. in length. Before use, they are boiled in dil. nitric acid and heated to redness in a bunsen flame.

The other end of the combustion tube contains a well-fitting rubber stopper, through which passes a thick-walled capillary, joined to a bubbler U-tube (*e*) or a flowmeter, which, in turn, is attached to a wash bottle (*f*) containing a saturated dilution of sodium carbonate. The wash bottle is directly secured to the oxygen supply, either a cylinder fitted with a good reducing valve or a gas holder.

Filtration Apparatus (Fig. 64 (*C*)).—For the filtration of the halide precipitate, a wide-mouthed suction flask (*l*) is fitted with a one-holed rubber stopper, carrying an 80 mms. length of glass tubing (*k*), 8 mms. bore. The upper end of this tube is fitted with a clean, tightly-fitting, one-holed rubber stopper, through which passes the limb of the filter tube (*j*). This special tube is 150 mms. long, the limb being 100 mms. long, 3–4 mms. external diameter, and expanding to form a tube 45 mms. long, and 10

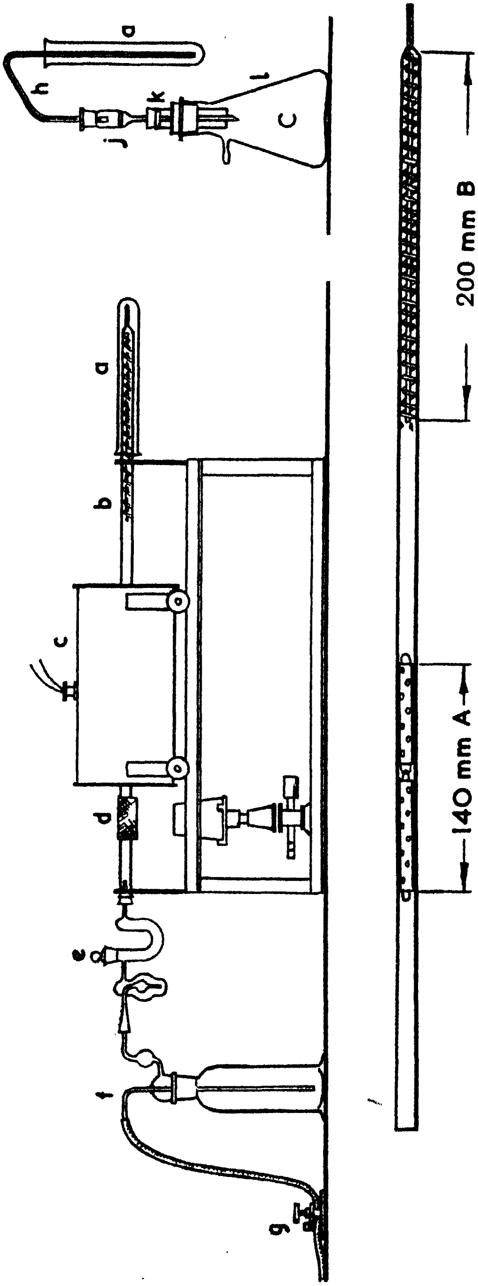


FIG. 64.

mms. diameter, 2–2·5 mms. internal diameter at the bottom of which is a sintered glass filter 1·5–2 mms. thick. This filter is covered with a 2 mms. layer of specially purified asbestos. The upper part of the filter tube is fitted with a rubber stopper, through which passes the shorter limb of the siphon (*h*), a glass tube 1·5–2 mms. bore. This tube is bent at an angle slightly less than a right angle, and 100 mms. farther along is bent again forming a limb 250 mms. long and parallel to the shorter limb. The end of this limb dips to the bottom of the test-tube (*a*) containing the precipitated halide, and on applying suction to the flask, the precipitate is deposited on the asbestos of the filter pad.

Before fixing the filter tube in position, it is dried in a current of air at 120° until constant in weight. The drying is carried out in a drying or regenerating block, which consists essentially of two superimposed copper or brass sections, each cut with two superimposable half holes, forming when assembled two holes into which the narrow limb, and the wider part of the filter tube fit. The lower section is heated by a micro burner to 120° registered on a thermometer inserted into a hole in this section. The filter tube is fitted with an air filter, made from glass tubing packed with cotton wool. The other end is attached to the suction pump and air slowly drawn through. When cool, the tube is wiped with chamois, and weighed with the usual precautions, see p. 462.

Course of Analysis.—The combustion tube and a wide-mouthed test tube (*a*) are first cleaned with warm chromic acid (conc. sulphuric acid plus potassium dichromate), thoroughly washed with distilled water, drained and dried. The spiral *B* (or beads) is then moistened with a solution containing three drops of saturated sodium bisulphite per 2 mls. saturated sodium carbonate solution, sucking the solution from the test-tube to the top of the spiral, allowing it to drain back slowly and then blowing out the residue from the tip. This solution is then discarded, and the test tube placed over the snout end of the combustion tube, after which this is positioned in the furnace, so that the nearer end of the spiral (*b*) is not less than 40 mms. distant from the furnace (*c*), the open end closed by a stopper and a movable roll (40 mms.) of gauze (*d*) placed round the tube. The stopper is then removed, the cleaned platinum contacts placed in position, and the platinum boat (or open capillary) containing the substance (5–10 mgms.) placed about 50 mms. from the first contact (*A*). The oxygen supply is then connected and turned on at the rate of not more than 4 mls. per minute, measured as described under carbon and hydrogen determination (p. 459). The furnace is then switched on, and when the platinum contacts are red hot as shown by the thermocouple, combustion of the substance is begun, which is exactly as described for carbon and hydrogen but should take not less than thirty minutes. The bunsen and the furnace are then shut off and the tube allowed to cool in a current of oxygen.

When cold, the movable gauze, platinum boat and contacts are removed. The combustion tube with the test tube in position is withdrawn from the furnace and clamped just off the perpendicular, the snout projecting 40 mms. into the test tube. Two drops bisulphite solution are added via the wide end of the tube and the spiral (or beads) washed with pure distilled water. Two washings with 0·5% nitric acid follow, and the end and snout of the combustion tube are rinsed with distilled water, giving about 20 mls. in the test tube. Two drops perhydrol are added (*care!*) to oxidise the bisulphite, the test tube being immersed for five minutes to about 50 mms. in a boiling water bath, a clean inverted beaker protecting from dust. A solution of 1 ml. conc. nitric acid and 2 mls. 5% silver nitrate is carefully added to the hot solution, and the mixture heated for a further five minutes, after which precipitation is quantitative. The coagulated precipitate settles to the bottom, is cooled, and the test tube placed under the long limb of the siphon tube (*h*), slow suction being applied (rate about two drops filtrate per second). Care is taken that all particles of halide are removed by washing with alcohol (96%) and acidified water (0·5% nitric acid), alternatively.

When filtration is complete, the rubber stopper and siphon (*h*) are removed, the end washed with alcohol, the filter tube (*j*) filled with alcohol which is sucked through. Finally, the air filter is attached, the filter tube removed, dried and weighed as before.

Calculation.

Let a = wt. of substance in mgm.

b = wt. of silver halide in mgm.

$$\% \text{ halogen} = \frac{b \times \text{factor} \times 100}{a}.$$

Factor for Chlorine = 0·2474

,, ,, Bromine = 0·4255

Volumetric Determination of Iodine.

This method (Microchemica Acta, 1938, 78, 147) is essentially one of combustion similar to that described for chlorine and bromine. The iodine, however, is absorbed in caustic soda, oxidised to iodate by bromine, the iodine liberated by potassium iodide, and titrated with sodium thiosulphate.

Course of Analysis.—The apparatus and combustion procedure are the same as for Pregl's estimation of chlorine and bromine, except that the spiral (or beads) is moistened with 5% caustic soda solution. After combustion is complete and the tube cooled, the latter and the test tube are placed in a stand just off the perpendicular. Into the test tube are run 4 mls. 10% solution of sodium acetate in glacial acetic acid and two or three drops of bromine. This solution is sucked up to 10–12 mms. beyond the end of the spiral, held there and allowed to drain slowly into a conical flask fitted with a sunken ground-glass stopper (Fig. 66 (*n*)) and containing 5 mls. 20% sodium acetate solution. The combustion tube and test tube are then rinsed in the same way with 6 mls. water, and the rinsings run into the conical flask. The combustion tube and test tube are then rinsed via the mouth of the former with a further 6 mls. water.

To reduce the bromine, two or three drops of formic acid are added, followed by a drop of methyl red indicator. Absence of bromine is indicated by retention of the pink colour. 2 mls. 10% potassium iodide solution and 5 mls. N. sulphuric acid are added, the glass stopper inserted, the solution shaken, and after five mins. (in dark preferably), distilled water is poured round the glass joint, the stopper removed and it and sides of the flask washed with a fine spray into the flask. The liberated iodine is titrated with 0·02 N. sodium thiosulphate, using methyl red as indicator and titrating until a pale pink colour is obtained.

Calculation.

$$1 \text{ ml. } 0{\cdot}02 \text{ N. sodium thiosulphate} = 0{\cdot}4231 \text{ mgm. iodine}$$

$$\% \text{ Iodine} = \frac{\text{ml. thiosulphate solution} \times 0{\cdot}4321 \times 100}{\text{Wt. of substance in mgm.}}.$$

Determination of Chlorine and Bromine by Carius Method

This is essentially a small scale adaptation of the classical macro method, with obvious precautions required for micro procedure. The substance is treated in sealed tubes with conc. nitric acid in the presence of silver nitrate, and the halogen estimated as silver halide. The method is not suitable for volatile liquids or solids with high vapour pressure.

Pressure Tubes.—These can be made from halogen-free glass tubing, 10–20 mms. internal diameter with walls 1–1·3 mms. thick. Their length depends on the size of the furnace, but about 200–250 mms. is convenient, as several estimations can be done with the same tube. The tubes are cleaned with chromic acid mixture, washed thoroughly with distilled water, and dried in the oven at 115°–120°.

Furnace.—Any type of small-scale Carius furnace (see Fig. 40) can be used, though one electrically-heated and fitted with an automatic cut-off after five hours heating, is convenient. The sealed pressure tubes need not be enclosed in cast-iron cylinders, though such a precaution is desirable and if used the cylinders may be open at one or both ends.

Course of Analysis.—3–8 mgms. of the substance are weighed into the cleaned pressure tube using the long-handled weighing tube described in the estimation of nitrogen (p. 468) taking care that all the substance lies at the bottom of the tube. Liquids, if non-volatile, can be weighed directly using an open capillary, or in a micro weighing bottled fitted with a ground-glass stopper. About 10–25 mgms. pure silver nitrate crystals are added followed by 0·5–1·0 ml. halogen-free conc. nitric acid, allowing the acid to run down the sides of the tube from a micro pipette. Substances which evolve halogen acid readily on contact with nitric acid are weighed either in a weighing bottle fitted with a ground-glass stopper which is easily removed, or by the Friedrich method in hard glass tubes 15 mms. long, 3 mms. bore, sealed at one end.

Sealing the Tube.—A glass rod is first fused on to the open end of the pressure tube, using a small blow-pipe flame, then the pressure tube, at a slight slant, is heated, 10–20 mms. from its mouth, rotating the tube all the time, until the glass softens, collapses and fuses (see p. 48). On no account must the tube be drawn out until the glass is fully softened. The rod is then pulled and the tube is drawn out, cut, and the end rounded off in a small flame. If cooling is slowed down by covering the hot tube with a deposit of carbon from a non-luminous flame, the danger of cracking is lessened. When the tube is cool, it is inserted in the furnace and heated slowly to 280°–300° and maintained at this temperature for five hours. After cooling in the furnace, the tube is partially withdrawn at a slant from the furnace and any liquid in the capillary end removed by warming with a small non-luminous flame. The capillary end is then softened by heat so that the pressure inside blows a small hole in the tube. The tube is cut at this hole by scratching with a glass cutter away from each side of the hole to form a circle, wiping and applying a hot rod to the scratch. Great care is necessary to avoid glass splinters falling into the tube. The rough edges are then rounded off in a small blow-pipe flame. The precipitate, if coagulated to a ball, is broken up with a thin clean glass rod, and the rod washed with acidified water. The precipitate is then filtered off as described in the Pregl tube spiral method (p. 472) and the silver halide estimated.

Determination of Sulphur

This may be done (*a*) by catalytic combustion in a spiral or bead tube (Pregl), or in the Gröte apparatus as modified by Schöberl (Z. a., 1933, 103 ; 1937, 334), (*b*) by a micro modification of the Carius method in a tube or bomb. The sulphur is finally weighed as barium sulphate or estimated volumetrically (see text-books, p. 457 ; also Z. a., 1932, 401 ; J. Eng. *Anal. Ed.*, 1940, 53, 357, 360 ; 1946, 719 ; Analyst, 1935, 522 ; Ang. Chem. 1941, 479 ; Die Chemie, 1942, 245). Direct titration of sulphuric acid obtained in the catalytic combustion methods is possible if nitrogen and halogens are absent.

Pregl's catalytic combustion method, the apparatus for which is identical with that used (Fig. 64) for the determination of chlorine and bromine, is the most accurate and the most generally used. Combustion is carried out in oxygen in presence of platinum, the oxides of sulphur absorbed in perhydrol which oxidises sulphurous to sulphuric acid ; and this last isolated as barium sulphate.

The filtering apparatus (Fig. 65) is similar to that used for the determination of chlorine (Fig. 64*C*) but the filter stick is replaced by a micro Neubauer crucible (*a*) fitted with a lid and also with a capsule which protects the base during ignition. The crucible specified by Pregl is 14 mms. high while that specified by Royer *et al* (J. Eng. *Anal. Ed.*, 1943, 230) is 35 mms. high and is glazed black inside. Prior to each determination the crucible is cleaned inside with cotton wool wrapped round a piece of soft wood and washed several times with distilled water. The filter bed is composed of compressed iridio-platinum sponge on to which has been filtered a small amount of precipitated barium sulphate. Alternatively, Wintersteiner's automatic filtration method (J. Eng., *Anal. Ed.*, 1924, 14) may be used.

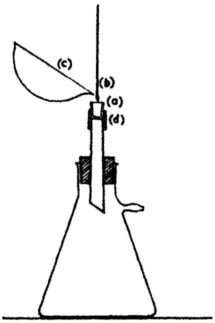


Fig. 65.

During the course of the determination the barium sulphate is transferred from the dish (*c*) to the crucible with the aid of a stiff feather ; a snipe feather sealed with Krönig cement into a glass capillary 120–150 mms. long, 20–25 mms. diameter and closed at one end is suitable. Excess cement is removed with benzene, and the feather washed with benzene, alcohol and ammoniacal soap solution—and finally with water—before use.

Course of Analysis.—This is conducted as described for chlorine (p. 472) except that the spiral is moistened with perhydrol and that the combustion tube and test tube when cold, after the combustion, are washed with 1% hydrochloric acid into a basin (*c*) 5–10 cms. diameter. This is preferably of platinum, but a good quality glass or Pyrex dish is satisfactory provided it has been well steamed out beforehand. About 40 mgms. barium chloride in the form of small crystals are added, the dish covered with a clean clock glass, convex side down, and the mixture evaporated to dryness on a water bath. The residue is treated with 1–2 mls. water, the clock glass washed with 1–2 mls. water into the dish, and the barium sulphate filtered into the crucible.

Preparation of crucible (*a*).—This, held in the moistened rubber collar (*d*) of the apparatus, is washed two or three times with 1% hydrochloric acid. After removal it is fitted with its lid and protective base, heated gently on a large platinum lid until dry, and then to redness for three minutes. After cooling somewhat it is removed to a copper or brass block in a desiccator until cold. It is then transferred by platinum-tipped forceps to the balance and weighed.

With its lid and base left in the desiccator, the crucible is inserted into the filtering apparatus. Without disturbing the precipitate, the clear supernatant liquor from the dish is decanted down the feather (*b*) held vertically over the centre of the crucible. When the crucible is full, gentle suction is applied and more decanted as the crucible empties until all the liquor has been transferred. The dish is rinsed with 1–2 mls. 1% hydrochloric acid, the precipitate stirred with the tip of the feather, and at once transferred to the crucible. The dish is washed with a few drops of water, and brushed from the edge to the centre with the feather, and the contents transferred to the crucible as before. On no account must the tip of the feather touch the top of the liquid in the crucible otherwise the precipitate will creep up the feather. In this connection pouring of the solution is facilitated if the edge of the lip of the basin is touched previously with the finger. A thin stream of alcohol is then used to wash out the residual barium sulphate, and the last traces are transferred with the aid of the feather, washing alternately with alcohol and water and finally with water. When washing is completed, the crucible is carefully removed, fitted with its lid and base, and dried and ignited as before. Washing, drying and igniting are continued until the loss in weight does not exceed 0·005 mgm.

Calculation.

$$\% \text{ Sulphur} = \frac{\text{Wt. of BaSO}_4 \times 32 \times 100}{\text{Wt. of sample} \times 233{\cdot}5}.$$

In Pregl's Carius method 3–8 mgms. of the compound are decomposed in a sealed tube at 270° for 5 hours with conc. nitric acid in the presence of finely-powdered barium chloride. Good quality Supremax or similar glass should be used, as results are liable to be high with ordinary glass due to the presence of silica. If the temperature is too high, results are sometimes low due to fusion of the barium sulphate to the glass.

The course of analysis is exactly as described for halogen (p. 474) except that barium chloride replaces silver nitrate. The tube is opened and the barium sulphate removed into a dish, and dealt with as already described. Should the substance contain both sulphur and halogen, it is heated in the sealed tube with silver nitrate and nitric acid, the halide filtered and estimated as described before, the sulphuric acid in the filtrate being estimated as barium sulphate.

Determination of Alkoxy Groups

This is based on the method of Zeisel (M., 1885, 989) in which the compound is refluxed with hydriodic acid whereby the alkoxy group is split off as alkyl iodide. The iodide is either absorbed in (1) alcoholic silver nitrate and the silver iodide estimated gravimetrically, or (2) a solution composed of bromine, glacial acetic acid, and sodium acetate (B., 1930, 3207) when the following reactions occur :

$$CH_3I + Br_2 \longrightarrow CH_3Br + IBr$$

$$IBr + 3H_2O + 2Br_2 \longrightarrow HIO_3 + 5HBr.$$

The sodium acetate neutralises the hydrobromic acid formed, and on addition of potassium iodide the liberated iodine is titrated with standard thiosulphate.

The apparatus (Fig. 66) is a modification of that described by Pregl adapted for volumetric estimation (see also Niederl and Niederl, p. 240). It consists of a spherical reaction flask (*a*), 20–25 mls. capacity, sealed to a condenser (*b*), 60 mms. long with internal tube 8 mms. diam. The side tube (*c*), drawn to a capillary 1 mm. internal diameter at its lower end, and fitted to (*a*) by a ground glass joint, serves for the introduction of a current of carbon dioxide. The washer (*defg*) is attached to the top of (*b*) by a ground glass joint, the bulb (*d*) being of 14 mms. diam., the spiral (*e*) fitting closely into the surrounding tube which is 55 mms. high and 8 mms. diam. The ground glass cap (*f*), held in position by rubber bands, is removed and replaced during the charging of the trap. The splash bulb (*g*), about 14 mms. diam., is attached to a perpendicular tube (*h*) open at both ends. This tube has a constriction (*i*) just above its junction to the side arm and is fitted at the top with a ground glass stopper. The tube (*h*) is attached to a receiver (*k*) 110 mms. long and 9 mms. diam., by a ground glass joint. Inside the receiver this tube (*h*) is surrounded by a glass spiral. The bottom of the receiver is narrowed to 2 mms. diam., bent up and then down to form a siphon, the end of which is attached by a ground-glass stopper and springs to a flask (*l*) of about 2 mls. capacity. A horizontal tube (*m*) having a ground-glass joint attached to the top of the receiver contains a small amount of cotton wool impregnated with formic acid which prevents escape of bromine vapour into the atmosphere.

The spiral in the receiver fits closely causing the carbon dioxide to ascend slowly, thereby ensuring the complete absorption of the alkyl halide.

The conical titration flask (*n*) of 200 mls. capacity, has a special ground-glass stopper with a handle, sunk to accommodate a water seal.

Course of Analysis.—The apparatus is thoroughly cleaned with warm chromic acid, washed with distilled water and dried. A drop of water, to act as a seal impermeable to alkyl halide, is placed above the constriction (*i*). One ml. 5% cadmium sulphate solution and one ml. 5% sodium thiosulphate solution are introduced via the side arm into the washer and the ground-glass cap (*f*) held in place by rubber bands. 2 mls. of a solution of glacial acetic acid containing 10% by weight of solid sodium acetate and 5 drops bromine are run into the receiver (*k*).

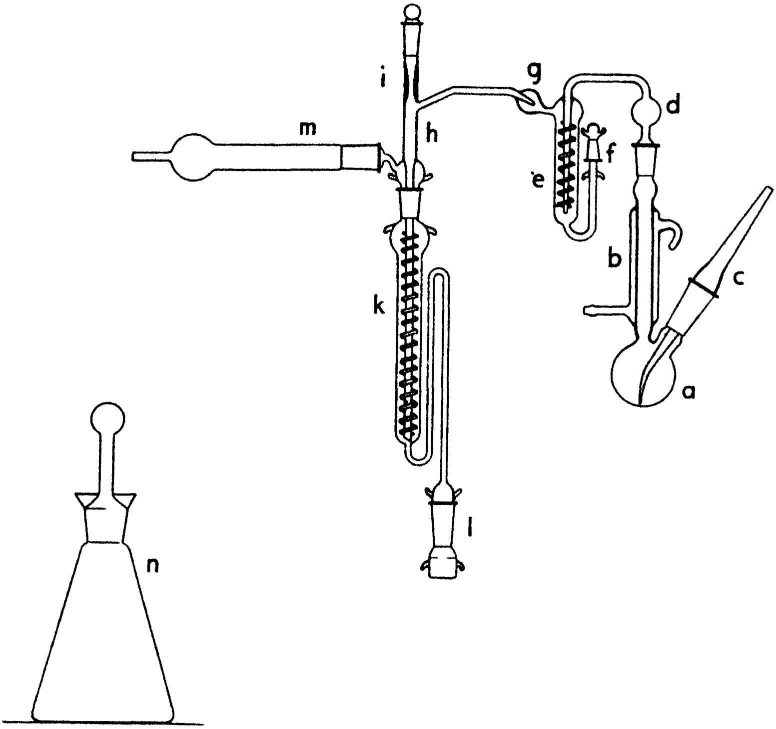


FIG. 66.

The substance (3–5 mgms.) if solid and non-volatile, is weighed from a weighing tube (p. 468) and placed in (*a*). About 5 small crystals of phenol, 5 drops of acetic anhydride and 5 mls. of iodine-free hydriodic acid (1·7 S.G.) are also introduced. If the substance is appreciably volatile it is weighed in a micro weighing bottle but in this event 12–20 mgms. tinfoil are added to reduce bumping. A stream of carbon dioxide generated from the solid (p. 467) and scrubbed through a saturated aqueous solution of sodium carbonate is adjusted by means of a precision screw clip to allow not more than two bubbles in the receiver at a time. If the substance is insoluble or undecomposed during the procedure about to be outlined it is heated with phenol and acetic anhydride in a sealed tube at 130° for 2 hours before being placed in (*a*).

A very small non-luminous flame from a micro burner placed about 20–30 mms. below the bulb of the reaction flask, or a copper block into which the bottom of the flask fits closely and heated with a micro burner, is used to boil the reaction mixture gently for 60 minutes, when reaction is complete. The heating medium is removed, the receiver disconnected at the ground-glass joint, and lowered so that the delivery tube is about 10 mms. above the sodium acetate solution. Flask (*l*) is disconnected, flask (*n*) containing 5 mls. 20 per cent. aqueous sodium acetate is placed under the siphon and (*l*) washed out with distilled water into (*n*). The delivery tube (*h*) and spiral are then washed into the receiver with distilled water, when the solution siphons over into the conical flask. Washing is continued until the combined volume is 20–30 mls. Formic acid from a thin glass rod is run down the inside of the flask and the contents shaken. One drop of methyl red, from a fine capillary is added, and if the solution remains pink all the bromine has been reduced. If the reduction is not complete, further tests are made—adding one drop each of formic acid and of indicator—until the pink colour persists. 2 mls. 10% potassium iodide solution followed by 5 mls. 2N. sulphuric acid are run in, the flask stoppered, shaken, and kept in the dark for 2 minutes. Distilled water, to act as a seal, is poured round the stopper which is removed and washed with distilled water into the flask the inner sides of which are similarly washed. The iodine liberated is titrated to a pale pink end-point with 0·02N. sodium thiosulphate, using starch as indicator.

$$\%\ \text{Alkoxyl} = \frac{\text{ml. thiosulphate} \times \text{factor} \times 100}{\text{Wt. of substance in mgm.}}.$$

1 ml. 0·02N. thiosulphate ≡ 0·4231 mgms. iodine.

CHAPTER XXXV

ORGANIC ANALYSIS

MACRO METHODS

Determination of Nitrogen (Kjeldahl method)

Compounds which contain N can usually be oxidised by heating with conc. H_2SO_4, the C being converted into CO_2, and the N to $(NH_4)_2SO_4$. NH_3 can then be liberated from this solution and estimated.

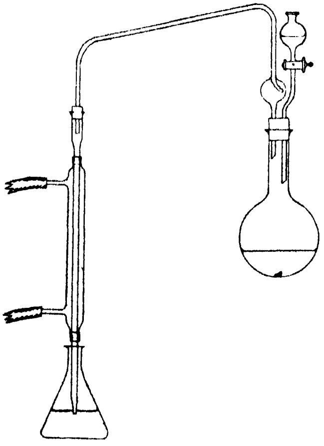


FIG. 67.

0·5–5 gms. of the substance are weighed into a long-necked, round-bottomed Kjeldahl flask of 300–500 c.cs. capacity, and 20–30 c.cs. of pure conc. H_2SO_4 added by means of a pipette. 10–20 gms. of pure $KHSO_4$ (or anhydrous K_2SO_4) and 0·2 gm. Se are then added, and the contents of the flask heated over a sand bath or small Bunsen flame until almost boiling. The neck of the flask can be partially closed with a loose-fitting, short-stemmed, glass funnel. On further heating the dark-coloured mass grows lighter until finally it is colourless, or only a faint straw colour.

The contents of the flask are then washed into the distilling flask of an ammonia estimation apparatus (Fig. 67) with successive small amounts of distilled water. The NH_3 is then determined in the usual manner.

An alternative form of ammonia distillation apparatus, Fig. 68, is due to Stock (Abs. A., 1892, 1516). The flask *A* contains the partially-neutralised solution of $(NH_4)_2SO_4$. Through the rubber stopper the stem of a dropping funnel containing conc. NaOH solution passes. This flask is attached to a second flask *B* by a glass connecting tube. The flask *B* contains distilled water, which is kept boiling vigorously during distillation. A delivery tube from flask *B* connects with the condenser *C*. The other end of the condenser tube passes through one hole in a rubber stopper into a wide-mouthed conical flask *D*. A second hole in the stopper carries a glass tube connection leading to the U-tube *E* (alternatively the end of the condenser may pass through a single-bored stopper into a filter flask, and the U-tube *E* can be attached to the suction tube of this flask). 50 c.cs. of standardised H_2SO_4 solution are distributed between the flask *D* and the U-tube *E*. A small amount of methyl red indicator is placed in *E*.

A few pieces of pure Zn foil, and excess of alkali from the dropping funnel are added to *A*, the contents of which are gradually heated to boiling. The vapour passes into the trap flask *B*, the contents of which are kept boiling, and the NH_3 distils from this flask into the receiver *D*. The unchanged acid is titrated in the usual manner.

$$\%\ \text{N} = \frac{\text{vol. of } \frac{\text{N}}{2} \text{ acid neutralised} \times 0{\cdot}7}{\text{wt. of substance taken}} \quad \left(\text{if } \frac{\text{N}}{2} \text{ acid used}\right).$$

(Chem. Rev., 1940, 331.)

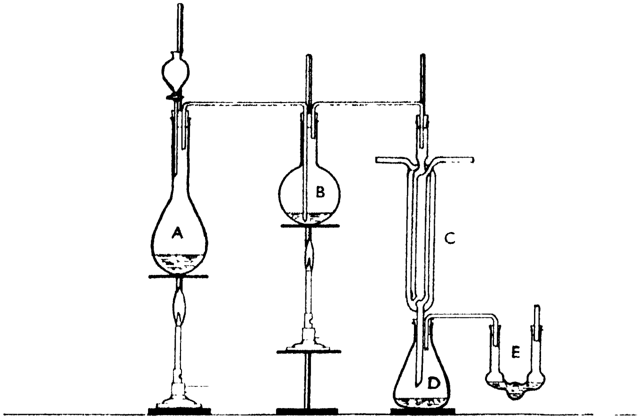


FIG. 68.

Determination of Sulphur (Fusion method)

This method is applicable only to substances which are not easily volatile.

About 6 gms. of Na_2O_2 are heated in a crucible immersed in a sand bath (the temperature of which may be taken with a thermometer bulb immersed in the sand) to about 150° for about 15 minutes in order to expel absorbed H_2O. After cooling, the peroxide is removed and finely powdered. A quantity of the substance, 0·2–0·4 gm., is intimately mixed with 4 gms. of the dried Na_2O_2 and 7 gms. Na_2CO_3 in an iron crucible. It is heated very cautiously with a small flame which does not touch the crucible at first. The flame is very gradually increased until the crucible is ultimately raised to a red heat, at which it is maintained for 30 minutes. (*Note.*—Great care is necessary in the early stages of the heating in order to avoid explosive reaction.)

The melt is allowed to cool, taking care to avoid loss of any material which may have crept up the sides of the crucible. It is then digested with H_2O, a few c.cs. of Br water added, and the resulting solution with the crucible and lid in it warmed on the water bath for 30 minutes. The crucible and lid are then removed, washed thoroughly, and the solution acidified with HCl and filtered. The S in the filtrate is finally precipitated and estimated as $BaSO_4$. The purest reagents available should be employed and a blank determination performed.

CHAPTER XXXVI

DETERMINATION OF THE EQUIVALENT OF AN ACID

By Titration with Standard Alkali.—$\frac{N}{10}$ aqueous and alcoholic potash as well as $\frac{N}{10}$ baryta solution are used for titrating organic acids, phenolphthalein being in all cases the best indicator. Baryta solution is the most suitable alkali since it can be prepared and kept free from carbonate. The baryta solution is contained in the apparatus, Fig. 69. The storage bottle is connected to the top and bottom of a burette having a 2-way stopcock and the baryta solution is protected from atmospheric carbon dioxide by a soda-lime tube inserted through the cork in the top of the storage bottle.

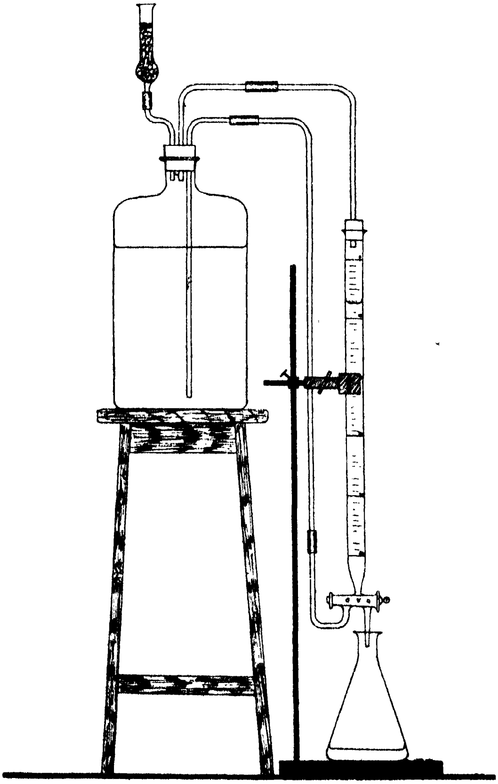


FIG. 69.

The baryta solution is prepared from pure crystalline barium hydroxide, $Ba(OH)_2.8H_2O$, by dissolving in distilled water. Any carbonate is allowed to subside and the clear supernatant liquor syphoned into the storage bottle after the latter has been filled with air free from carbon dioxide.

To determine the equivalent of an acid, a suitable quantity of it—determined by trial titrations—is dissolved in distilled water if soluble in water, and if insoluble in water in, aqueous alcohol, or in alcohol free from acid. The average of a few readings which should agree to within 0·5% is taken, and the amount of acid necessary to neutralise 85·5 gms. of barium hydroxide calculated.

Preparation and Analysis of Silver Salts.—The preparation of metallic salts and their analysis is the chief method of determining equivalents of organic acids. Salts of silver, calcium, barium, sodium, or potassium may be used, and a few preliminary tests will reveal which salt is the most suitable. Generally the silver salt, when sparingly soluble in water, is selected, since its isolation, purification, and decomposition can be readily effected. Silver salts of organic acids usually crystallise without water of crystallisation, but some have the disadvantage of being easily attacked by light.

A small quantity of the acid is neutralised with pure aqueous ammonia, and the excess of the latter boiled off. Sufficient silver nitrate is then added, and the liquid cooled. Crystals of the sparingly soluble silver salt separate and are filtered off These are recrystallised when possible from hot water, collected, well washed, dried in a steam oven for 30 minutes and allowed to cool in a vacuum desiccator. 0·2–0·3 gm. of the dry silver salt is weighed into a porcelain crucible and gently ignited until all organic matter is destroyed, and until the crucible containing the residue of silver is of constant weight—care being taken that heat is not applied too strongly, since silver is volatile at a high temperature.

$$\text{The equivalent of the acid} = 108\left(\frac{\text{wt. of silver salt}}{\text{wt. of silver}} - 1\right)$$

$$\text{and the M.W., when monobasic} = 108\,\frac{\text{wt. of silver salt}}{\text{wt. of silver}} - 107.$$

When the silver salt of an acid is soluble, the calcium or barium salt may be employed. These are prepared either by adding a soluble calcium or barium salt to a soluble salt of the acid, or by neutralising the acid itself with pure lime or baryta water. Ignition of a calcium salt is carried out either gently to the carbonate, or strongly to the oxide. A barium salt is first ignited until decomposition of organic matter is complete, then cooled and converted into the sulphate by addition of a few drops of conc. sulphuric acid, and finally ignited as sulphate. Calcium and barium salts often contain water of crystallisation and hence may require great care in drying.

When the sodium or potassium salt is available in a pure state, a known weight is ignited until only a residue of pure carbonate remains. A few drops of conc. sulphuric acid are then carefully added, and heat from a small flame applied until the excess of sulphuric acid is driven off. If any specks of carbon remain the last process is repeated. Finally the residue is weighed as alkali sulphate.

When an acid contains halogen, and the silver salt method is employed, the residue after ignition is treated with a few drops of nitric acid and a little ammonium halide to ensure complete conversion into silver halide.

Determination of the Equivalent of a Base

By Titration.—A crystalline salt of the base with some mineral or organic acid is prepared and purified, and the acid present in a weighed quantity of the salt titrated with standard alkali (preferably baryta solution, p. 484) in presence of phenolphthalein. From the average of several readings the amount of the salt which contains one equivalent of the acid is calculated, and from this is subtracted the weight of one equivalent of the acid, leaving the weight of one equivalent of the base.

Preparation and Decomposition of the Platinichloride.—Most organic bases form well-defined crystalline double salts with platinic and auric chlorides of the general formulae $B_2H_2PtCl_6$ and $B_2H_2AuCl_4$, where B represents one equivalent of the base. (Iridio-chlorides and cuprichlorides are sometimes used.) These salts are prepared by adding platinic or auric chloride to a solution of the base in dilute hydrochloric acid. The double salt is filtered off, recrystallised (generally from alcohol), and dried on a porous plate in a vacuum desiccator. When dry, a weighed quantity (0·5–1·0 gm.) is heated in a porcelain crucible, gently at first with the lid on, and afterwards strongly until all organic matter is burnt away. The residue is weighed as platinum or gold. Taking a platinum salt as example, the equivalent weight of the base is calculated as follows :

$$\text{Molecular weight of the double salt} = \frac{\text{wt. of salt taken} \times 195}{\text{wt. of platinum residue}}.$$

M.W. of the salt $-$ 409·9 (i.e. M.W. of H_2PtCl_6) = twice the equivalent of the base.

Determination of Molecular Weight

Rast's Method.—This method is easily carried out, using an ordinary thermometer graduated in 0·5°, and gives results accurate to within 5%. It is not applicable to compounds, which are not freely soluble in camphor or which react therewith or which decompose under the conditions. (B., 55, 1051, 3727.)

The method depends on the very high molecular constant (38–40) shown by camphor.

6–10 mgs. of the substance are accurately weighed and placed with about ten times the weight of pure camphor in a small, carefully-cleaned test tube, which is sealed off and heated over a small flame until the contents melt. The melt is allowed to solidify, the tube is broken, and the contents (freed from glass) ground on a watch-glass or agate mortar. A small portion is placed in a thin-walled, wide melting-point tube, pressed down with a thin glass rod, and heated to melting in the usual melting point apparatus. It is then allowed to cool until some crystals separate. After this, heating is conducted slowly and the temperature noted to within 0·5°, when the last crystal of camphor disappears. This is the freezing point of the solution. The freezing point of camphor is determined under the same conditions, using the same thermometer. The molecular weight (M) is given by the equation :

$$M = \frac{K \times w \times 100}{W \times d},$$

where w = weight of substance

W = „ „ camphor

d = difference in freezing point of camphor and that of mixture.

K = molecular depression constant for camphor.

The Molecular Depression Constant (K) for camphor is determined by using a substance of known molecular weight, say, naphthalene, and applying the following formula :

$$K = \frac{d \times M \times W}{w \times 100}.$$

The determination of this constant should precede that of each molecular weight.

The introduction of the substance and of camphor should be performed, even when working on the macro scale, with the aid of a wide capillary tube and ramrod as described by Pregl (Roth) in *Quantitative Organic Microanalysis*, p. 241. The object is to make sure that none of these substances is left adhering to the sides of the small test tube.

CHAPTER XXXVII

GROUP ESTIMATIONS

ESTIMATION OF PRIMARY OR SECONDARY AMINES BY ACETYLATION

THE primary aromatic amines are most readily estimated by means of nitrous acid (see p. 499). Primary or secondary amines, either alone or in presence of tertiary amines, may be estimated by acetylation, since the last do not react. About 1 gm. of the substance or mixture is weighed into a small flask provided with a reflux air condenser and 5 c.cs. of acetic anhydride added from a pipette having a soda-lime guard tube. In another flask, also provided with a similar condenser, 5 c.cs. acetic anhydride are placed. The two flasks are allowed to stand at room temperature for 30 minutes to 1 hour, after which time 50 c.cs. of water are added to each, and both are placed on the steam bath for an hour in order to convert the remaining acetic anhydride into acetic acid. After cooling, the amount of acetic acid in each flask is titrated with standard sodium hydroxide or standard baryta, using phenolphthalein as indicator. The difference in the two titrations corresponds to the amount of primary or secondary amine present.

$$2R.NH_2 + (CH_3CO)_2O = 2R.NH.COCH_3 + H_2O$$

$$2R.NH.R_1 + (CH_3CO)_2O = 2R.NR_1.CO.CH_3 + H_2O.$$

The blank experiment is necessary since it is difficult to obtain acetic anhydride in a pure state, and also since there is a slight loss of this reagent from the apparatus during the operation. (For Xylene Modification, see C. Z., 17, 465.)

Estimation of the Number of Hydroxyl Groups in a Compound

The acetyl derivative (each hydroxyl group acetylated) is prepared and purified, and a weighed quantity of it hydrolysed with benzene sulphonic acid. The acetic acid liberated is separated by steam distillation and titrated with baryta solution.

A solution of pure benzene sulphonic acid is prepared as follows :

100 gms. of barium benzene sulphonate $(C_6H_5SO_3)_2Ba$ are recrystallised twice from distilled water. 50 gms. of the dry purified salt are then subjected to steam distillation until the distillate is no longer acid to litmus, small amounts of volatile impurities which are generally present in the barium salt being thereby removed. To the hot liquid is added the requisite amount (avoiding excess) of pure sulphuric acid necessary to convert the barium salt into barium sulphate and benzene sulphonic acid. The barium sulphate is filtered off and washed, and the filtrate and washings made up with water to give a 10% solution of the acid.

Example.—**Mannitol.**—The hexa-acetyl derivative (p. 263) is prepared and purified, and a quantity of it—about 0·2 gm.—along with 100 c.cs. of 10% benzene sulphonic acid solution placed in a steam distillation flask. The flask is connected to a condenser on one side and to an apparatus for the generation of pure steam on the other. A suction flask to serve as receiver is attached by a cork to the condenser, and to the side tube of the suction flask a soda-lime tube to prevent the entrance of carbon dioxide is attached. Steam is blown through the flask until (1·5–3 hours) the distillate passing over is neutral. The whole distillate is then titrated with standard baryta, using phenolphthalein as indicator.

General Calculation.

W = weight of acetyl compound

w = ,, ,, acetic acid (by titration)

$\frac{w \times 17}{60}$ = ,, ,, OH $= a$

$W - \frac{w \times 42}{60}$ = ,, ,, corresponding OH compound $= b$.

Then $\frac{a}{b} \times 100 = \%$ OH, also $\frac{a}{b} \times \frac{M}{17}$ = no. of OH groups,

where M = molecular weight of OH compound.

It is obvious that this method serves for the estimation of acetyl groups present in esters of alcohols or phenols, or in substituted primary or secondary amines.

A widely applicable method of determining hydroxyl consists in boiling with acetic anhydride in pyridine to acetylate, the excess of anhydride being determined by titration following dilution with water (J. S. C. I., 1939, 74).

Many phenols are more conveniently estimated by " coupling " (see p. 499) or by bromination (see p. 508).

Estimation of Acyl Derivatives

When the substance under estimation is either an acyl derivative of an alcohol or phenol, which is not affected by alkali and air, or an acyl derivative of a volatile base, the estimation may be carried out as for esters with alcoholic potash (p. 516), any free base being removed by distillation before titrating the excess of alkali.

$$R.O.COR_1 + KOH = R.OH + R_1COOK$$

$$R.NH.COR_1 + KOH = R.NH_2 + R_1COOK.$$

When alcoholic potash cannot be employed, the acyl derivative may be hydrolysed with benzene sulphonic acid (see above) or phosphoric acid, provided that the acid produced is volatile in steam ; benzene sulphonic acid is a stronger acid than phosphoric.

Estimation of Methoxyl or Ethoxyl Groups (Macro Method)

All the usual determinations of these groups are based on the original method of Zeisel, which consists in decomposing the substance with hydriodic acid thus :

$$R.(OCH_3)x + xHI = R(OH)x + xCH_3I.$$

The resulting methyl (or ethyl) iodide is converted into silver iodide by the action of alcoholic silver nitrate, and the number of methoxyl (or ethoxyl) groups calculated from the weight of silver iodide formed.

The hydriodic acid used is purified as described on p. 514, selecting for the determination the fraction of constant B.P. 127° and D. 1·68. The alcoholic silver nitrate, which is prepared by dissolving 4 gms. of silver nitrate in 10 c.cs. of water and adding 90 c.cs. of absolute alcohol, is preserved in a well-stoppered bottle in the dark, and should be filtered and acidified with one drop of nitric acid immediately before use.

A reliable modification of the process for the estimation of methoxyl is that of the British Pharmacopœia, 1932. The apparatus is shown in Fig. 70. A Pyrex flask (*A*) of about 100 c.cs. capacity, having a bulb (*B*) of about 70 c.cs. capacity blown on the side tube, contains the mixture of substance (about 0·2 gm.) and hydriodic acid (10 c.cs.). The side tube is connected through a smaller bulbed tube (*C*) to a set of absorption bulbs (*D*), immersed in a water bath at 60° (95° for ethoxyl), containing red phosphorus suspended in a 2% aqueous solution of cadmium sulphate. To this is attached two absorption flasks (*E*), each containing about 20 c.cs. of the above alcoholic silver nitrate. To the flask (*A*) is attached a side tube (*F*) through which carbon dioxide passes to within a short distance of the surface of the reacting mixture. (Care should be taken to bring all glass connections into contact within the rubber tube).

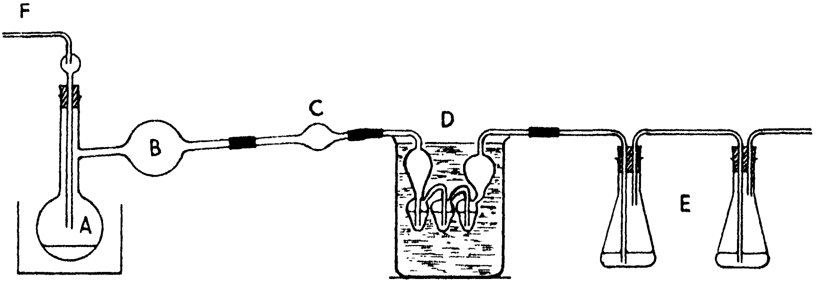


Fig. 70.

Carbon dioxide generated by interaction of sodium carbonate solution and dilute sulphuric acid and dried by passage through conc. sulphuric acid is delivered to the flask, which is maintained in a glycerine or metal bath at 140° for at least one hour until no further precipitate appears in the absorption flasks (*E*). (The mixture in the bulbs (*D*) absorbs iodine and hydriodic acid.) The silver nitrate flasks are then replaced by a Ushaped tube containing a few c.cs. of alcoholic silver nitrate, and the heating continued for 15 minutes. If no precipitate forms the operation is finished, but if a precipitate forms, the liquid in the U-tube is added to the contents of one of the small flasks and replaced by fresh alcoholic silver nitrate, the heating being continued for another 15 minutes, and so on until no more alkyl iodide passes over.

The contents of the two small flasks are diluted with water, allowed to stand for 5 minutes to ensure decomposition of the last traces of alkyl iodide, and finally poured gradually into 50 c.cs. of boiling water acidified with nitric acid, which is boiled until the alcohol is driven off. The precipitate is collected in a weighed Gooch crucible, washed, and dried in an air oven at 120°. The percentage is calculated as follows :

$$\text{Methoxyl} = \frac{\text{wt. of silver iodide}}{\text{wt. of substance}} \times 13{\cdot}21$$

$$\text{Ethoxyl} = \frac{\text{wt. of silver iodide}}{\text{wt. of substance.}} \times 19{\cdot}17$$

For micro method, see p. 479 ; also British Pharmacopœia, 1948, 762.

Estimation of Esters

1. By hydrolysis with standard alcoholic potash (p. 516). A quantity, 1–2 gms., of the ester is placed in a flask containing 50 c.cs. of seminormal alcoholic potash. The flask is fitted with a reflux condenser, and the mixture boiled on a water bath for 2–3 hours until hydrolysis is complete. A little water is then run down the inner surface of the condenser into the flask, and the excess of potash in the flask titrated with standard hydrochloric acid, using phenolphthalein as indicator. The quantity of potash used in the hydrolysis gives a measure of the value of the ester.

$$R.COOR_1 + KOH = R.COOK + R_1OH.$$

2. By use of benzene sulphonic acid or phosphoric acid. When the ester yields on hydrolysis products which become coloured in presence of alkali and air, Method 1 is inapplicable. If the acid produced on hydrolysis is volatile in steam, benzene sulphonic or phosphoric acid may be used as hydrolytic agent, and the acid (from the ester) after separation by steam distillation is titrated with standard alkali. (See Estimation of Acetyl Group, p. 489).

Estimation of Amides

Amides are estimated by hydrolysis with alkalis (generally aqueous or alcoholic potash) or with acids (sulphuric, phosphoric or benzene sulphonic). In the former case the ammonia set free is absorbed in standard acid (as in the Kjeldahl estimation of nitrogen) and the excess of acid titrated. In the latter the estimation is conducted similarly to a Kjeldahl estimation of nitrogen, the ammonium salt formed on hydrolysis being afterwards decomposed by alkali and the liberated ammonia collected in standard acid.

Estimation of Aldehydes (other than Formaldehyde)

The method depends on the combination of alkali bisulphites with aldehydes.

25 c.cs. of the solution to be examined, which must not contain more than 0·5% of total aldehyde, are run into 50 c.cs. of a solution of potassium bisulphite containing 12 gms. of $KHSO_3$ per litre, placed in a 150-c.c. flask which is then well corked and allowed to stand for 15 minutes. During this time another 50 c.cs. of the potassium bisulphite solution is titrated with $\frac{N}{10}$ iodine. The excess of bisulphite added to the aldehyde solution is then determined with the same iodine, and from the difference the bisulphite absorbed by the aldehyde, and hence the aldehyde present, can be calculated. The strength given for the bisulphite solution should be adhered to, otherwise the quantities of hydriodic acid liberated in more concentrated solutions reduce the sulphuric acid formed—i.e. the reverse reaction comes into play. The bisulphite method gives an accurate figure also for dilute solutions of mixed aldehydes ; combining it with the cyanide method (see p. 493), the amount of formaldehyde and of another aldehyde in a solution of the two can be estimated.

$$\begin{aligned} 1 \text{ c.c. } \frac{N}{10} \text{ iodine} &= 1{\cdot}5 \text{ mgs. } CH_2O \\ &= 2{\cdot}2 \text{ mgs. } CH_3.CHO \\ &= \frac{\text{mol. wt. of aldehyde in gms.}}{20} \text{ mgs.} \end{aligned}$$

Aldehydes insoluble in water should be dissolved in dilute aqueous alcohol, the concentration of alcohol being kept below 5%.

Aldehydes (e.g. benzaldehyde, cinnamic aldehyde, etc.) and certain ketones (e.g. acetone) react with hydroxylamine hydrochloride or preferably sulphate forming oximes with the liberation of free acid which can be accurately titrated in presence of methyl orange, or better with bromophenol blue (J. Eng. *Anal. Ed.*, 1942, 154). Pyridine may be used as solvent (Am. Soc., 1935, 57). See *British Pharmacopœia*, 1948, 764.

Estimation of Formaldehyde

Many methods are available for the estimation of formaldehyde.

1. For pure dilute solutions the following is recommended. 10 c.cs. of the formaldehyde solution which must, if necessary, be diluted so that it is not more than a 2% solution, is mixed with 25 c.cs. of N/10 iodine solution. 10% caustic soda solution, which is free from nitrite, is added, with shaking, drop by drop from a burette until a clear yellow liquid is obtained ; after standing for 10 minutes, an equal quantity of 10% hydrochloric acid, *plus* an extra 5 c.cs., are added to liberate the excess of iodine

which is back titrated with $\frac{N}{10}$ thiosulphate, using freshly made starch paste as indicator.

$$1 \text{ c.c. } \frac{N}{10} \text{ iodine} = 1{\cdot}5 \text{ mg. formaldehyde}$$

$$\begin{array}{l} 6NaOH + 3I_2 = NaIO_3 + 5NaI + 3H_2O \\ 3CH_2O + NaIO_3 = 3CH_2O_2 + NaI \\ \hline 3CH_2O + 6NaOH + 3I_2 = 3CH_2O_2 + 6NaI + 3H_2O \end{array}$$

$$CH_2O \equiv I_2 \equiv 2H.$$

The excess of iodine added forms iodide and iodate, and is liberated on addition of hydrochloric acid.

$$5NaI + NaIO_3 + 6HCl = 6NaCl + 3I_2 + 3H_2O.$$

This method is very satisfactory for formaldehyde provided other aldehydes are absent. In a solution containing 1 gm. CH_2O per litre, two titrations should not differ by more than 0·1 c.c. of $\frac{N}{10}$ thiosulphate; and the method will show 1 part of formaldehyde in 100,000 parts of water. It is necessary for such accuracy that the quantities of acid and alkali employed be carefully controlled as described; on no account must a great excess of alkali be used, as then there is a danger of some of the formaldehyde being converted to iodoform.

2. For impure dilute solutions of formaldehyde, especially those containing other aldehydes, the cyanide method should be used. The iodine method is not reliable in this case, as all aldehydes present are attacked. But while aldehydes, other than formaldehyde, combine similarly with potassium cyanide in the cold, they do so slowly; if the excess of cyanide is removed immediately with silver nitrate, only formaldehyde is estimated.

15 c.cs. of N/10 silver nitrate acidified with 6 drops of 50% nitric acid are mixed with 10 c.cs. of potassium cyanide solution (prepared by dissolving 3·1 gms. potassium cyanide in 500 c.cs. distilled water), the whole diluted to 50 c.cs., well shaken, filtered through a dry filter, and 20 c.cs. of the filtrate titrated with N/10 ammonium thiocyanate. Another 15 c.cs. portion of N/10 silver nitrate, to which is added 6 drops of the nitric acid, 10 c.cs. of the potassium cyanide solution and 10 c.cs. of the formaldehyde (content should not exceed 25 mgms. of the aldehyde), is diluted as before to 50 c.cs., filtered through a dry filter, and 25 c.cs. titrated with N/10 thiocyanate for the excess of silver nitrate. The difference between the volumes of thiocyanate used in these two titrations multiplied by two is the volume of thiocyanate corresponding to the potassium cyanide reacted upon by the formaldehyde.

$$1 \text{ c.c. } \frac{N}{10} \text{ thiocyanate} = 3 \text{ mgs. } CH_2O.$$

CHAPTER XXXVIII

ESTIMATIONS BASED ON THE USE OF TITANOUS SALTS

This energetic reducing agent can be maintained at constant strength in aqueous hydrochloric acid solution for a reasonable period. It is advisable, however, to re-standardise it after 24 hours' standing. It serves for the reduction of aromatic nitro compounds, some nitroso bodies, many azo dyes, and of nearly all the dyes which yield leuco-compounds. It is easily standardised against a ferric salt—say ferric alum—using potassium thiocyanate as indicator. From the equations :

$$TiCl_3 + FeCl_3 = TiCl_4 + FeCl_2$$

$$6TiCl_3 + 6HCl + R.NO_2 = 6TiCl_4 + R.NH_2 + 2H_2O$$

it is seen that

$$6TiCl_3 \equiv 6Fe \equiv 6H \equiv NO_2.$$

Preparation and Storage of Titanous Chloride Solution for Analysis.—50 c.cs. of the commercial titanous chloride solution (15%) are boiled with 100 c.cs. of conc. hydrochloric acid for 1 minute and then made up to about 2 litres in a storage bottle, *A* (Fig. 71). The solution when freshly prepared should fill the bottle completely ; otherwise air remains which must be displaced by hydrogen. *A* is connected to both top and bottom of a burette by means of glass and rubber tubing. The burette has a 2-way glass stopcock at *B*, so that it can receive solution from *A*, or deliver solution through its orifice. The second tube from the top of *A* leads to a hydrogen generator *H*, which consists of 2 parts, (*a*) an inner tube, made by drawing a test tube out to a fine point ;

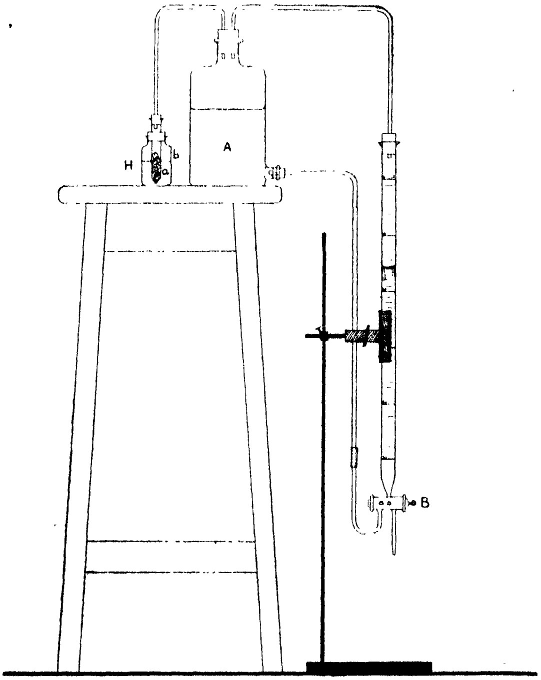


Fig. 71.

this contains granulated zinc, and is connected by a rubber stopper and delivery tube to *A* ; (*b*) an outer vessel containing hydrochloric acid (15%). To replace all the air in the apparatus by hydrogen, the stopcock is turned to allow solution from *A* to fill the tube leading to the bottom of the burette. The stopcock is then turned as for delivery from the burette, and hydrogen allowed to escape from the apparatus for 5 minutes. The burette is filled, emptied and refilled, after which the apparatus is ready for use.

A layer of medicinal paraffin on the surface of the titanous chloride is helpful in preventing oxidation.

Standardisation.—3·5 gms. of pure ferrous ammonium sulphate are dissolved in distilled water, 100 c.cs. of 5N sulphuric acid added, and the whole made up to 250 c.cs. 25 c.cs. of this are oxidised with potassium permanganate solution of approximately $\frac{N}{50}$ strength until a faint pink colour persists. A large excess of potassium thiocyanate (0·2–0·3 gm.) is added, and titanous chloride solution run in from the burette until the red colour due to ferric thiocyanate just disappears. If 25 c.cs. of iron solution require x c.cs. of titanous chloride solution to reduce it, then each c.c. of the latter is equivalent to $\frac{0{\cdot}05}{x}$ gm. iron.

A solution of iron alum, containing about 14 gms. per litre, and acidified with sulphuric acid until the solution assumes a pale straw colour, is prepared. By titrating 25 c.cs. of this with titanous chloride, using potassium thiocyanate as indicator, its strength is determined, and as it will retain its strength for a long period, this alum solution may be used in all subsequent cases for standardising the titanous chloride solution.

Titanous sulphate (p. 511) may be similarly employed. (J. S. C. I., 41, 158.) It has the advantage of not giving rise to halogenated compounds as are given by titanous chloride in some instances.

Nitro Compounds.—(*a*) *Those Soluble in Water.*—A known amount of a nitro body is dissolved in water in a conical flask, hydrochloric acid is added, and the solution is boiled with a stream of carbon dioxide passing through. If the nitro compound is volatile in steam the heating should be done in a vessel provided with a " ground in " reflux condenser, (J. S. C. I., 41, 158.) Heating is momentarily stopped, and a large excess of titanous chloride solution run in. The contents are boiled for 10 minutes to ensure complete reduction. Carbon dioxide is passed through the flask during the entire operation. The solution is then cooled and the excess of titanous chloride determined by titration with ferric alum solution, using potassium thiocyanate as indicator. A control experiment without the nitro compound present is performed under exactly the same conditions. 6 equivalents of titanous chloride (6H atoms) are required for the reduction of each NO_2 group.

Example.—0·4979 gm. *p*-nitroaniline is dissolved in hydrochloric acid on the water bath, and made up to 500 c.cs. 20 c.cs. of this solution are reduced with 50 c.cs. titanous chloride as described above, and the excess of the latter titrated back with ferric alum. Excess $TiCl_3 = 9{\cdot}7$ c.cs. A control experiment having no *p*-nitroaniline used 0·76 c.c. $TiCl_3$.

$TiCl_3$ used = 39·54 c.cs. 1 c.c. $TiCl_3$ = 0·0012228 gm. Fe.

138 *p*-nitroaniline require 336 Fe.

$$\therefore\ 0{\cdot}4979 \text{ gm. contains } \frac{0{\cdot}0012228 \times 39{\cdot}54 \times 138 \times 25}{336} \text{ } p\text{-nitroaniline}$$

$$= 99{\cdot}7\%.$$

Picric acid and Naphthol Yellow S may be estimated in a similar manner.

(*b*) *Those insoluble in water* must first be sulphonated by heating with 20 parts by weight of fuming sulphuric acid on a water bath for 2 hours. The product is made up to a definite volume with water (*caution!*) and an aliquot part titrated with titanous chloride as described for soluble nitro compounds.

Example.—1·01 gms. nitrobenzene are sulphonated as described above, then cooled and the volume carefully diluted to 1 litre. 20 c.cs. are withdrawn and reduced with 50 c.cs. $TiCl_3$ solution (as for *p*-nitroaniline).

Excess $TiCl_3$ = 18 c.cs. Control experiment = 0·8 c.c. $TiCl_3$.

Vol. $TiCl_3$ used = 31·2 c.cs. = 31·2 × 0·001700 gm. Fe.

123 nitrobenzene = 336 Fe.

$$\therefore\ 1{\cdot}002 \text{ gms. contain } \frac{0{\cdot}0017 \times 31{\cdot}2 \times 123 \times 50}{336} = 0{\cdot}9709$$

$$= 96{\cdot}1\%.$$

(*c*) Nitro compounds *insoluble and yet not easily sulphonated*, e.g. dinitrobenzene or dinitronaphthalene, are dissolved in alcohol, and the solution poured into a known volume of titanous chloride solution acidified with hydrochloric acid, through which carbon dioxide is passed. The mixture is boiled, allowed to cool, and the excess of titanous chloride estimated with ferric alum.

Example.—0·110 gm. commercial dinitronaphthalene is dissolved in 250 c.cs. alcohol. 50 c.cs. $TiCl_3$ solution are placed in a conical flask, 10 c.cs. conc. HCl added, carbon dioxide passed through, and 25 c.cs. of the dinitronaphthalene solution run in. The mixture is boiled, then allowed to cool, and the excess of $TiCl_3$ titrated.

Excess $TiCl_3$ = 31·60 c.cs. Control experiment = 0·90 c.c. $TiCl_3$.

Vol. $TiCl_3$ used = 17·5 c.cs. = 17·5 × 0·001750 Fe.

218 dinitronaphthalene = 672 Fe.

$$\therefore\ 0{\cdot}110 \text{ gm. contains } \frac{0{\cdot}00175 \times 17{\cdot}5 \times 10 \times 218}{672} = 0{\cdot}09933$$

$$= 90{\cdot}3\%.$$

The method is not applicable to polynitro compounds.

Nitroso Compounds.—Owing to the intense colour which these compounds yield in hydrochloric acid solution they may be titrated directly with titanous chloride until the yellow colour disappears. A weighed quantity is dissolved in hydrochloric acid and made up to a known volume. An aliquot part of this solution is warmed to 40°–50° in a conical flask with carbon dioxide passing through and titanous chloride solution is run in until the yellow colour disappears. 4 equivalents of titanous chloride are required for each nitroso group.

Example.—1·005 gms. nitrosodimethylaniline are dissolved in 20 c.cs. conc. hydrochloric acid and sufficient water to make volume up to 500 c.cs. 10 c.cs. of this solution required 17·5 c.cs. $TiCl_3$ solution.

$$1 \text{ c.c. } TiCl_3 = 0{\cdot}001700 \text{ gm. Fe.}$$

$$150 \text{ nitrosodimethylaniline} = 224 \text{ Fe.}$$

$$\therefore\ 1{\cdot}005 \text{ gms. contains } \frac{17{\cdot}5 \times 0{\cdot}0017 \times 150 \times 50}{224} = 0{\cdot}9983 \text{ gm.}$$

$$= 99{\cdot}3\%.$$

Azo Dyes.—(1) Azo dyes which are soluble in dilute hydrochloric acid may be titrated directly, the disappearance of the colour indicating the end point.

(2) Many azo dyes which are insoluble in dilute hydrochloric acid can be titrated directly in presence of Rochelle salt. Since Rochelle salt forms a compound with titanium, which is pale yellow in dilute solution, this method is inapplicable for the estimation of yellow dyes.

(3) A number of azo dyes which cannot be estimated according to (1) or (2), may be estimated indirectly. A weighted quantity of dye is boiled in aqueous solution in a flask through which a stream of carbon dioxide is passing. After adding hydrochloric acid an excess of titanous chloride is run into the boiling mixture. The reduction is usually complete in about 2 minutes, after which the flask is cooled under the tap with the current of carbon dioxide still passing. When cold, the excess of titanous chloride is estimated with ferric alum solution, using potassium thiocyanate as indicator. The azo group requires 4 equivalents of titanous chloride.

Example of (1).—1·003 gms. of Orange II ($C_{16}H_{11}N_2O_4SNa, 5H_2O$) are dissolved in water and made up to 500 c.cs. 50 c.cs. are withdrawn into a conical flask, 5 c.cs. conc. hydrochloric acid added, and after boiling for 1 minute titrated with titanous chloride.

$$\text{Vol. } TiCl_3 \text{ required} = 29{\cdot}15 \text{ c.cs.} = 29{\cdot}15 \times 0{\cdot}00165 \text{ gm. Fe.}$$

$$350 \text{ Orange II} = 224 \text{ Fe.}$$

$$\therefore\ 1{\cdot}003 \text{ gms. contain } \frac{29{\cdot}15 \times 0{\cdot}00165 \times 10 \times 350}{224} = 0{\cdot}7522 \text{ gm.}$$

$$= 75\%.$$

Example of (2).—1·10 gms. of Diamine Black ($C_{34}H_{24}O_{14}N_6S_4Na_4$) are dissolved in 250 c.cs. water. 50 c.cs. of this solution are withdrawn, 25 c.cs. of Rochelle salt solution (about 20%) added, and titrated with titanous chloride until the colour of the dye disappears.

$$\text{Vol. } TiCl_3 \text{ used} = 20{\cdot}22 \text{ c.cs.} = 20{\cdot}22 \times 0{\cdot}00165 \text{ gm. Fe.}$$

$$960 \text{ diamine black} = 448 \text{ Fe.}$$

$$\therefore\ 1{\cdot}10 \text{ gms. contains } \frac{20{\cdot}2 \times 0{\cdot}00165 \times 5 \times 960}{448} = 0{\cdot}44 \text{ gm.} = 40\%.$$

Example of (3).—0·99 gm. of Chrysophenine G ($C_{30}H_{26}N_4O_8S_2Na_2$) is dissolved in a litre of water. 100 c.cs. of this solution are withdrawn and boiled, with a current of carbon dioxide passing through ; 10 c.cs. of conc. hydrochloric acid and 50 c.cs. of titanous chloride are then added, and the mixture boiled until the precipitate dissolves and the solution turns a slight violet colour. After cooling, the excess of titanous chloride is titrated with ferric alum.

$$\text{Excess } TiCl_3 = 34{\cdot}2 \text{ c.cs.}$$

$$\text{Vol. } TiCl_3 \text{ used} = 15{\cdot}8 \text{ c.cs.} = 15{\cdot}8 \times 0{\cdot}00165 \text{ gm. Fe.}$$

$$680 \text{ chrysophenine} = 448 \text{ Fe.}$$

$$\therefore\ 0{\cdot}99 \text{ gm. contains } \frac{15{\cdot}8 \times 0{\cdot}00165 \times 10 \times 680}{448} = 0{\cdot}396 \text{ gm.}$$

$$= 40\%.$$

Dyes which Yield Colourless Leuco Compounds.—Approximately 1 gm. is dissolved in 250 c.cs. water ; 50 c.cs. of this solution and about 2 c.cs. conc. hydrochloric acid are introduced into a conical flask fitted with a rubber stopper having 3 holes. Through one hole a current of carbon dioxide is introduced, another serves for the escape of this gas, and the third is left for the delivery tube of the titanous chloride burette. The solution is boiled, and then titrated with titanous chloride, until the colour just disappears.

Example.—1 gm. crystallised zinc-free Methylene Blue ($C_{16}H_{18}N_3SCl$) is treated as described above. 50 c.cs. of this solution required 41·64 ccs. titanous chloride solution, of which 1 c.c. = 0·00165 gm. Fe.

$$319{\cdot}5 \text{ Methylene Blue} = 112 \text{ Fe.}$$

$$\therefore\ 1 \text{ gm. contains } \frac{41{\cdot}6 \times 0{\cdot}00165 \times 5 \times 319{\cdot}5}{112} = 0{\cdot}98 \text{ gm.}$$

$$= 98\%.$$

The zinc double chloride of Methylene Blue has the formula $C_{16}H_{18}N_3SCl$, $ZnCl_2$, H_2O, and is much less soluble in dilute hydrochloric acid. A drop of weak Methylene Blue solution may be used as indicator in the direct titration of substances with titanous chloride where a selective reduction takes place. The end point is perfectly sharp if the solution is warmed to 35°.

Of other examples which yield leuco compounds, Indigo may be estimated by titrating the sulphonated dye in presence of Rochelle salt ; Magenta in Rochelle salt solution ; Eosin and Rhodamine in presence of Rochelle salt and alcohol, the latter to keep the leuco compound in solution. All these titrations are carried out on the boiling dye solution and in presence of carbon dioxide.

For many other valuable applications of titanous chloride, see Knecht and Hibbert, *New Reduction Methods in Volumetric Analysis* (Longmans, Green & Co.).

CHAPTER XXXIX

ESTIMATIONS BASED ON DIAZOTISATION OR COUPLING

PREPARATION OF STANDARD REAGENTS

(*a*) **Sodium Nitrite.**—Sodium nitrite is often estimated by the use of permanganate and oxalic acid. When impure sodium nitrite is estimated in this manner, the values obtained are often too high, owing to the presence of other oxidisable substances. For reactions such as those which follow, it should be estimated with pure sulphanilic acid, pure benzidine, or pure aniline.

Commercial sulphanilic acid is purified by dissolving in sufficient aqueous sodium carbonate to give an alkaline solution, which is boiled until all trace of aniline disappears. The solution is filtered and acidified with hydrochloric acid, and after 12 hours the product is filtered off and washed with a little water. It is again dissolved by means of hot water and sodium carbonate to a neutral solution ; the solution is quickly cooled along with stirring to 0°, and the sodium sulphanilate filtered off. These crystals are dissolved in distilled water, and acidified with pure conc. hydrochloric acid. The crystals which separate are filtered off and washed free of sodium chloride with distilled water ; they are once more recrystallised from distilled water, and afterwards dried in an air oven at 120° until of constant weight. The product should be preserved in a bottle having a ground-glass stopper. To prepare a semi-normal solution, exactly 86·5 gms. are dissolved in 50 c.cs. pure (20%) ammonia, and made up to 1 litre ; the solution when preserved in the dark will keep for many months.

Benzidine may be purified by crystallisation from boiling water in which it is soluble to about 1%. When crystallised from water above 80° (i.e. from an aqueous solution heated to boiling, cooled to 80° and filtered through a funnel maintained at 80°), the anhydrous base (M.P. 127°) is obtained in meagre quantity ; under 80° a hydrate (M.P. 104°–105°) is formed. By crystallisation in the ordinary way, the bulk of the product is the monohydrate. This should be exposed in a desiccator over conc. sulphuric acid until (about 24 hours) a M.P. of 127° is reached. *N.B.*—The melting points must be taken quickly. (J. S. C. I., 46, 209.) The product obtained by vacuum distillation (see Fig. 22) is also suitable for standardisation purposes.

To prepare semi-normal nitrite solution, about 37·5 gms. of commercial sodium nitrite (or rather less of a purer salt) are dissolved in water, filtered, and made up to 1 litre. 50 c.cs. of the $\frac{N}{2}$ sulphanilic acid or $\frac{N}{2}$ benzidine solution are then titrated with it in the following manner :

The solution is measured by means of a pipette into a 500-c.c. beaker ; 200 gms. of ice and 13 gms. of conc. hydrochloric acid are also added. The beaker is slightly tilted to one side, and the nitrite solution, run in from a burette, is allowed to trickle down the side of the beaker and thus to sink quickly to the bottom. When about 45 c.cs. nitrite have been added, the solution is stirred with a glass rod, and more nitrite is run in, drop by drop (tests being carried out at intervals), until a drop of the solution just causes an immediate blue coloration on starch-iodide paper.* After standing a few minutes, a test is again applied to see if the excess of nitrite still remains, and if not, more nitrite is added, until a slight positive test is obtained after a few minutes' standing. It is advisable to repeat the operation, all but 1 c.c. of the total volume of nitrite being used in the previous test being run in at once along the side of the beaker; this obviates as much as possible the escape of free nitrous acid on mixing. The remainder of the nitrite is run in, drop by drop, as before. From the volume of nitrite necessary, a calculation is made to ascertain what volume of water must be added to make the remaining nitrite exactly semi-normal.

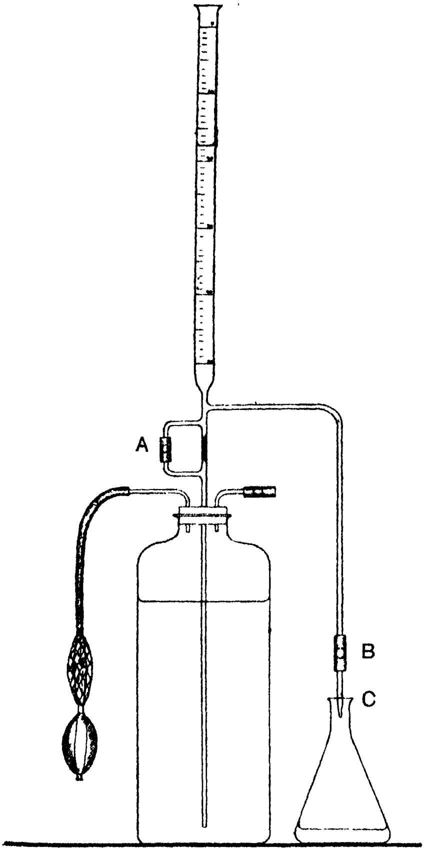


Fig. 72.

Fig. 72 shows a convenient type of burette for use in cases where many titrations have to be performed. The burette is fixed to the storage bottle and the liquid is blown up into the burette by compressed air from the hand bulb, the bead at *A* being opened by pressure between the fingers. The titration is effected by opening the bead at *B*.

(*b*) $\frac{N}{2}$ **Aniline Solution.**—About 250 c.cs. of the purest commercial aniline are carefully redistilled, and the fraction passing over within half a degree at its boiling point reserved for the preparation of the standard solution. Exactly 46·5 gms. of the above fraction are weighed ; to this

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* A certain amount of practice is necessary to judge the end point accurately, as the paper when moistened with diazonium solution generally develops a blue colour on standing a short time. As the end point is approached the eye detects a brief interval between the moistening of the test paper and the development of the colour; at the end point this interval disappears and the colour develops instantaneously. (See p. 512.)

are added 50 c.cs. ice-water, and 75 c.cs. of conc. hydrochloric acid, the object of the ice-water being to prevent the escape of fumes when the acid and amine come together. The solution is then made up to 1 litre with distilled water; when prepared in this way, it is generally accepted as exactly semi-normal, and may be used as such for the standardisation of sodium nitrite solution; however, if any doubt exists, it is standardised against the previously prepared $\frac{N}{2}$ sodium nitrite.

(*c*) $\frac{N}{20}$ **Phenyldiazonium Solution.**—50 c.cs. of the $\frac{N}{2}$ aniline solution are measured out into a 500-c.c. flask, 10 c.cs. of conc. hydrochloric acid are added, and the flask immersed in ice-water. When thoroughly cold, 50 c.cs. of $\frac{N}{2}$ sodium nitrite are run in from a burette, the contents of the flask being gently rotated at intervals. After standing for 15 minutes, the solution is made up to 500 c.cs.; it may be preserved for a few hours at 0° in the dark, but should always be freshly prepared before use.

(*d*) $\frac{N}{20}$ **R Salt Solution.**—20 gms. of commercial "R Salt" (β-naphthol-3 : 6-disodium-disulphonate) are dissolved in water and made up to 1 litre to give an approximately $\frac{N}{20}$ solution. A $\frac{N}{20}$ phenyldiazonium solution is prepared and 100 c.cs. of it poured into a 100-c.c. measuring cylinder which has been previously cooled in an ice chest. The cylinder is then immersed in a vessel containing ice-water. 50 c.cs. of the R salt solution are measured out into a beaker, 8 gms. sodium carbonate added, and stirred to dissolve. 15 c.cs. of the phenyldiazonium solution are then added from the measuring cylinder. A red dye is formed which is thrown out of solution by addition of common salt. After addition of sufficient salt, a drop "spotted" on filter paper leaves a sediment of dye in the centre, and the outspread is colourless. A small quantity of diazonium solution from the stock solution is poured into a small beaker to be used for testing. If the outspread on filter paper of a drop from the solution containing the dye is touched with a glass rod dipped in the diazonium test solution, a red dye is formed, provided an equivalent quantity or more of diazonium solution has not been added. Proceeding in this way, and testing after each addition, small quantities of diazonium solution from the measuring cylinder are added until a drop tested on filter paper no longer forms a red dye.

When the dyestuff is very soluble in water, a clear outcrop can frequently be secured by the following procedure. The coloured solution is "spotted" on to a small heap of common salt placed on good filter paper and allowed to soak through to the paper. The salt may then be removed by shaking the paper, and the test applied to the clear outcrop as before.

Since 1 mol. of R salt couples with 1 mol. diazonium compound, the strength of the R salt solution can be easily calculated, and hence the quantity of water which must be added to make it $\frac{N}{20}$.

Standard "R salt" is used for estimating amines (see below).

Estimation of Amines

(*a*) *By Diazotisation.*—Many amines which diazotise readily can be accurately estimated with standard nitrite. The principle of the method is exactly the same as that underlying the standardisation of sodium nitrite with sulphanilic acid, benzidine or aniline. As a general rule 1/100 mol. wt. of the amine is dissolved along with rather more than three times its acid equivalent of hydrochloric acid in water ; the solution is cooled to 0° by the addition of ice, and $\frac{N}{2}$ sodium nitrite solution is run in until an end point is indicated by starch-iodide paper (see preparation of standard sodium nitrite, p. 499).

$$\% \text{ purity} = \text{c.cs. of } \frac{N}{2} \text{ nitrite} \times 5.$$

Those amines which, when treated as above, give diazoamino compounds or dyes and also those whose diazonium compounds blacken starch-iodide cannot be estimated directly. They may be estimated either by (1) coupling with a standard diazonium solution, or (2) by adding excess of nitrous acid and coupling with alkaline β-naphthol of known strength.

(*b*) *By Diazotisation and Coupling.*—Exactly $\frac{1}{100}$ mol. wt. of the amine is diazotised as described under (*a*). 8 gms. sodium carbonate are added to the diazotised solution and stirred until dissolved. The solution is diluted and cooled, so that its strength is equivalent to about 1% amine and its temperature about 5°. $\frac{N}{20}$ R salt solution is then run in until an excess of diazonium solution no longer appears on spotting on paper (see p. 501), the dye being first salted out by the addition of common salt. By the above method, two values are obtained—a " nitrite " value, and an " R salt " value, and these should approximate.

The above outline is general, but is subject to variation for the particular amine under estimation. For instance, the amount of sodium carbonate—the essential point is to have the mixture alkaline during the coupling—depends on the acidity of the diazonium solution, and the presence of acid groups, such as sulphonic. When the coupling is carried out in acetic acid solution, sodium acetate is added in place of sodium carbonate and in three times the quantity.

Estimation of Phenolic Compounds

Phenolic compounds which couple readily and completely with diazonium compounds can be estimated by titration with a standard diazonium solution. The standardisation of R salt affords one example of the method (p. 501).

Example.—β-**Naphthol.**—1·44 gms. ($\frac{1}{100}$ mol.) of β-naphthol are dissolved in 10 c.cs. caustic soda solution (15%) ; to this is added 100 c.cs. water and 3 gms. of anhydrous sodium carbonate. The whole is then made up to 200 c.cs. in a flask. 50 c.cs. of this are placed in a beaker, and ice-cold $\frac{N}{20}$ phenyl-diazonium solution run in until a drop on filter paper no longer shows an excess of β-naphthol when tested with diazonium solution. (For end point, see R salt, p. 501).

$$\% \text{ purity} = \text{c.cs. of diazonium solution} \times 2.$$

Estimation of H Acid (Acid Sodium Salt)

(*a*) *By Diazotisation.*—3·41 gms. ($\frac{1}{100}$ mol.) are dissolved in 5 c.cs. of 10% sodium carbonate solution, and diluted to 250 c.cs. 25 c.cs. of conc. hydrochloric acid are then added, and the solution diazotised at 5° with $\frac{N}{2}$ sodium nitrite.

$$\% \text{ of H acid} = \text{c.cs. of nitrite} \times 5.$$

(*b*) *By Coupling.*—3·41 gms. H acid are dissolved in 50 c.cs. of 10% sodium carbonate solution and diluted to 300 c.cs. $\frac{N}{20}$ phenyldiazonium solution is then added until the end point is obtained as determined by "spotting" (see p. 501).

$$\% \text{ of H acid} = \frac{\text{c.cs. of diazonium solution}}{2}.$$

For a good quality of H acid, the percentage determined by diazotisation should only be slightly higher than that determined by coupling.

CHAPTER XL

MISCELLANEOUS ESTIMATIONS

Estimation of *p*-Phenylenediamen

THE *para*-diamines cannot be estimated by means of the diazo reaction. The following estimation is based on the formation of benzoquinone dichloro-imide when *p*-phenylenediamine in hydrochloric acid solution is added to a solution containing excess of sodium hypochlorite and sodium carbonate.

A solution of sodium hypochlorite is prepared by diluting 50 c.cs. of a commercial solution containing about 12–15% available chlorine to 1,000 c.cs. Or, a corresponding solution may be prepared by passing chlorine into caustic soda (p. 519). 50 c.cs. of this solution are titrated with $\frac{N}{10}$ sodium arsenite solution, using starch-iodide paper as indicator. 100 c.cs. of hypochlorite solution are then measured out, diluted with an equal volume of cold water, and about 1 gm. of solid sodium carbonate added. 10 c.cs. of the solution to be determined, containing 2–6% of *p*-phenylenediamine dissolved in slight excess of hydrochloric acid, are added slowly with stirring. The mixture should then give a strong reaction with starch-iodide paper, otherwise the experiment must be repeated, using either less diamine or more sodium hypochlorite solution. On the addition of the diamine solution, the dichloro-imide is rapidly precipitated as an almost colourless solid.

$$C_6H_4(NH_2)_2 + 3Cl_2 \longrightarrow C_6H_4 : (NCl)_2 + 4HCl.$$

The turbid solution is then titrated, without filtration, with $\frac{N}{10}$ sodium arsenite solution, using starch-iodide paper as external indicator, the end point being sharply defined by the non-appearance of the blue colour on spotting. At the end of the titration the solution should be alkaline; the dichloro-imide in alkaline solution has no action on the test-paper. The difference in the volume of the $\frac{N}{10}$ arsenite solution required for the titration of the sodium hypochlorite itself and for the titration of the hypochlorite *plus* diamine is equivalent to the amount of active chlorine removed from the solution as benzoquinone dichloro-imide, each c.c. of $\frac{N}{10}$ arsenite solution corresponding to 0·0018 gm. of diamine.

The method gives good results, the error varying from 0·3–0·7%. (J. S. C. I., 38, 408.)

Estimation of Thiophen in Benzene

2 c.cs. of commercial benzene and 20 c.cs. of Denigès' reagent (see below) are introduced into a strong test tube (2 cms. × 15 cms.), which is after-

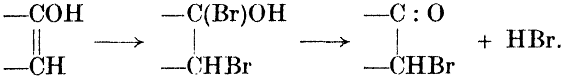
wards closed with a good wet cork, and placed in a shaking machine for 3 hours. (Even without shaking, the reaction takes place to some extent.) At the end of this time, the precipitate is collected in a weighed Gooch crucible, washed with hot water until neutral to litmus, dried at 110°–115° until constant, and weighed as $2(HgO.HgSO_4)C_4H_4S$. The weight of this precipitate × 0·0757 gives the weight of thiophen.

To prepare the above reagent, 20 c.cs. of pure conc. sulphuric acid are poured into 110 c.cs. distilled water, 5 gms. of finely-powdered mercuric oxide are added and the mixture stirred until almost all dissolves. The solution is then filtered and the filtrate preserved in a stoppered bottle.

The Gooch crucible is prepared with a filtering layer of good fibrous asbestos on top of which is placed a perforated porcelain plate. The asbestos should be previously purified by boiling first with *aqua regia* for a short time, and then with conc. hydrochloric acid for a week, the acid being renewed each day. (J. S. C. I., 38, 189.) Alternatively, asbestos of sufficiently good quality can now be purchased.

Estimation of Enol Modification in a Compound exhibiting Keto-enol Tautomerism

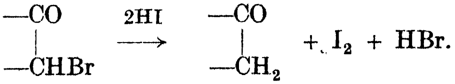
The enolic form reacts instantly with an alcoholic solution of bromine, and the amount of bromine used corresponds with the formation of a dibromide, which body, however, cannot be isolated since it decomposes as soon as formed into hydrogen bromide and a bromo-ketone.



$$\begin{array}{l}\text{—COH}\\ \|\\ \text{—CH}\end{array} \longrightarrow \begin{array}{l}\text{—C(Br)OH}\\ |\\ \text{—CHBr}\end{array} \longrightarrow \begin{array}{l}\text{—C : O}\\ |\\ \text{—CHBr}\end{array} + \text{HBr}.$$

The amount of enolic compound can be estimated by adding a standard solution of bromine in alcohol, until the yellow colour just persists, but the method has the disadvantage that such a solution of bromine is unstable.

In the following method a slight excess of an alcoholic solution of bromine is added to an alcoholic solution of the tautomeric mixture; the excess of bromine is immediately removed by the addition of a few drops of alcoholic β-naphthol solution; potassium iodide solution is next added, and the hydrogen iodide formed by interaction with the hydrogen bromide present reduces the bromo-ketone with liberation of free iodine, which is estimated by titration with standard thiosulphate (in absence of starch). One molecule of iodine ≡ one molecule of enolic compound. For review of this method, see Ann. Rep., 1930, 100.



$$\begin{array}{l}\text{—CO}\\ |\\ \text{—CHBr}\end{array} \xrightarrow{2HI} \begin{array}{l}\text{—CO}\\ |\\ \text{—CH}_2\end{array} + I_2 + \text{HBr}.$$

Example.—**Ethyl Acetoacetate.**—The following reagents are prepared:

1. An approximately $\frac{N}{10}$ alcoholic bromine solution; the bromine itself being previously purified by shaking up with sulphuric acid, then separating and distilling.

2. A 10% solution of potassium iodide.
3. $\frac{N}{10}$ sodium thiosulphate solution.
4. 1 gm. of β-naphthol dissolved in 20 c.cs. alcohol.

1·625 gms. ester are dissolved in 100 c.cs. alcohol in a flask, and cooled to −7°. The contents are given a swirling motion, and ice-cold bromine solution (21 c.cs.) added until a faint yellow colour is produced. Alcoholic β-naphthol sufficient to remove colour is then added. The time for the addition of bromine and β-naphthol should not exceed 20 seconds. 5 c.cs. of the potassium iodide solution are added, and the contents titrated with $\frac{N}{10}$ thiosulphate. Volume of thiosulphate = 18·7 c.cs., which is equivalent to 18·7 × 0·0127 gm. iodine, or to 18·7 × 0·0065 gm. enolic ester.

$$\therefore \% \text{ Enol} = \frac{100 \times 18{\cdot}7 \times 0{\cdot}0065}{1{\cdot}625} = 7{\cdot}49.$$

Estimation of Anthracene in Commercial Anthracene

The estimation of anthracene depends on its oxidation by means of chromic acid to anthraquinone.

1 gm. of the sample is dissolved in 45 gms. of glacial acetic acid by heating on a sand bath under a long reflux condenser. When the contents of the flask are boiling, 15 gms. of crystallised chromic acid dissolved in 50% acetic acid are very gradually added (2 hours). When the addition of chromic acid is complete, the mixture is boiled for another 2 hours. After cooling, the contents are treated with 400 c.cs. water, and the precipitated anthraquinone filtered off, washed with cold water, then with boiling dilute alkali and finally with boiling water, until the washings are free from alkali. The residue is then washed into a small porcelain basin and dried at 100°. 10 gms. of fuming sulphuric acid (about 5% SO_3) are added, and the mixture heated for 10 minutes at 100°. After cooling, it is carefully poured (*caution!*) into 200 c.cs. of cold water, the anthraquinone filtered, washed with dilute alkali, and finally with water as before. It is then dried and weighed. The anthraquinone is volatilised by heating on a sand bath and the residue is weighed. The difference gives the weight of anthraquinone.

$$\text{Wt. of anthraquinone} \times \frac{178}{208} = \text{weight of anthracene.}$$

Estimation of Acetone

1. *Volumetrically.*—Iodine in alkaline solution reacts with acetone to give iodoform, a reaction which is used in the estimation of the ketone.

$$1 \text{ mol. acetone} \equiv 3 \text{ mols. iodine.}$$

$$CH_3COCH_3 + 3KIO \longrightarrow CH_3COCI_3 + 3KOH$$

$$CH_3COCI_3 + KOH \longrightarrow CHI_3 + CH_3COOK.$$

The excess of iodine may be decomposed as follows :

$$I_2 + 2KOH = KIO + KI + H_2O$$
$$KIO + KI + 2HCl = I_2 + 2KCl + H_2O$$

and is titrated with thiosulphate solution.

A weighed quantity (about 2 c.cs.) of acetone is made up to 500 c.cs. with water. 15 c.cs. of this solution are shaken with 50 c.cs. of approximately normal caustic potash in a 250-c.c. stoppered flask. About 100 c.cs. of $\frac{N}{10}$ iodine solution are then run in from a burette, and the mixture shaken for ten minutes. It is then acidified with about 50 c.cs. of approximately normal sulphuric acid. The excess of iodine which is thereby liberated is titrated with $\frac{N}{10}$ thiosulphate; this amount deducted from the quantity of iodine originally added gives the amount of iodine used.

$$1 \text{ c.c. of } \frac{N}{10} \text{ iodine} \equiv 0{\cdot}000968 \text{ gm. acetone.}$$

Example.

	Weight of acetone	= 2·0 gms.
	Volume of acetone solution	= 15 c.cs.
	,, $\frac{N}{10}$ iodine added	= 82·5 c.cs.
	,, $\frac{N}{10}$ thiosulphate	= 21·0 c.cs.
∴	,, $\frac{N}{10}$ iodine used up	= 61·5 c.cs.

∴ Wt. of acetone in 15 c.cs. solution = 61·5 × 0·000968 gm.

$$\text{,,} \quad \text{,,} \quad 500 \text{ c.cs. solution} = \frac{61{\cdot}5 \times 0{\cdot}000968 \times 500}{15} \text{ gms.}$$

$$\therefore \% \text{ Acetone} = \frac{61{\cdot}5 \times 0{\cdot}000968 \times 500 \times 10}{15 \times 2}$$
$$= 99{\cdot}38.$$

2. *Gravimetrically.*—Mercuric sulphate combines with aliphatic ketones to give insoluble precipitates which, when dried *in vacuo*, have the general formula $(2HgSO_4.3HgO).4COR_2$. These compounds have such high molecular weights that very small quantities of the ketone suffice.

5 gms. of mercuric oxide are dissolved in 120 c.cs. of cold 30% sulphuric acid. 25 c.cs. of this solution and 25 c.cs. of the acetone solution, containing about 0·05 gm. of acetone are placed in a strong glass bottle of about 200 c.cs. capacity. The glass stopper is wired in, and the bottle heated to 100° in a water bath for 10 minutes. When cold, the whole is

filtered through a weighed filter paper, and the residue washed with cold water, dried *in vacuo* for 12 hours and weighed.

Wt. of acetone = weight of precipitate × 0·0584.

Example.

Wt. of acetone in 25 c.cs. of water = 0·052 gm.
„ precipitate = 0·886 „
∴ „ acetone = 0·886 × 0·0584
= 0·0517 gm.

$$\therefore \ \% \text{ acetone} = \frac{0{\cdot}0517 \times 100}{0{\cdot}052}$$

$$= 99{\cdot}4.$$

See Methods of Analysis, Association Official Agricultural Chemists, p. 195 ; also p. 492 (Oxime Method).

Estimations using Potassium Bromate

The method depends on the direct bromination of a substance by means of nascent bromine liberated from potassium bromate and potassium bromide in hydrochloric acid solution.

$$5KBr + KBrO_3 + 6HCl = 6KCl + 6Br + 3H_2O.$$

Excess potassium bromide and hydrochloric acid is added to a solution of the substance to be estimated ; and the bromate, in the form of a volumetric solution (usually N/5) is run in. The end point, (shown by the presence of free bromine) is detectable, quite sharply, by spotting on starch iodide paper as external indicator. Alternatively, the end point may be determined by adding a known amount of bromate in excess, then potassium iodide, and titrating the liberated iodine with thiosulphate.

Preparation of N/5 Bromate Solution.—5·567 gms. (1/30) mol. of potassium bromate are dissolved in water to 1,000 c.cs. 25 c.cs. are withdrawn, diluted to 200 c.cs. with water, 3–5 gms. of potassium bromide (free from bromate), 3–5 gms. potassium iodide (free from iodate) and 5 c.cs. conc. hydrochloric acid (free from chlorine or iron) added. The liberated iodine is titrated with thiosulphate in the usual way, and the bromine equivalent of the bromate solution thus obtained.

The reagent is particularly suitable for the determination of amines and phenols and their derivatives, and also for unsaturated compounds. Temperature has a marked effect on the rate and on the extent of bromination. It is necessary to know or to determine what bromo compound is being formed.

In the case of amines and phenols, bromine enters the ring in the ortho- or para-position ; if there is no unoccupied ortho- or para-position bromination does not take place except when this position is occupied by a carboxyl or sulphonic group, and in such cases the group is split off and replaced by bromine.

General Procedure.—Dissolve 0·2–0·5 gm. of the compound to be estimated in 200 c.cs. of water, using a slight excess of hydrochloric acid for amines or a similar excess of caustic soda in the case of phenols, carboxylic- and sulphonic-acids. To the solution thus prepared 10 c.cs. of a 20% solution of potassium bromide and 5–10 c.cs. of concentrated hydrochloric acid are added ; the mixture is brought to the required temperature and N/5 bromate solution run in slowly until a sample withdrawn gives a reaction on starch-iodide paper. The presence of free bromine should be again tested for after 5 minutes.

Examples.—Aniline is rapidly tribrominated at room temperature, the end point is very sharp, and this estimation of aniline is preferable to the nitrous acid method. At ordinary temperature ortho- and para-toluidines are dibrominated and meta-toluidine is tribrominated. Dimethylaniline is monobrominated at 0°–5°, dibrominated at 40°–50° and tribrominated at 60°–70°, an interesting example of the effect of temperature. Sulphanilic acid at 60°–70° yields tribromoaniline, and at this temperature *p*-nitroaniline reacts quantitatively. Phenol at about 22° yields tribromophenol. For reference to the estimation of *m*-diamines, *m*-dihydroxy compounds, R salt, cresols, *p*-nitroaniline, diphenylamine, *p*-nitrophenol, and other notes, see J. S. C. I., 41, 161.

Estimation of Formic Acid

This acid can be estimated by reduction of mercuric chloride (*a*) volumetrically (*b*) gravimetrically (Abs., 1923, ii, 95), or by reduction of potassium permanganate (Abs., 1906, ii, 907). In presence of homologues it can be estimated by the method given in Abs., 1912, ii, 499, the total acidity being determined by titration with alkali and the formic acid by reduction of permanganate. See also, Methods of Analysis, Association Official Agricultural Chemists, p. 535.

PART IV

CHAPTER XLI

INORGANIC SECTION

REAGENTS

Sulphuric Acid.—The acid used in the laboratory is the commercial 96–98% acid. The 100% acid (monohydrate) can be made from this by adding the requisite amount of oleum (see p. 320). Usual impurities: lead or iron sulphate and oxides of nitrogen.

Oleum.—Oleum is supplied in all strengths up to 70% free SO_3. From 0–40% free SO_3 it is liquid; from 40–60% free SO_3 it is solid; from 60–70% free SO_3 it is liquid; above 70% it is solid. The acid should be kept in well-stoppered, stout glass bottles, and when it is necessary to melt the acid, the stopper is withdrawn, a watch-glass placed on the mouth of the bottle, and the bottle placed on a layer of sand in a large vessel or oil bath which is warmed with a small flame. The bottle is fitted with a wash-bottle attachment, and any desired quantity is forced out by gentle air pressure from hand or foot bellows (the mouth must not be used). For the preparation of oleum of definite strengths, see p. 320. Usual impurities: ferric sulphate, sulphur dioxide and lead sulphate. For estimation, see p. 319.

Hydrochloric Acid.—The pure concentrated aqueous acid contains about 33% HCl. The commercial acid containing about 30% HCl serves for most organic preparations. The yellow colour is due to iron. Usual impurities: chlorine, sulphuric acid and iron.

Hydriodic Acid.—Both the conc. acid and the acid of constant boiling point (D. 1·7, 57% HI (see p. 514)) are on the market. Usual impurity: iodine.

Hydrofluoric Acid.—Commercial strength varies from 50–98%. Anhydrous acid (B.P. 19°) is also available. Usual impurities: sulphuric acid, fluorosulphonic acid, fluosilicic acid, iron, lead, arsenic.

Nitric Acid.—The commercial conc. acid generally contains about 70% HNO_3. Synthetic nitric acid (see p. 522) containing up to 99% HNO_3 (D. 1·5) is available commercially. Usual impurities: oxides of nitrogen, sulphuric acid, hydrochloric acid, chlorine and iodine.

Phosphoric Acid.—The commercial acid (D. 1·5) contains 65% H_3PO_4; syrupy phosphoric acid contains about 90% H_3PO_4. Usual impurities: sulphuric acid, iron and arsenic acid.

Anhydrous Aluminium Chloride.—It is best to buy this reagent from a reliable manufacturer. As a high pressure frequently exists in bottles containing this reagent, such bottles should be opened with care, a cloth being wrapped round the vessel during the operation. If the commercial product is not available, it may be prepared (see p. 514). Contains adsorbed hydrogen chloride up to 9 c.cs. per gm. (C J. R., 1, 400); absorbs moisture very readily.

Titanous chloride comes on the market in the form of a 15% solution (see p. 494). Usual impurities: oxidation products. For the many reducing reactions in which titanous chloride is used it may be replaced by titanous sulphate (obtainable as 15% solution), which should be used when there is possibility of chlorination.

Copper Bronze.—This product can be used for the Gattermann reaction (p. 72) in place of copper powder (p. 515). The bronze should be washed with ether to remove oil and grease.

Zinc Dust.—Commercial varieties vary much in character and are subject to deterioration; they contain usually 90–95% **Zn** (for estimation, see p. 518). It should be preserved in airtight vessels and should be occasionally analysed. Usual impurities: zinc oxide, iron and arsenic.

Caustic soda.—This is supplied in powder, stick, flake and pellet forms, the last two being convenient in use. The pure variety comes on the market in the form of sticks. In weighing out a quantity the sticks should not be handled. Pieces of a desired size can be broken off by elevating one end and dealing a sharp blow with a knife or file at the desired point. The same remark applies to caustic potash sticks. 30–40% solutions of caustic soda are available in commerce. Usual impurities: chloride, carbonate, and chlorate of sodium.

Ammonia.—A solution, D. 0·88, containing 35% **NH_3** comes on the market. Cylinders of anhydrous liquid ammonia are also available.

Sodium Nitrite.—The commercial product contains 97–98% **$NaNO_2$**, and is suitable for most organic reactions. For estimation, see p. 499. Usual impurity: sodium nitrate.

Sodium Sulphide (Na_2S, $9H_2O$).—The commercial variety consists of deliquescent crystals. It can be used for most purposes. Usual impurities: polysulphides and sulphate. For evaluation, see p. 520.

Sodium Bisulphite (see p. 517).—This is available commercially in the solid form, and as a 30% solution. The product as prepared on p. 517 is the most reactive in many cases. Usual impurity: bisulphate.

Sodium Hypochlorite (see p. 519).—The commercial solution (about 15%) is available. Usual impurities: caustic soda, sodium chloride and sodium chlorate.

Iron Filings and Iron Powder.—These are recommended for many operations in place of zinc and tin, on account of cheapness. Usual impurities: oxides.

Stannous Chloride.—The product should be obtained from a reliable firm. It should be frequently estimated, as it deteriorates through oxidation (see p. 521).

Tables of the gravities and strengths of some reagents are given on pp. 522-524.

Indicators

1. **Litmus Paper.**—Used as an indicator for all weak and strong acids and bases. Turned red by acids and blue by alkalis. Range: *p*H 5·0–8·0.

4–5 gms. litmus are dissolved in 1 litre of water. For red litmus a few drops of acetic acid are added and for blue litmus, ammonia ; good quality filter paper is soaked in the solution and dried by hanging on threads. It is then cut into small pieces.

2. **Phenolphthalein Paper.**—Used in acidimetry and alkalimetry. Turned red by alkalis, reacting with ammonia and sodium carbonate, but not with bicarbonate. Range : *p*H 8·3–10·0.

0·5 gm. of phenolphthalein is dissolved in 500 c.cs. of hot water, and filter paper is soaked in the hot solution and dried.

A few drops of a very dilute alcoholic solution may be used as an internal indicator.

3. **Congo Red Paper.**—Used as an indicator for acids. Turned pure blue by mineral acids and violet by strong organic acids. Range : *p*H 3·0–5·0.

1 gm. Congo Red is dissolved in 1 litre of water to which a few drops of ammonia have been added. Filter paper is soaked in the warm solution and dried in an atmosphere free from fumes.

4. **Brilliant Yellow Paper.**—Used as an indicator for alkalis. Turned red by alkalis, alkali carbonates and ammonia. Range : *p*H 6·4–9·4.

1 gm. of the dye is dissolved in 1 litre of water and filter paper dipped in the solution and dried.

The alkali salts of phenols and naphthols also give an alkaline reaction, so that free alkali must be tested for in the following way. A crystal of ammonium chloride is added to a few drops of the solution placed on a watch-glass, and the latter warmed with a very small flame. Another watch-glass with a piece of moistened red litmus paper adhering to its concave side is placed over the other one, and if the liquid is alkaline the litmus paper will be turned blue. This method can also be used where the colour or solubility of the substance to be tested prohibits the direct use of test papers.

5. **Thiazole Paper (Mimosa Paper).**—Used as an indicator for free alkali and is preferable to turmeric. Turned red by alkalis, but not by ammonia even in high concentrations. Range : *p*H 12·0–13·0.

Prepared similarly to Congo Red paper, the dye thiazole yellow (Clayton Yellow) being employed.

6. **Starch-Iodide Paper.**—Used as an indicator for nitrous acid, and for halogens and other oxidising agents. Turned bluish-violet by a trace of oxidising agent and brown by excess.

10 gms. of pure starch are ground up with 100 c.cs. of cold water and the mixture poured slowly into 2 litres of boiling water with good stirring. The whole is boiled for a few minutes, then cooled rapidly. 2 gms. of potassium iodide are added and 1 gm. of cadmium iodide. When all is dissolved, filter paper is immersed, drained, and dried in an atmosphere free from fumes.

The solution does not keep and should be freshly prepared.

The solution may be used as an indicator by " spotting " on filter paper.

When the paper is used, a drop of the test solution is removed on a glass rod, and *lightly* drawn across the paper.

The papers should be tested from time to time by treating with a 1% solution of hydrochloric acid containing 1 drop of very dilute sodium nitrite solution.

7. **Lead Acetate Paper.**—Used for detecting H_2S, with which it gives a brown coloration. Filter paper is soaked in a solution of 5 gms. lead acetate (or nitrate) per litre, and dried in an atmosphere free from H_2S. Ferrous sulphate paper may also be used for detection of H_2S, but does not keep.

8. **Methyl Orange.**—Used as an internal indicator in acidimetry and alkalimetry. Turned red with acid and yellow with alkali. Can be used in the presence of carbonates to detect free alkali. Is acted upon by bicarbonate. Range : *p*H 2·9–4·6.

1 gm. of methyl orange is dissolved in 1 litre of water.

9. **Methyl Red.**—Used as an internal indicator like methyl orange, but more sensitive, giving similar colour change. Range : *p*H 4·2–6·3.

1 gm. of methyl red (water soluble) is dissolved in 1 litre of water.

10. **Bromophenol Blue.**—Used in acidimetry and alkalimetry. Change, yellow to violet. Range : *p*H 2·8–4·6.

Note.—All test papers and solutions should be preserved in well-stoppered bottles.

Booklets may be purchased containing indicator papers which give a close approximation to the *p*H of a solution. Each booklet carries a reproduction of the colour assumed by the indicator at various *p*H values, against which the colour produced by the solution may be matched. Thus, the " Universal " test papers cover the range *p*H 1 to 10 in unit steps ; other indicator papers are now available for colour matching at intervals of 0·3 *p*H unit.

Inorganic Preparations, etc.

Chlorine.—Manganese dioxide is placed in a flask and just covered with conc. hydrochloric acid. On heating, a regular current of chlorine is obtained which is passed through water and through conc. sulphuric acid. Chlorine can also be prepared by heating a mixture of conc. hydrochloric acid (5 parts) with ground potassium dichromate (1 part). Another convenient method, which does not necessitate the use of heat, consists in treating good bleaching powder—cubes consisting of bleaching powder and plaster of Paris are sold for this purpose—with conc. hydrochloric acid.

Bromine.—When nascent bromine is required, a mixture of sodium bromide and bromate is added to the solution of the substance. The quantity of hydrochloric or of sulphuric acid required by the following equation is then added.

$$5NaBr + NaBrO_3 + 6H_2SO_4 = 6NaHSO_4 + 3H_2O + 6Br.$$

For most purposes commercial bromine is used, although this form sometimes contains as much as 10% of impurities, the chief of which is bromoform. It may be purified by shaking with conc. sulphuric acid.

Hydrochloric Acid.—Gaseous hydrochloric acid is conveniently prepared in a Kipp apparatus charged with fused ammonium chloride in lumps, and conc. sulphuric acid.

The most convenient method is to run concentrated hydrochloric acid from a dropping funnel (drawn to a capillary) underneath conc. sulphuric acid contained in a suction flask or other suitable vessel. (In. S., I, 147.)

Hydrobromic Acid.—Sulphur dioxide is passed on to the surface of a mixture of 35 c.cs. bromine and 200 c.cs. ice-water until a uniform pale yellow solution remains, which is distilled.

$$SO_2 + Br_2 + 2H_2O = 2HBr + H_2SO_4.$$

The distillate which may contain traces of sulphuric acid is redistilled over barium bromide. When large quantities are required, it is advisable to pass sulphur dioxide into a mixture of crushed ice and bromine until a uniform pale yellow solution is obtained. (C. V., I, 26.)

In. S., 1, 149, gives preparation from tetralin and bromine.

Hydriodic Acid.—11 parts by weight of iodine are placed in a small round-bottomed flask, and 1 part of yellow phosphorus, cut into small pieces and dried, is gradually added. The addition of each piece causes a flash of light and the contents of the flask become liquid. When all the phosphorus has been added, solid phosphorus tri-iodide separates on cooling. The product is treated with 1½ parts of water and, when gently heated, evolves hydrogen iodide, which is passed over some red phosphorus moistened with a little water in a U-tube. Heating is continued until the liquid just becomes colourless ; otherwise, if heating is continued further, phosphine and phosphonium iodide are formed, which may cause explosion. If a solution of hydriodic acid is required, the gas is led through an inverted funnel into a small quantity of cold water. This solution, if dilute, may be concentrated by distillation. At 127° a solution of constant boiling point passes over, containing 57% of hydrogen iodide and of density 1·70. (In. S., I, 157.)

For methoxyl and ethoxyl group estimations (p. 490) hydriodic acid (B.P. 127°) is distilled over phosphorus in a current of carbon dioxide.

Ammonia.—Ammonia gas can be conveniently obtained by gently heating conc. ammonium hydroxide solution (D. 0·88) which contains 35% of the gas. This is dried by passing it over quicklime or soda-lime.

A very convenient method consists in dropping conc. ammonia solution on to solid caustic potash or soda packed in a drying tower or in a flask. If a relatively large quantity of alkali is used the gas evolved is dry.

Zinc-Ammonium Chloride ($ZnCl_2.2NH_3$).—This compound is formed by passing a current of dry ammonia gas into molten zinc chloride. It can also be obtained by passing the gas over pulverised anhydrous zinc chloride. This compound gives up ammonia on heating and is used in place of the concentrated solution in certain reactions (p. 309).

Anhydrous Aluminium Chloride.—Aluminium shavings are freed from oil by boiling with alcohol, and then dried in an air bath at 120°. These are then packed in a thoroughly dry, hard glass tube, and kept in position by asbestos plugs. To one end of the tube is attached a drying apparatus consisting of two sulphuric acid wash-bottles. To the other end is attached a receiving apparatus in the form of a wide-mouthed bottle, which is closed with a cork suitably bored to admit the hard glass tube and a calcium chloride tube. The air is displaced from the apparatus by passing a stream of hydrochloric acid from a Kipp apparatus through the drying apparatus. This is accomplished when the gas issuing from the calcium chloride tube of the receiver is completely soluble in water. The hard glass tube is heated in a small furnace, or by means of a few Ramsay burners, the heating being gradual at first, and commencing at the end nearer the hydrochloric acid generator. White vapours of aluminium chloride condense in the receiver, and it is necessary to maintain a rapid current of hydrochloric acid. The reaction is finished when there is only a small dark-coloured residue of aluminium left in the tube. The aluminium chloride should be preserved in well-stoppered bottles (see p. 510), or in a desiccator. Aluminium chloride of reliable quality can now be purchased.

Cuprous Chloride.—To 100 gms. crystallised powdered copper sulphate and 28 gms. common salt in 320 c.cs. hot water, 22 gms. sodium bisulphite and 15 gms. sodium hydroxide in 160 c.cs. water are added, with shaking during 5 to 10 minutes. The mixture is cooled, decanted, and the precipitate of cuprous chloride washed by decantation with water. The white precipitate (wet) is dissolved in a mixture of 110 c.cs. conc. hydrochloric acid and 40 c.cs. water in a flask, corked to minimise oxidation. (In. S., II, 1.)

Cuprous Bromide.—100 gms. of crystallised copper sulphate, 288 gms. potassium bromide, 640 c.cs. of water, 610 gms. of copper turnings, and 88 gms. of conc. sulphuric acid are boiled until the whole is decolorised. The solution is decanted from unchanged copper.

Sodium Plumbite.—To 25 gms. lead acetate dissolved in 200 c.cs. distilled water are added 60 gms. sodium hydroxide in 100 c.cs. distilled water. The mixture is heated on a steam bath for 30 minutes, diluted to 1 litre with distilled water and stored in a stoppered bottle. It should be filtered if necessary before use.

Lead Dioxide.—100 gms. of bleaching powder are shaken up with 1,500 c.cs. of water and filtered. The filtrate is added gradually to a hot solution of 50 gms. lead acetate in 250 c.cs. of water ; the addition is continued until the precipitate turns dark brown, and until no precipitate is formed by further addition of bleaching powder solution to a filtered test portion. The liquid is decanted, and the precipitate washed several times with water, then filtered and washed with water. It is preserved in a well-stoppered bottle in the form of a thick paste.

Evaluation.—0·5 to 1 gm. of the paste is treated (with cooling) with hydrochloric acid (approximately 15% solution). The chlorine liberated on heating is passed into a solution of 4 gms. of potasium iodide in water, and the iodine liberated is titrated with $\frac{N}{10}$ sodium thiosulphate. 1 c.c. of this thiosulphate solution is equivalent to 0·012 gm. of pure lead peroxide.

Copper Powder.—100 gms. of crystallised copper sulphate are dissolved in 350 gms. of water in a beaker, to which is attached a mechanical agitator. After cooling to laboratory temperature, the stirrer is set in motion, and 35 gms. (or more if necessary) of good quality zinc dust are gradually added until the solution is decolourised. The precipitated copper is washed by decantation with water. Dilute hydrochloric acid is added to the precipitate (to remove excess zinc), and agitation continued until evolution of hydrogen ceases. The powder is filtered off and preserved in a moist condition in a stoppered bottle.

Sodium Amalgam.—*Weighing of Sodium.*—A lump of sodium is removed from a storage bottle and the surface cleaned with a knife. The bright lump is covered with petroleum ether (60°–80°) in a porcelain dish, and cut into small pieces. A second dish (or beaker) containing petroleum ether is weighed. Small lumps of sodium are removed from the first dish, quickly dried with filter paper, and added to the second until the required weight of sodium is obtained.

Sodium amalgam is usually made to contain 2½% of sodium, as such a product is solid and easily pulverised.

Pure dry mercury is placed in a porcelain mortar and warmed in an oven to 60°–70°. It is then removed to a fume cupboard, and the metallic sodium removed a piece at a time from the petroleum ether, quickly dried with filter paper, and plunged under the surface of the mercury with a pointed glass rod. The hand should be covered with a towel during the operation. When preparing a large quantity of amalgam it is advisable to place only a portion of the mercury in the mortar at first, and to charge this with sodium before adding another portion of mercury to the contents. Proceeding in this way, the sodium dissolves quietly, and there is practically no spluttering with the second or later instalments of mercury. For a pure amalgam possessing special properties, see B., 61, (B), 876. See also O. S., VII, 89; In. S., I, 10.

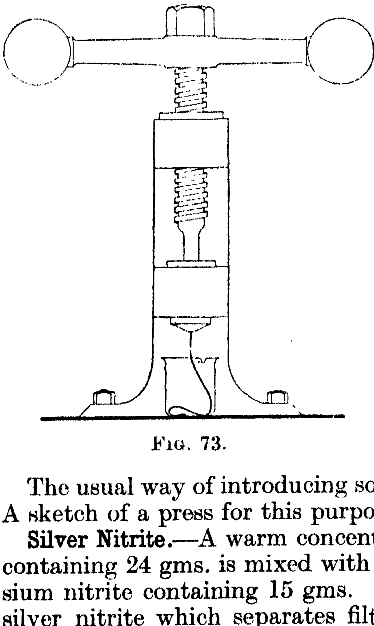


FIG. 73.

The usual way of introducing sodium into a liquid is in the form of wire. A sketch of a press for this purpose is shown in Fig. 73.

Silver Nitrite.—A warm concentrated aqueous solution of silver nitrate containing 24 gms. is mixed with a warm concentrated solution of potassium nitrite containing 15 gms. The mixture is allowed to cool and the silver nitrite which separates filtered off, purified from silver oxide by crystallisation from water at 70°, washed with water and dried.

Sodium Ethoxide (or Ethylate).—100 c.cs. of absolute alcohol are placed in a flask and clean metallic sodium in small strips added until it no longer dissolves. Gentle heat is then applied to effect solution of the last particle of metal. The excess of alcohol is then distilled off up to 200°, and the dry residue warmed for some time in a current of hydrogen. It is then preserved in a well-stoppered bottle.

It is not always necessary to isolate the solid sodium ethoxide, the alcoholic solution being sufficient for most purposes.

A very reactive sodium ethylate can be obtained by adding the calculated quantity of absolute alcohol diluted with 2 vols. of dry xylene to granulated sodium under xylene (see below). During the addition the whole is well cooled and shaken. The xylene is then distilled off in a current of dry hydrogen.

Alcoholic Potash.—*Method I.*—10 gms. of caustic potash sticks are dissolved in an equal quantity of water and diluted with absolute alcohol to 400 c.cs. The solution is agitated with 10 gms. of anhydrous sodium sulphate until clarified, after which the clear solution is decanted.

Method II.—15 gms. of caustic potash sticks are agitated with 500 c.cs. of 90% alcohol at ordinary temperature until dissolved. After settling, the clear solution is decanted.

When the solution is required for analytical purposes, caustic potash " purified from alcohol " should be employed. The solution is standardised with hydrochloric acid, using phenolphthalein as indicator.

Granulated Sodium.—1 part of sodium is covered with 10 parts of dry xylene and heated to 120°. The flask is then corked and wrapped in a thick dry cloth and well shaken for a short time. The metal is thus obtained in the form of a powder. No more than 20 gms. of sodium should be granulated at one time. A dry bucket should be kept at hand to drop the flask into in case of breakage. (B., 21, 1464 ; 35, 3516 ; J. pr., [2], 54, 116 ; O. S., XIII, 23 ; XX, 7.)

Anhydrous Sodium Acetate.—Crystallised sodium acetate ($CH_3.COONa. 3H_2O$) is heated in a basin over a small flame. The salt melts and for some time steam is evolved until all the water of crystallisation is driven off, at which stage the mass becomes solid. The flame is then increased, and heating continued until the mass melts again. Care must be taken not to char the product by using too large a flame. On cooling, the mass solidifies ; it is broken up into small lumps and preserved in a stoppered bottle.

Anhydrous Zinc Chloride.—Crystallised zinc chloride is fused in a porcelain basin for a short time until no more steam is evolved, then cooled and broken up into small pieces which are preserved in a well-stoppered bottle.

Sodium Bisulphite.—Sodium carbonate is covered with a layer of water—insufficient to dissolve it—and sulphur dioxide is passed into the mixture. After a time the solid disappears and an apple-green solution remains which smells strongly of sulphur dioxide. Sulphur dioxide may be obtained from a siphon of the liquid or generated by the action of conc. sulphuric acid on sodium sulphite.

Sodium bisulphite solution may be obtained by dissolving the sodium bisulphite in water, but the solution so prepared does not act so readily with aldehydes and ketones as the syrupy apple-green solution described above. A freshly-prepared solution should always be used for aldehydes and ketones for which a saturated solution of sodium metabisulphite ($Na_2S_2O_5$) is also applicable.

Sodamide.—This is prepared by the action of ammonia gas on sodium heated to 300°–400°. For the preparation of quantities of 20 gms. or more the most convenient apparatus consists of some form of closed iron pot provided with inlet and outlet tubes for ammonia. The apparatus, Fig. 37, or an autoclave from which any copper fittings have been removed, can easily be adapted to suit the purpose. If the apparatus is free from rust, the sodium may be placed directly on the bottom of the pot. Or, it may be contained in a large nickel or iron crucible. Before commencing to heat, the air should be displaced from the pot by ammonia, after which the temperature is raised to and maintained at 300°–400° while a current of the dry gas is passed over the molten metal. The reaction takes place readily. If, after cooling and opening the pot, any soft lumps of sodium remain on the surface, these can be picked out with a knife, or else the apparatus may be closed again and more ammonia passed over the heated metal. The sodamide forms a hard mass which is chipped out with a knife or chisel. It is now available commercially and should be preserved in stoppered bottles. (O. S., XX, 86 ; In. S., I, 74 ; II, 128.)

Sodamide can be dangerous (see O. S., XX, 90 ; *Organic Preparations*, Weygand, p. 409). When exposed to limited amounts of air, as in badly-sealed containers, it may give rise to highly-explosive products generally coloured yellow or brown. These should be destroyed by covering with benzene and adding aqueous alcohol while stirring.

The preparation on a small scale of sodamide, described in *Organic Reactions*, Vol. 1, Adams, p. 98, from metallic sodium and liquid ammonia has the advantage over the foregoing method in that the amide can be prepared in the same flask in which the subsequent reaction is performed ; the method is recommended.

Evaluation of Zinc Dust.—0·5 gm. of zinc dust is quickly weighed out and placed in a *dry* 250-c.c. graduated flask and 50 c.cs. of saturated solution of ferric alum added. The flask is stoppered and vigorously shaken until the zinc dust disappears. The reaction is represented by the equation :

$$Zn + Fe_2(SO_4)_3 = ZnSO_4 + 2FeSO_4.$$

25 c.cs. of conc. sulphuric acid are then added gradually, cooling being applied. When all the acid is added, the volume is made up to 250 c.cs. with distilled water. 50 c.cs. of this solution are then withdrawn and titrated with $\frac{N}{5}$ permanganate.

$$1 \text{ c.c. } \frac{N}{5} KMnO_4 \equiv 0{\cdot}00654 \text{ gm. Zn.}$$

Sulphur Monochloride (S_2Cl_2).—In a dry retort are placed 100 gms. of sulphur, which are melted by gentle heating. The retort is connected to a receiver having an exit tube. Chlorine, dried by passing through conc. sulphuric acid and fused calcium chloride, is passed into the melted sulphur. Sulphur monochloride distils over, and the passage of gas is continued until very little sulphur remains. The brownish-yellow liquid which collects is redistilled, the fraction 138°–139° being collected, and preserved in a sealed bottle.

Sulphuryl Chloride (SO_2Cl_2).—Dry sulphur dioxide is passed into a flask-containing camphor and cooled in water, until it liquefies and no more gas is absorbed. Dry chlorine is now passed until absorption is complete, when sulphur dioxide is again passed, and so on, until the volume of liquid no longer increases. The liquid is then distilled, the fraction up to 100° being collected. This is then fractionated, collecting the colourless liquid, B.P. 70°.

Dry chlorine and sulphur dioxide when passed into sulphuryl chloride containing activated carbon combine to give sulphuryl chloride. (J. Eng., 16, 279 ; In. S., I, 114.)

Thionyl Chloride ($SOCl_2$).—A mixture of carbonyl chloride and sulphur dioxide is passed over wood charcoal heated to above 200°. The liquid which distils is purified by distillation over dimethylaniline or quinoline. D. 1·677, B.P. 78·8°. (J. S. C. I., 45, 36 and 55.)

Lead Tetra-acetate.—To a mixture of 108 gms. glacial acetic acid and 36 gms. acetic anhydride in a 500 c.cs. 3-necked flask provided with mercury seal stirrer, are added 60 gms. dry red lead in small portions, the temperature being kept about 65°. When the conversion is complete, the mixture is cooled, filtered, and washed with glacial acetic acid and crystallised therefrom. M.P. 175°–180°; unstable in air.

$$Pb_3O_4 + 8CH_3COOH \longrightarrow Pb(OCOCH_3)_4 + 2Pb(OCOCH_3)_2 + 4H_2O.$$

(In. S., I, 47.)

Phosphorus Di-iodide (PI_2).—5 parts of phosphorus are dissolved in carbon disulphide, and to the well-cooled solution 41 parts of dry, powdered iodine are added. The carbon disulphide is then distilled off from the phosphorus di-iodide (*Care!*).

Phosphorus Trisulphide (P_2S_3).—The calculated quantities of dry amorphous phosphorus and sulphur are carefully melted together in a fireclay crucible. The product is then cooled and broken up.

Chlorosulphonic Acid (SO_3HCl).—A mixture of common salt and conc. hydrochloric acid is placed in a flask and hydrochloric acid gas produced by dropping conc. sulphuric acid on to it. The gas is dried and passed into fuming sulphuric acid in a retort until no further absorption takes place, cooling being applied to the retort, if necessary. The retort is then heated to 140°–153°, when chlorosulphonic acid distils over. A pure acid can be obtained, if necessary, by a further distillation, the fraction boiling at 149°–151° being retained. The yield is nearly theoretical. *N.B.*—The acid is severely corrosive to the skin and the vapour is poisonous. A dilute chlorosulphonic acid can be readily obtained by adding common salt to fuming sulphuric acid.

Fuming Nitric Acid.—This can be prepared by distilling 2 mols. sodium nitrate with 1 mol. conc. sulphuric acid at over 200°; or by distilling a mixture of strong nitric acid and conc. sulphuric acid. The addition of 3–5% starch is effective. Its specific gravity at 15° is 1·533.

Sodium Hypochlorite ($NaOCl$).—1. Excess of sodium carbonate is added to a solution of bleaching powder. The filtrate, after removing the $CaCO_3$, contains the available chlorine, and the solution can be kept for some time.

2. Chlorine gas is passed into a cold solution of sodium hydroxide until chlorination is almost complete. The solution is usually made to contain 14–15% available chlorine. (J. S. C. I., 18, 1096.)

Sodium Hyposulphite ("Hydrosulphite," $Na_2S_2O_4$).—SO_2 is passed into a strong solution of $NaHSO_3$ until saturated, and the mixture reduced with zinc dust.

$$NaHSO_3 + SO_2 + Zn = ZnSO_3 + Na_2S_2O_4 + H_2O.$$

Milk of lime is then added to precipitate **ZnO** and **$CaSO_3$**, and the liquor is saturated with salt at 50°, and cooled to crystallise the hyposulphite. By adding excess of sodium hydroxide to a conc. solution of the crystals at 50°, the anhydrous salt is precipitated as a powder, which may be filtered and washed with alcohol.

Various hyposulphite compounds are used for industrial purposes including stable aldehyde compounds. Of these the formaldehyde compound (Formosul) is the most important, since it is the reducing agent almost universally employed in applying vat dyes by *printing* methods to textile materials. The less stable sodium " hydrosulphite " is used in *dyeing* with vat dyes. Stable zinc compounds (Rongalite) are also on the market.

Ammonium Sulphite.—SO_2 from a siphon is passed in a vigorous stream into 2 parts of conc. ammonia solution (D. 0·880) and 1 part of ice, surrounded by a freezing mixture. The solution gradually assumes a light yellow colour. When no more SO_2 is absorbed, the solution is neutralised with conc. ammonia, giving a saturated solution of ammonium sulphite which sometimes deposits crystals on standing.

Sodium Sulphide ($Na_2S.9H_2O$).

Evaluation.—5 gms. sodium sulphide are dissolved in water up to 250 c.cs. and carefully neutralised with dilute acetic acid in presence of phenolphthalein until the latter is colourless. A $\frac{2}{5}$N solution of crystallised zinc sulphate (57·514 gms. $ZnSO_4.7H_2O$ per litre) is run in from a burette until all the soluble sodium sulphide is converted into zinc sulphide. A conc. solution of cadmium sulphate is spotted on thick blotting-paper, and a drop of the liquid being analysed is placed near it. A yellow stain will be produced as long as any soluble sulphide remains. The zinc sulphate is added until no yellow colour is given.

Example. Volume of zinc sulphate = 9·3 c.cs.

$$Na_2S \text{ in 25 c.cs.} = \frac{9{\cdot}3 \times 0{\cdot}078}{5} = 0{\cdot}1451 \text{ gm.}$$

$$\% \; Na_2S = \frac{0{\cdot}1451 \times 10 \times 100}{5} = 29{\cdot}02.$$

Carbonyl Chloride (Phosgene).—100% sulphuric acid, to which is added 2% dry ignited kieselguhr, is placed in a flask which is attached to a small reflux condenser and a dropping funnel. Carbon tetrachloride is placed in the funnel, and from the top of the condenser is led a delivery tube passing through an empty wash-bottle, and then under the surface of toluene contained in a Buchner flask, the side tube of which is led to a draught duct. The sulphuric acid is heated to 140°, when the carbon tetrachloride is allowed to drop slowly. After the reaction commences the temperature may be lowered to about 120°, and this temperature maintained by gentle heat. The carbonyl chloride passes over and is absorbed in the toluene, while the hydrogen chloride which is formed passes over. The whole operation should be conducted in a good draught chamber as phosgene is very poisonous.

$$2H_2SO_4 + 3CCl_4 \longrightarrow 3COCl_2 + 4HCl + S_2O_5Cl_2.$$

Nitrous Fumes.—Arsenious acid (As_2O_3) is broken into small pieces and placed in a flask with a two-holed cork, which carries a dropping funnel and a delivery tube. The delivery tube is connected to an empty wash-bottle surrounded by cold water to condense any nitric acid which passes over. Nitric acid (D. 1·3) is dropped in gradually from the funnel, while the flask is gently heated ; a stream of nitrous fumes is readily evolved.

Chromic Anhydride (CrO_3).—1·5 vols. of conc. sulphuric acid are added gradually, and with shaking, to 1 vol. of a saturated solution of potassium chromate. The mixture is allowed to cool, when the anhydride separates out as scarlet crystals. The crystals are filtered off, washed with a little nitric acid, and dried in a desiccator. The crystals are hygroscopic, and should be preserved in a well-stoppered bottle.

$$K_2CrO_4 + H_2SO_4 = K_2SO_4 + CrO_3 + H_2O.$$

Chromyl Chloride (CrO_2Cl_2).—A mixture of 4 parts sodium chloride, 5 parts potassium dichromate and 9 parts fuming sulphuric acid is placed in a retort and distilled until coloured liquid no longer passes over. The chromyl chloride is then redistilled (B.P. 116°). (In. S., II, 205.)

$$K_2Cr_2O_7 + 4NaCl + 3H_2SO_4.SO_3 = 2CrO_2Cl_2 + 2KHSO_4 + 4NaHSO_4.$$

Anhydrous Stannous Chloride.—Powdered stannous chloride (**$SnCl_2$, $2H_2O$**) is treated with an equal weight of acetic anhydride. Much heat is evolved and the anhydrous salt separates. When collected, and washed free of acetic acid with dry ether, it does not appear to be hygroscopic, and may be preserved indefinitely in a desiccator. It is readily soluble in acetone and in anhydrous methyl or ethyl alcohol ; insoluble in benzene or chloroform ; and it may be crystallised from acetic acid containing a little acetic anhydride. (For uses, see p. 241, and J. C. S., 1931, 82.)

Raney Nickel (Catalyst).—50 gms. aluminium are melted in a salamander (half clay, half graphite) crucible in a gas-fired furnace to a temperature of approximately 1000°. A layer of lithium chloride is added as flux. After further heating for 15 minutes to ensure superheating, 50 gms. nickel shot are added and heating continued for a few minutes. The reaction becomes violent and the crucible is removed from the furnace before premature ignition occurs. The alloy is allowed to cool in the crucible, washed with water, and dried with filter paper, and ground. The alloy in 2 to 4 gm. lots is added to 128 gms. caustic soda in 500 c.cs. water at 50° with good mechanical agitation for 30 minutes. The temperature is controlled at 50 ± 2° by rate of addition of alloy. When addition is complete, the temperature is maintained at 50° by heat if necessary for 50 minutes with gentle agitation. The catalyst is then washed several times with distilled water by decantation, then with absolute alcohol, and finally stored under alcohol. For full details, see Am. Soc., 68, 1471. For application, see Ann. Rep., 1945, 100.

Copper Chromite (Catalyst).—20 gms. barium nitrate are dissolved in 600 c.cs. water at 70° and 170 gms. copper nitrate added with stirring. until solution is complete. 10 gms. ammonium dichromate in 500 c.cs. water and 120 c.cs. conc. ammonia solution is then poured in with stirring The precipitate is filtered, dried at 110°, placed in a nickel pan covered with a watch glass, and heated in a muffle to 350°–450°. The residue is pulverised, stirred with a litre of 10% acetic acid, allowed to settle, and decanted. The acid treatment is repeated four times and the residue filtered, dried at 110°, and ground in a mortar. C.V.II, 142.

SPECIFIC GRAVITIES AND CONCENTRATIONS OF AQUEOUS ACID SOLUTIONS.

Hydrochloric		Nitric		Sulphuric		Acetic	
%	D.^{15}	%	D.^{15}	%	D.^{15}	%	D.^{15}
0·15	1·005	1·000	1·005	4.49	1·030	1.0	1·0007
2·14	1·010	1·90	1·010	10·19	1·070	5	1·0067
3·12	1·015	2·80	1·015	15·71	1·110	10	1·0142
4·13	1·020	3·70	1·020	20·91	1·150	15	1·0214
5·15	1·025	4·60	1·025	26·04	1·190	20	1·0284
6·15	1·030	5·50	1·030	31·11	1·230	25	1·0350
7·15	1·035	6·38	1·035	35·71	1·270	30	1·0412
8·16	1·040	7·26	1·040	40·35	1·310	35	1·0470
9·16	1·045	8·99	1·050	44·82	1·350	40	1·0523
10·17	1·050	9·84	1·055	50·11	1·400	45	1·0571
11·18	1·055	10·68	1·060	55·03	1·450	50	1·0615
12·19	1·060	11·51	1·065	60·65	1·510	55	1·0653
13·19	1·065	12·33	1·070	65·08	1·560	60	1·0685
14·17	1·070	13·95	1·080	70·32	1·620	65	1·0712
15·16	1·075	15·53	1·090	75·42	1·680	70	1·0733
16·15	1·080	17·11	1·100	80·68	1·740	75	1·0746
17·13	1·085	18·67	1·110	85·70	1·790	80	1·0748
18·11	1·090	22·30	1·120	90·05	1·820	85	1·0739
19·06	1·095	22·54	1·135	90·40	1·822	90	1·0713
20·01	1·100	24·08	1·145	91·00	1·825	91	1·0705
20·97	1·105	26·36	1·160	91·50	1·827	92	1·0696
21·92	1·110	28·63	1·175	92·10	1·830	93	1·0680
22·86	1·115	31·30	1·185	92·52	1·832	94	1·0674
23·82	1·120	32·36	1·200	93·05	1·834	95	1·0660
24·78	1·125	34·55	1·215	93·43	1·835	96	1·0644
25·75	1·130	36·78	1·230	94·20	1·837	97	1·0625
26·70	1·135	39·05	1·245	94·60	1·838	98	1·0604
27·66	1·140	41·34	1·260	95·00	1·839	99	1·0580
28·61	1·145	44·41	1·280	95·60	1·840	100	1·0553
29·57	1·150	46·72	1·295	95·95	1·8405		
30·55	1·155	49·07	1·310	97·00	1·8410		
31·52	1·160	52·37	1·330	97·70	1·8415		
32·49	1·165	55·79	1·350	98·20	1·8410		
33·46	1·170	58·48	1·365	98·70	1·8405		
34·42	1·175	61·27	1·380	99·20	1·8400		
35·39	1·180	63·23	1·390	99·45	1·8395		
		65·30	1·400	99·70	1·8390		
		67·50	1·410	99·95	1·8385		
		69·80	1·420				
		75·98	1·445				
		79·98	1·460				
		84·45	1·475				
		89·60	1·490				
		95·08	1·502				
		96·39	1·505				
		97·50	1·508				
		98·53	1·512				
		99·07	1·515				
		99·67	1·520				

SPECIFIC GRAVITIES AND CONCENTRATIONS OF AQUEOUS ALKALINE SOLUTIONS.

Caustic Soda		Caustic Potash		Ammonia	
%	D.^{15}	%	D.^{15}	%	D.^{15}
0·61	1·007	1	1·009	0·45	0·998
2·00	1·022	3	1·025	1·37	0·994
3·35	1·036	5	1·041	2·31	0·990
4·26	1·052	7	1·058	3·30	0·986
5·87	1·067	9	1·074	4·30	0·982
6·55	1·075	11	1·092	5·30	0·978
7·31	1·083	13	1·110	6·30	0·974
8·68	1·100	15	1·128	7·31	0·970
9·42	1·108	17	1·146	8·33	0·966
10·97	1·125	19	1·166	9·35	0·962
12·64	1·142	21	1·188	10·47	0·958
14·37	1·162	23	1·209	11·60	0·954
15·91	1·180	25	1·230	12·74	0·950
16·77	1·190	27	1·252	13·88	0·946
17·67	1·200	29	1·276	14·46	0·944
19·58	1·220	31	1·300	15·04	0·942
21·42	1·241	33	1·324	15·63	0·940
23·67	1·263	35	1·349	16·82	0·936
25·80	1·285	37	1·374	18·03	0·932
27·80	1·308	39	1·400	19·25	0·928
29·93	1·332	41	1·425	20·49	0·924
32·47	1·357	43	1·450	21·75	0·920
34·96	1·383	45	1·475	23·03	0·916
36·25	1·397	47	1·499	24·33	0·912
37·47	1·410	49	1·525	25·65	0·908
38·80	1·424	51	1·552	26·98	0·904
39·99	1·438	53	1·578	28·33	0·900
41·41	1·453	55	1·604	29·69	0·896
42·83	1·468	57	1·630	30·37	0·894
44·38	1·483	59	1·655	31·75	0·890
46·15	1·498	61	1·681	32·50	0·888
47·60	1·514	63	1·705	33·25	0·886
49·02	1·530	65	1·729	34·95	0·882
		67	1·754		
		69	1·780		

VAPOUR PRESSURES.

Vapour pressure of water at different temperatures				Vapour pressure of conc. KOH solution at different temperatures		
Temperature	Pressure	Temperature	Pressure	Temperature	40 gms. KOH : 100 c.cs. H_2O	49 gms. KOH : 100 c.cs. H_2O
	mms.		mms.		mms.	mms.
0°	4·6	16°	13·5	10°	6·5	5·6
2°	5·3	18°	15·4	12°	7·5	6·5
4°	6·1	20°	17·4	14°	8·4	7·3
6°	7·0	22°	19·7	16°	9·6	8·3
8°	8·0	24°	22·2	18°	10·9	9·5
10°	9·2	26°	25·0	20°	12·4	10·8
12°	10·5	28°	28·1	22°	13·9	12·1
14°	11·9	30°	31·6			

GAS REDUCTION TABLE.

Logarithm of the weight of 1 c.c. nitrogen at $t°$ and p mm.

$t°$ / p	15	16	17	18	19	20	21	22	23	24
720	05034	04883	04733	04583	04434	04285	04137	03989	03842	03695
721	05095	04944	04794	04644	04495	04346	04198	04050	03903	03756
722	05155	05004	04854	04704	04555	04406	04258	04110	03963	03816
723	05215	05064	04914	04764	04615	04466	04318	04170	04023	03876
724	05275	05124	04974	04824	04675	04526	04378	04230	04083	03936
725	05335	05184	05034	04884	04735	04586	04438	04290	04143	03996
726	05395	05244	05094	04944	04795	04646	04498	04350	04203	04056
727	05454	05303	05153	05003	04854	04705	04557	04409	04262	04115
728	05514	05363	05213	05063	04914	04765	04617	04469	04322	04175
729	05574	05423	05273	05123	04974	04825	04677	04529	04382	04235
730	05633	05482	05332	05182	05033	04884	04736	04588	04441	04294
731	05693	05542	05392	05242	05093	04944	04796	04648	04501	04354
732	05752	05601	05451	05301	05152	05003	04855	04707	04560	04413
733	05811	05660	05510	05360	05211	05062	04914	04766	04619	04472
734	05871	05720	05570	05420	05271	05122	04974	04826	04679	04532
735	05930	05779	05629	05479	05330	05181	05033	04885	04738	04591
736	05989	05838	05688	05538	05389	05240	05092	04944	04797	04650
737	06048	05897	05747	05597	05448	05299	05151	05003	04856	04709
738	06107	05956	05806	05656	05507	05358	05210	05062	04915	04768
739	06165	06014	05864	05714	05565	05416	05268	05120	04973	04826
740	06224	06073	05923	05773	05624	05475	05327	05179	05032	04885
741	06283	06123	05982	05832	05683	05534	05386	05238	05091	05944
742	06341	06190	06040	05890	05742	05593	05445	05297	05150	05003
743	06400	06249	06099	05949	05800	05651	05503	05355	05208	05061
744	06458	06307	06157	06007	05858	05709	05561	05413	05266	05119
745	06517	06366	06216	06066	05917	05768	05620	05472	05325	05178
746	06575	06424	06274	06124	05975	05826	05678	05530	05383	05236
747	06633	06482	06332	06182	06033	05884	05736	05588	05441	05294
748	06691	06540	06390	06240	06091	05942	05794	05646	05499	05352
749	06749	06598	06448	06298	06149	06000	05852	05704	05557	05410
750	06807	06656	06506	06356	06207	06058	05910	05762	05615	05468
751	06865	06714	06564	06414	06265	06116	05968	05820	05673	05526
752	06923	06772	06622	06472	06323	06174	06026	05878	05731	05584
753	06980	06829	06679	06529	06380	06231	06083	06935	05788	05641
754	07038	06887	06737	06587	06438	06289	06141	05993	05846	05699
755	07096	06945	06795	06645	06496	06347	06199	06051	05904	05757

GAS REDUCTION TABLE—*Continued.*

p \ t°	15	16	17	18	19	20	21	22	23	24
756	07153	07002	06852	06702	06553	06404	06256	06108	05961	05814
757	07211	07060	06910	06760	06611	06462	06314	06166	06019	05872
758	07268	07117	06967	06817	06668	06519	06371	06223	06076	05929
759	07325	07174	07024	06874	06725	06576	06428	06280	06133	05986
760	07382	07231	07081	06931	06782	06633	06485	06337	06190	06043
761	07439	07288	07138	06988	06839	06690	06542	06394	06247	06100
762	07496	07435	07195	07045	06896	06747	06599	06451	06304	06157
763	07553	07402	07252	07102	06953	06804	06656	06508	06361	06214
764	07610	07459	07309	07159	07010	06861	06713	06565	06418	06271
765	07667	07516	07366	07216	07067	06918	06770	06622	06475	06328
766	07724	07573	07423	07273	07124	06975	06827	06679	06532	06385
767	07781	07630	07480	07330	07181	07032	06884	06736	06589	06442
768	07837	07686	07536	07386	07237	07088	06940	06792	06645	06498
769	07894	07743	07593	07443	07294	07145	06997	06849	06702	06555
770	07949	07798	07648	07498	07349	07200	07052	06904	06757	06611
771	08005	07854	07704	07554	07405	07256	07108	06960	06813	06667
772	08062	07911	07761	07611	07462	07313	07165	07017	06870	06724
773	08118	07967	07817	07667	07518	07369	07221	07073	06926	06780
774	08147	08023	07873	07723	07574	07425	07277	07129	06982	06836
775	08230	08079	07929	07779	07630	07481	07333	07185	07038	06892
776	08286	08135	07985	07835	07686	07537	07389	07241	07094	06948
777	08342	08191	08041	06891	07742	07593	07445	07297	07150	07004
778	08398	08247	08097	07947	07798	07649	07501	07353	07206	07060
779	08454	08303	08153	08003	07854	07705	07557	07409	07262	07116
780	08509	08358	08208	08058	07909	07760	07612	07464	07317	07171

TABLE OF APPROXIMATE ATOMIC WEIGHTS
(O = 16)

Element		Approximate Atomic Weight	Element		Approximate Atomic Weight
Aluminium	Al	27	Lithium	Li	7
Antimony	Sb	121·5	Magnesium	Mg	24·5
Arsenic	As	75	Manganese	Mn	55
Barium	Ba	137·5	Mercury	Hg	200·5
Bismuth	Bi	209	Molybdenum	Mo	96
Boron	B	11	Nickel	Ni	58·5
Bromine	Br	80	Nitrogen	N	14
Cadmium	Cd	112·5	Oxygen	O	16
Caesium	Cs	133	Palladium	Pd	107
Calcium	Ca	40	Phosphorus	P	31
Carbon	C	12	Platinum	Pt	195
Chlorine	Cl	35·5	Potassium	K	39
Chromium	Cr	52	Silicon	Si	28
Cobalt	Co	59	Silver	Ag	108
Copper	Cu	63·5	Sodium	Na	23
Fluorine	F	19	Strontium	Sr	87·5
Gold	Au	197	Sulphur	S	32
Hydrogen	H	1	Tin	Sn	119
Iodine	I	127	Titanium	Ti	48
Iron	Fe	56	Vanadium	V	51
Lead	Pb	207	Zinc	Zn	65·5

CHAPTER XLII

TESTS FOR COMMON ORGANIC ACIDS, ALKALOIDS, CARBOHYDRATES

PRELIMINARY TESTS

I. Effect of Heat.—Heat about 0·25 gm. on a crucible lid—carefully at first, noting any odour evolved and whether the substance chars with or without melting. If the substance chars, as many organic compounds do, continue the heating, using the blowpipe if necessary, until all the carbon is burnt away. Note any flame tests.

Melts, vaporises, vapours may catch fire—oxalic, benzoic, or salicylic acid.

Chars and emits odour of burnt sugar—carbohydrate, tartrate.

Ammonia evolved—ammonium salt.

Coloured residue—salt of metal giving coloured oxide.

White residue—salt of metal giving white oxide or carbonate. Touch residue with moist litmus paper ; an alkaline reaction indicates presence of **Na, K, Li, Ca, Ba, Sr** or **Mg**.

Organic salts of **Hg, As,** and $\mathbf{NH_4}$ volatilise completely on ignition.

II. Heat in a Dry Test Tube.—Note evolution of odour or inflammable gas.

Cyanogen evolved, burns with a peach-coloured flame—cyanide of **Hg** or **Ag**.

Melts and forms a sublimate—oxalic, benzoic or salicylic acid.

Odour of benzene evolved—benzoate.

Odour of phenol evolved—salicylate.

Chars, emits odour of burnt sugar—carbohydrate, glucoside, tartrate.

Chars, evolves irritating fumes—citrate.

Chars, emits tarry odour—alkaloid.

III. Test Reaction of Substance to moist litmus and its Solubility in water.—Free acids and some acid salts—acidic.

Benzoic and salicylic acids—soluble on heating, crystallise on cooling.

Alkaloids—sparingly soluble, alkaline.

Alkaloid salts—usually soluble and acidic.

Starch—insoluble in cold, opalescent solution on boiling.

IV. Heat with dilute Sulphuric Acid.—Odour of formic acid, acetic acid—formates, acetates respectively.

Odour of hydrocyanic acid—cyanide, ferro- or ferri-cyanide.

Crystals, soluble in alkali, separate on cooling—benzoate, salicylate.

Precipitate after boiling and cooling—salicin.

V. Treat with conc. Sulphuric Acid.—If there is no apparent action, heat the mixture.

Deep red coloration in the cold—glucoside.

Odour of acetic acid on warming—acetate.

Charring with odour of burnt sugar on warming—carbohydrate, tartrate.

Carbon monoxide (test inflammability) on heating, no charring—formate, cyanide, ferrocyanide, ferricyanide.

Carbon monoxide and carbon dioxide (test with lime water) on heating, no charring—oxalate.

VI. Heat with Caustic Soda Solution.—Ammonia evolved—ammonium salt.

Substance (sparingly soluble in water) dissolves—benzoic, salicylic acid.

Substance (soluble in water) yields precipitate—salt of alkaloid.

Soluble, resinifies on warming—glucose, lactose.

VII. Heat with Soda-lime.—Grind about 0·5 gm. with 2 gms. soda-lime in a mortar. Transfer to small hard glass tube, cover with a layer of ground soda-lime and heat. Detect odour and inflammability of any gases evolved.

Ammonia evolved—ammonium salt, alkaloid.

Phenol evolved—salicylic acid, salicylate.

Benzene evolved—benzoic acid, benzoate,

Inflammable gas—formate, acetate, oxalate.

Organic Acids

Identification of these in many substances is facilitated by the preparation of their benzthiouronium salts (p. 452), their hydroxamic acids (p. 272) or their hydrazides, all of which have well defined melting points.

Preparation of Hydrazides.—These like the hydroxamic acids are prepared from esters. The ester (1 gm.) is dissolved in alcohol (2 c.cs.) and hydrazine hydrate (0·5 gm.) added. If the product does not separate in the cold, the mixture is heated under reflux until, on cooling, the hydrazide crystallises out.

$$RCOOR_1 + NH_2.NH_2 \longrightarrow RCONH.NH_2 + R_1OH.$$

Aqueous solutions of calcium chloride, ferric chloride or silver nitrate give precipitates or colorations with certain organic acids which are valuable for the detection of these acids. It is important to use neutral solutions of the acids which at the same time do not contain metallic radicles likely to react with the reagents added. Thus the addition of calcium chloride to a solution of lead acetate may produce a precipitate of lead chloride. A neutral solution, which should be of about 10% concentration, prepared as follows, usually avoids such complications :

Neutral Solution.—If the acid is combined with a metal other than an alkali metal or ammonia, about 2 gms. of the compound are boiled with 10 c.cs. concentrated sodium carbonate solution. Metals which would otherwise interfere during the tests with the above reagents will remain undissolved or be precipitated in the form of their hydroxides or carbonates. The precipitate is filtered off and examined for metals. The filtrate is acidified with a slight excess of nitric acid (testing with litmus), boiled to expel carbon dioxide, then made slightly alkaline with ammonia and finally boiled to expel this excess of ammonia. Portions of this neutral solution are taken for the appropriate tests. Neutral solutions from free acids are conveniently prepared by dissolving in a slight excess of ammonia and boiling off the latter.

Solubility of Salts.—The calcium salts of oxalic and tartaric acids are very sparingly soluble in cold water, calcium citrate is sparingly soluble in hot water. In some instances, as in the analysis of mixtures where an acid is present in low concentration, it may be advisable to add solid calcium chloride.

The ferric salts of benzoic, succinic, hydroferrocyanic, gallic and tannic acids are sparingly soluble in cold water, while basic ferric salts of formic and acetic acids formed on boiling are also sparingly soluble. Solutions of ferric thiocyanate and salicylate exhibit characteristic colorations.

A number of acids form sparingly soluble silver salts. Formates and tartrates reduce ammoniacal silver nitrate.

Oxalic, $COOH.COOH + 2H_2O$.—White crystalline solid. Loses $2H_2O$ at 100°, then melts and sublimes partly with decomposition, giving off CO_2 and $H.COOH$. Easily soluble in water and in alcohol.

Oxalic acid and oxalates give with :

Conc. H_2SO_4, on heating, usually no charring ; CO and CO_2 evolved.

Neutral solutions of oxalates give with :

1. $CaCl_2$, white precipitate—CaC_2O_4, soluble in HCl and HNO_3, almost insoluble in acetic acid.
2. $AgNO_3$, white precipitate—$Ag_2C_2O_4$, soluble in HNO_3 and ammonia.
3. $KMnO_4$ in warm dilute H_2SO_4 solution, decolorised and CO_2 given off.

Tartaric, $COOH.CH(OH).CH(OH).COOH$.

Colourless crystals. M.P. 167°–170°.

Readily soluble in water, moderately in alcohol, sparingly in ether.

Tartaric acid and tartrates :

1. On heating, charring takes place ; burnt sugar smell, and acid vapours evolved.
2. With conc. H_2SO_4, on heating, turn brown then black, and acid vapours evolved.

Neutral solutions of tartrates give with :

1. $CaCl_2$, white precipitate—$CaC_4H_4O_6$, usually only after vigorous shaking ; soluble in HCl, HNO_3 and, if precipitate has not assumed the crystalline form, in acetic acid.
2. $AgNO_3$, white precipitate—$Ag_2C_4H_4O_6$, soluble in HNO_3, and ammonia. Precipitate dissolved in minimum quantity of ammonia, with addition of crystal of $AgNO_3$, deposits silver mirror on gently heating.
3. Small crystal of $FeSO_3$, two drops of H_2O_2 solution, and making strongly alkaline (Fenton's reagent)—violet coloration.

Citric, $COOH.CH_2.C(OH)(COOH).CH_2.COOH + H_2O$.

Colourless crystals ; M.P. 100° (anhydrous acid, M.P. 153°) ; readily soluble in water and alcohol, sparingly in ether. On heating, melts and gives off water and acid vapours ; no smell of burnt sugar.

Citric acid and citrates, in the solid, on heating with conc. H_2SO_4 for 10 minutes at 90°–95° effervesce and give yellow solutions, which after dilution and making alkaline give red coloration with nitroprusside solution due to acetone or its carboxylic acid.

Neutral solutions of citrates give with :

1. $\mathbf{CaCl_2}$ on boiling, white precipitate—$\mathbf{Ca_3(C_6H_5O_7)_2}$; no precipitate in the cold.

2. $\mathbf{AgNO_3}$, white precipitate—$\mathbf{Ag_3C_6H_5O_7}$, soluble in ammonia. No mirror formed as in tartrates.

3. $\mathbf{Ca(OH)_2}$ on boiling, white precipitate—$\mathbf{Ca_3(C_6H_5O_7)_2}$, which redissolves on cooling.

4. 5 gms. $\mathbf{HgSO_4}$ are dissolved in dil. $\mathbf{H_2SO_4}$ (20 c.cs. conc. acid, 100 c.cs. water). A mixture of 1 c.c. of this solution with 5 c.cs. of dil. citrate solution decolourises dil. $\mathbf{KMnO_4}$ with formation of white ppt. (Denigès' test).

Benzoic $\mathbf{C_6H_5COOH}$.—white needles or scales ; M.P. 121° ; sparingly soluble in cold, fairly readily in boiling water ; readily soluble in alcohol and in ether. On heating, melts and volatilises.

All benzoates give benzoic acid with mineral acids.

On heating acid or salts with soda-lime, benzene evolved.

Conc. $\mathbf{H_2SO_4}$, on heating, dissolves ; no charring ; acid precipitated on dilution with water.

Neutral solutions of benzoates give with :

1. $\mathbf{CaCl_2}$, no precipitate even on addition of alcohol.

2. $\mathbf{FeCl_3}$, buff precipitate—$\mathbf{Fe(C_7H_5O_2)_3}$, soluble in **HCl** with liberation of benzoic acid.

3. **HCl**, free acid precipitated.

Succinic, $\mathbf{COOH.CH_2CH_2.COOH}$.—Colourless prisms ; M.P. 181° ; soluble in water, sparingly soluble in cold alcohol and ether.

On heating, with acetic anhydride, yields anhydride (see p. 271).

Succinates char at high temperature.

Conc. $\mathbf{H_2SO_4}$ added to succinates and heated, solution turns dark and sublimates forms on cold part of dry tube.

Neutral solutions of succinates give with :

1. $\mathbf{CaCl_2}$, no precipitate even on boiling.

2. $\mathbf{FeCl_3}$, brownish-red precipitate of basic ferric succinate easily soluble in **HCl**.

3. $\mathbf{BaCl_2}$ in presence of ammonia, white precipitate on addition of alcohol.

Formic, H.COOH.—Colourless liquid ; M.P. 8° ; B.P. 101°. Pungent odour ; vapour burns with blue flame. Miscible in all proportions with water, alcohol and ether.

Formates, when heated, evolve **CO**, yielding carbonates, oxides or metals.

Conc. $\mathbf{H_2SO_4}$, **CO** evolved on heating.

Neutral solutions of formates give with :

1. $\mathbf{FeCl_3}$, red coloration, which on boiling yields reddish precipitate of basic ferric formate.

2. $\mathbf{AgNO_3}$ in conc. solutions, white precipitate—$\mathbf{AgCHO_2}$, turning dark even in cold, owing to deposition of metallic silver. This decomposition of silver formate does not take place in presence of excess ammonia.

3. $\mathbf{HgCl_2}$, on warming, white precipitate—$\mathbf{Hg_2Cl_2}$, or grey precipitate of metallic mercury.

4. Formates or formic acid decolourise $KMnO_4$ solution.

5. Solutions of formates or formic acid, with few drops alcohol and few drops conc. H_2SO_4, on warming, give ethyl formate, recognised by sweet smell.

Acetic, $CH_3.COOH$.—Colourless crystals; M.P. 17°; B.P. 119°; characteristic odour; vapour burns with bluish flame; miscible in all proportions with water, alcohol and ether.

Acetates, when heated alone, give acetone; with conc. H_2SO_4, acetic acid.

Solid acetates with conc. H_2SO_4 and a few drops of alcohol, on heating, give ethyl acetate, recognised by pleasant odour.

Dry acetates mixed with a trace of As_2O_3, when heated, give vapours of cacodyl oxide, $As_2(CH_3)_4O$, recognised by smell (*caution!* vapours are very poisonous).

Neutral solutions of acetates give with:

1. $FeCl_3$, red coloration, which on boiling yields brownish precipitate of basic ferric acetate. The red colour is destroyed by HCl, but not by $HgCl_2$.

2. $AgNO_3$ in conc. solutions, white crystalline precipitate—$AgC_2H_3O_2$, soluble in hot water and in ammonia. Silver acetate is not reduced when the solution is boiled.

Hydrocyanic, HCN.—Colourless volatile liquid; B.P. 26°; burns with reddish-violet flame; soluble in water, alcohol and ether. Aqueous solution does not redden blue litmus.

Cyanides with conc. H_2SO_4, on heating, liberate **CO**.

Dilute HCl, in cold, liberates HCN, recognised by smell (*caution!*).

Solutions of cyanides give with:

1. $AgNO_3$, white precipitate—AgCN, insoluble in dilute HNO_3, soluble in ammonia and KCN solutions.

2. NaOH with few drops $FeSO_4$ and $FeCl_3$ solutions, acidified with HCl, precipitate of Prussian blue.

3. Yellow ammonium sulphide, on evaporation to dryness—thiocyanate, which gives with $FeCl_3$ in dilute HCl deep red colour.

Cyanic, HCNO.—Unstable liquid; smell similar to acetic acid.

Cyanates with HCl give CO_2 and NH_4Cl.

Aqueous solution of KCNO on standing gives NH_3, and K_2CO_3

Solutions of cyanates give with $AgNO_3$, white precipitate—AgCNO, soluble in ammonia; decomposed by acids with liberation of CO_2 and formation of an ammonium salt.

For conversion to urea, see p. 446.

Thiocyanic, HCNS.—Unstable liquid; salts are decomposed when heated.

Solid salts heated with H_2SO_4 yield CO_2, HCN and H_2S.

Solutions of thiocyanates give with:

1. $AgNO_3$, white precipitate—AgCNS, insoluble in dilute HNO_3, sparingly soluble in ammonia; also soluble in KCNS.

2. $FeCl_3$ to dilute solution, deep red coloration—$Fe(CNS)_3$, colour is unchanged by HCl, but destroyed by $HgCl_2$.

For conversion to thiourea, see p. 446.

Hydroferrocyanic, $H_4Fe(CN)_6$.—Colourless crystalline solid, readily soluble in water.

All ferrocyanides are decomposed by heat.

Conc. H_2SO_4, on heating, CO evolved.

Solutions of ferrocyanides give with :

1. $FeCl_3$, dark blue precipitate—Prussian blue, $Fe_4\{Fe(CN)_6\}_3$, insoluble in HCl, soluble in aqueous oxalic acid.
2. $FeSO_4$, pale blue precipitate, which rapidly darkens on exposure to air.
3. $AgNO_3$, white precipitate—$Ag_4Fe(CN)_6$, insoluble in dilute HNO_3 and in ammonia, soluble in KCN.
4. $CuSO_4$, brown precipitate—$Cu_2Fe(CN)_6$, insoluble in dilute acids.

Hydroferricyanic, $H_3Fe(CN)_6$.—Yellow crystalline solid, readily soluble in water.

All metallic ferricyanides are decomposed by heat.

Conc. H_2SO_4, on heating, CO and CO_2.

Solutions of ferricyanides give with :

1. $FeCl_3$, brown or dark green coloration.
2. $FeSO_4$, dark blue precipitate—Turnbull's blue, $Fe_3\{Fe(CN)_6\}_2$, insoluble in acids, decomposed by KOH.
3. $CuSO_4$, greenish-yellow precipitate—$Cu_3\{Fe(CN)_6\}_2$.
4. $AgNO_3$, orange precipitate—$Ag_3Fe(CN)_6$, insoluble in dilute HNO_3, soluble in ammonia and KCN.

Salicylic, $C_6H_4OH.COOH$ [1 : 2].—Colourless needles ; M.P. 157° ; sparingly soluble in cold, moderately in hot water ; easily soluble in alcohol and in ether.

Salicylates give salicylic acid with mineral acids. When strongly heated gives CO_2 and phenol. Salicylic acid or salicylates mixed with soda-lime and heated give phenol, recognised by its smell.

The acid is soluble in conc. H_2SO_4, and is reprecipitated on dilution with water.

Dry salicylates, with few drops methyl alcohol and conc. H_2SO_4, on warming, methyl salicylate (oil of winter green) ; recognised by smell.

Neutral solutions of salicylates give with :

1. $FeCl_3$, violet coloration ; colour destroyed by acids or alkalis.
2. Bromine water, yellowish-white precipitate.

Uric, $C_5H_4N_4O_3$.—White crystalline powder ; sparingly soluble in water and all solvents ; insoluble in cold Na_2CO_3, but soluble in NaOH. On heating, NH_3, HCNO, HCN and urea are formed.

Conc. H_2SO_4, in cold, soluble ; on heating, CO_2 and SO_2 evolved.

The Murexide Test.—Evaporate a little uric acid and dilute HNO_3 to dryness. Add few drops of ammonia to the red residue when cold ; purple coloration. Uric acid reduces Fehling's solution on prolonged boiling.

Tannic (Gallo-tannic), $C_{14}H_{10}O_9 + 2H_2O$.—Colourless, amorphous, glistening mass ; decomposes on heating ; very soluble in hot water.

Action of caustic alkalis same as for gallic acid.

Conc. H_2SO_4, on warming, dark green coloration, and brownish-black precipitate on dilution.

Neutral solutions of tannates give with :

1. **$FeCl_3$**, bluish-black precipitate, soluble in **HCl**, but reprecipitated by ammonia.
2. **KCN**, no coloration.
3. Tartar emetic, precipitate.
4. Gelatin, greyish precipitate.
5. **$AgNO_3$**, metallic silver.
6. **NH_4Cl** and ammonia, precipitate.

Gallic, $C_6H_2(OH)_3COOH$ [3 : 4 : 5 : 1].—Colourless, silky needles ; decomposes on heating, giving pyrogallol and leaving charred residue ; sparingly soluble in cold water ; readily soluble in hot water, and in alcohol.

Gallates when mixed with caustic alkalis oxidise in air, giving coloured solutions.

Conc. **H_2SO_4**, on warming, dark red solution, and dark red precipitate on dilution with water.

Neutral solutions of gallates give with :

1. **$FeCl_3$**, bluish-black precipitate, soluble in excess to a green solution, also soluble in **HCl**.
2. **KCN**, pink coloration, which disappears on standing and reappears on shaking.
3. Solution of gelatin, no precipitate.
4. Fehling's solution, precipitate of **Cu_2O**.
5. **$AgNO_3$**, metallic silver.
6. **NH_4Cl** and ammonia, no precipitate.

Lactic, $CH_3.CHOH.COOH$.—Syrupy liquid ; decomposes on heating, giving acetaldehyde.

Lactic acid and lactates :

1. On warming with conc. **H_2SO_4**, effervesce, and acetaldehyde evolved ; solution darkens.
2. On warming with iodine dissolved in **KI**, and adding **NaOH** to make alkaline, giving iodoform.

Neutral solutions of lactates give with :

1. **$AgNO_3$**, no precipitate.
2. **$CaCl_2$**, no precipitate.
3. **$KMnO_4$** acidified, on warming, decoloration.

Alkaloids

Most of the alkaloids, with the exception of coniine and nicotine, are crystalline solids ; they are usually insoluble or sparingly soluble in water, but being basic they dissolve in acids forming soluble salts, from which the base is usually precipitated by dilute **NaOH** or **Na_2CO_3**. In a few cases, e.g. morphine, the alkaloid is soluble in excess of alkali, while the solubility in water of a base such as nicotine prevents its precipitation by the addition of alkali to solutions of its salts. The liquid alkaloids coniine and nicotine are volatile in steam.

The majority are optically active and possess a bitter astringent taste, as well as an extremely poisonous character.

Alkaloids in general give precipitates with certain reagents amongst which may be mentioned :

1. Solution of iodine in **KI**—brown amorphous ppt.
2. Nessler's solution—white or discoloured amorphous ppt.
3. Potassium mercuric iodide—white or yellowish-white ppt.
4. Phosphomolybdic acid—light to brownish-yellow gelatinous ppt.
5. Chloroplatinic acid—yellow crystalline solid.
6. Tannic acid or picric acid in aqueous solution—almost all the alkaloids precipitated.
7. Hydroferro- and hydroferri-cyanic acids—yellow ppts.

Some give definite colorations with oxidising agents, e.g. conc. H_2SO_4 and $K_2Cr_2O_7$. The hydroferro- and hydroferri-cyanides are usually of definite crystalline form under the microscope, while the picrates and picrolonates usually possess the added advantage of a definite melting point.

Morphine, $C_{17}H_{19}O_3N + H_2O$.—White amorphous or crystalline substance, sparingly soluble in cold water and in ether ; soluble in **NaOH** solution ; M.P. 230°.

1. Conc. H_2SO_4—Pale orange solution.
2. Conc. H_2SO_4 + crystal of $K_2Cr_2O_7$—Greenish-brown coloration.
3. Conc. H_2SO_4 containing a few drops HNO_3—A violet coloration on standing.
4. Conc. HNO_3—Red coloration, changing to yellow on warming.
5. One drop of formalin in 1 c.c. conc. H_2SO_4—Purple colour, changing to blue.
6. Solid Na_3AsO_4—Slate-blue coloration.

To aqueous solution of salt add :

1. **NaOH**—Base precipitated, soluble in excess.
2. $FeCl_3$ (neutral solution)—Blue coloration.
3. KIO_3 crystal and warm—Iodine liberated ; cool and test with starch.

Cinchonine.—$C_{19}H_{22}ON_2$.—White powder or crystalline compound ; almost insoluble in water ; *d*-rotatory ; M.P. 255°.

Solutions of salts do not exhibit fluorescence.

1. Conc. H_2SO_4—Pale green solution.
2. Conc. H_2SO_4 + crystal of $K_2Cr_2O_7$—Olive-green coloration.

To aqueous solution of salt add :

1. **NaOH**—Base precipitated, insoluble in excess.
2. $K_4Fe(CN)_6$ to neutral or slightly acid solution—Yellowish-white ppt., soluble in excess on warming.

Quinine, $C_{20}H_{24}O_2N_2 + 3H_2O$.—White powder (anhydrous) or crystalline compound ; sparingly soluble in water ; *l*-rotatory ; M.P. 177° (anhydrous) or 67° (hydrated). Dilute solutions of its salts, acidified with H_2SO_4, exhibit a bluish fluorescence in daylight, which is discharged by **HCl**.

1. Conc. H_2SO_4—Pale green solution.
2. Conc. H_2SO_4 + crystal of $K_2Cr_2O_7$—Dark olive-green coloration.

To aqueous solution of salt add :

1. Conc. chlorine water ($\frac{1}{5}$ its volume), and then excess of conc. NH_4OH—Emerald-green colour.

2. Chlorine water, $K_4Fe(CN)_6$ and NH_4OH—Red coloration. Quinine hydrochloride, on heating alone, assumes a violet colour, and gives off violet vapours.

Strychnine, $C_{21}H_{22}O_2N_2$.—Colourless needles; M.P. 268°; sparingly soluble in water, alcohol, and ether; very soluble in $CHCl_3$; *l*-rotatory in alcohol.

1. Conc. H_2SO_4—Colourless solution (even at 100°).
2. Conc. H_2SO_4 + crystal of $K_2Cr_2O_7$—Bluish-violet coloration.

To solution of salt add:

1. **NaOH**—Base precipitated, soluble in excess of NH_4OH.
2. $K_3Fe(CN)_6$ or K_2CrO_4—Yellow crystalline ppt. in neutral and fairly conc. strychnine salt solution.

Brucine, $C_{23}H_{26}O_4N_2 + 4H_2O$.—Colourless needles or prisms; M.P. 168°; sparingly soluble in water, readily soluble in alcohol and in chloroform; $[\alpha]_D$ = about $-120°$ (in $CHCl_3$).

1. Conc. H_2SO_4—Rose-red coloration, changing to yellow.
2. Conc. H_2SO_4 + crystal of $K_2Cr_2O_7$—Yellowish-brown coloration.
3. Conc. HNO_3—Red coloration, turning yellow on heating, and turning to purple with $SnCl_2$.
4. Conc. **HCl**, followed by dilution with water and addition of chlorine water—Red coloration.

To solutions of its salts add:

$Hg(NO_3)_2$, to a neutral solution—Crimson colour on continued boiling.

Coniine, $C_8H_{17}N$.—Colourless, oily liquid, turning brown on exposure to air; volatile in steam; B.P. 167°; readily soluble in water and organic solvents; *d*-rotatory.

1. Conc. HNO_3—Orange-red coloration.
2. Phenolphthalein—Turned pink in 50% alcoholic solution.
3. After standing for 5 minutes with alcoholic CS_2, the mixture gives a brown or black ppt. with a drop of very dilute $CuSO_4$.
4. Albumen—Coagulated.

Nicotine, $C_{10}H_{14}N_2$.—Colourless, oily liquid, turning brown on exposure to air; volatile in steam; B.P. 247°; readily soluble in water and organic solvents; *l*-rotatory.

1. Conc. **HCl**—A light violet or brown coloration on warming, changing to orange with conc. HNO_3.
2. Conc. HNO_3—Orange coloration.
3. Phenolphthalein—Pink colour in very dilute alcohol.
4. Albumen—Not coagulated.
5. On warming 1 drop with 2 c.cs. epichlorohydrin gives a red colour.

Caffeine (Theine), $C_8H_{10}N_4O_2 + H_2O$.—Colourless needles; M.P. 234°; sparingly soluble in cold water and in alcohol, readily soluble in chloroform; sublimes unchanged.

1. Conc. H_2SO_4 + crystal of $K_2Cr_2O_7$—Green coloration.
2. Conc. **NaOH** and boiling—Methylamine evolved.
3. Murexide test—Treat with a crystal $KClO_3$ and a few drops of **HCl**, evaporate to dryness; the red residue turns purple with ammonia.

To aqueous solution add:

1. Iodine in **KI**—A precipitate (after acidification); M.P. 215°.
2. $K_4Fe(CN)_6$ and HNO_3 (iron free)—Yields Prussian blue on warming.

Atropine, $C_{17}H_{23}NO_3$.—Silky needles or prisms; M.P. 115°; very sparingly soluble in water, fairly soluble in ether or benzene, readily in alcohol or chloroform; optically inactive.

1. Conc. H_2SO_4 + crystal of $K_2Cr_2O_7$—Dark brown coloration.
2. Conc. HNO_3—Boiled and evaporated to dryness, and residue treated with alcoholic potash; yields violet colour.
3. Bromine in **HBr**—Yellow crystalline precipitate.
4. Baryta water on evaporation to dryness—Odour of hawthorn blossom.

Cocaine, $C_{17}H_{21}NO_4$.—Colourless prisms; M.P. 98°; slightly soluble in water, readily in organic solvents; *l*-rotatory.

1. Conc. H_2SO_4 + crystal of $K_2Cr_2O_7$—Brownish-green coloration, SO_2 evolved.
2. Conc. H_2SO_4 and a few drops of alcohol—Characteristic odour of ethyl benzoate.
3. Acids (on heating)—Yields benzoic acid and ecgonine (M.P. 205°).
4. $KMnO_4$ to conc. solution—Violet precipitate of the permanganate.
5. K_2CrO_4 in presence of **HCl**—Yellow precipitate.
6. Aqueous iodine on solutions of salts yields—per-iodide, M.P. 161°.

Carbohydrates

The carbohydrates are crystalline or amorphous solids which char on heating and emit an odour of burnt sugar. They are non-volatile. Some are soluble in water, e.g. sugars; some are insoluble or sparingly soluble, e.g. cellulose and the starches; lactose is much less soluble than glucose. Some reduce Fehling's solution on warming e.g. glucose, fructose, lactose. Polysaccharides on hydrolysis with dilute mineral acids yield monosaccharides and in consequence the reaction mixture, after neutralisation, reduces Fehling's solution.

General Test for Carbohydrates.—To a small portion of carbohydrate in 5 c.cs. water, 2–3 drops of alcoholic solution of α-naphthol (20%) are added, and 2 c.cs. conc. sulphuric acid poured carefully down sides of tube. A violet colour discharged by alkalis (*Molisch*).

Glucose, Grape Sugar or Dextrose, $C_6H_{12}O_6$.—Glucose is readily soluble in water and crystallises therefrom in granules, containing 1 molecule of water of crystallisation, which melt at 86°. From alcohol the anhydrous compound, M.P. 146°, separates. It has a sweet taste, but not so sweet as cane sugar. It is dextrorotatory, $[\alpha]_D = +52{\cdot}5°$ (basis of estimation).

1. Heat a small portion in a dry test tube. The hydrated variety melts, then gives off water vapour, and finally blackens owing to deposition of carbon. Odour of burnt sugar emitted.
2. Treat with conc. sulphuric acid. Pure glucose does not char in the cold; on heating a yellow colour is developed which gradually darkens (cf. cane sugar). Ordinary commercial glucose is impure and blackens readily on heating.

Use portions of a 10% aqueous solution of glucose for the following tests:

3. Warm gently with a few drops of sodium hydroxide solution. The colour of the solution changes through yellow to brown (cf. cane sugar).

4. Add a few drops to 10 c.cs. ammoniacal silver nitrate solution and warm in a bath of hot water. Silver mirror formed.

5. Add copper sulphate solution and then excess sodium hydroxide. Solution turns violet, but precipitation of copper hydrate does not take place. On warming, reduction of the cupric compound occurs and red cuprous oxide is precipitated (*Trommer's test*).

6. Add a few drops of Fehling's solution and warm. Cuprous oxide is precipitated (cf. cane sugar).

7. Treat with lime water. Glucose, unlike fructose, yields no precipitate.

8. Examine in a polarimeter (p. 53). It is dextrorotatory.

9. Glucose yields an osazone (cf. cane sugar).

Fructose, Fruit Sugar or Laevulose, $C_6H_{12}O_6$.—Fructose is more soluble in water and in alcohol than glucose. From alcoholic solution it may be obtained in crystals. M.P. 95°, but from aqueous solution it is usually obtained as a syrup. It is laevorotatory, $[\alpha]_D = -95{\cdot}5°$. With phenylhydrazine it yields the same osazone as glucose (p. 296). In most of its reactions it behaves like glucose from which it may be distinguished by its laevorotation, by its yielding a precipitate with lime water, and by its melting point.

Perform similar tests with fructose as described for glucose.

Sucrose, Cane Sugar or Saccharose, $C_{12}H_{22}O_{11}$.—Sucrose is very soluble in water from which it crystallises in large monoclinic prisms. It is sparingly soluble in alcohol. It is dextrorotatory, $[\alpha]_D^{20°} = +66{\cdot}5°$ (basis of estimation), M.P. about 160°.

1. Heat a few crystals in a tube to melting : on cooling, an amorphous glassy mass of " barley sugar " remains. Heat once more (in an oil bath) to 200° ; " caramel "—a dark brown mass—is formed. On further heating charring takes place.

2. Cover a few crystals with water in a beaker, add an equal volume of conc. sulphuric acid and stir. Much frothing takes place, sulphur dioxide and carbon dioxide being evolved, and a bulky deposit of carbon left (glucose is slowly charred).

3. Warm a few crystals with conc. nitric acid. Note energetic action (see Preparation 184).

Use a 10% aqueous solution of cane sugar for the following tests :

4. Treat with caustic soda solution and heat. Not turned brown (cf. glucose).

5. Add Fehling's solution and heat. No reduction (cf. glucose).

6. Add a little dilute sulphuric acid, boil a short time, and neutralise. Then add Fehling's solution and heat. The mixture of glucose and fructose, known as " invert sugar ", brings about reduction to cuprous oxide.

7. Examine in a polarimeter and note dextrorotation. Then heat with a little dilute sulphuric acid, neutralise carefully, and again examine in polarimeter. Note laevorotation. Fructose is more laevorotatory than glucose is dextrorotatory.

Lactose, Milk Sugar, $C_{12}H_{22}O_{11}$.—Lactose is much less soluble in water and in alcohol than the other sugars. It is not very sweet. $[\alpha]_D^{20°} = +52{\cdot}5°$; M.P. 205°.

Perform tests for lactose similar to those described under cane sugar. It reduces Fehling's solution on warming, and yields an osazone (distinctions from cane sugar) ; the osazone does not separate very readily from the hot solution (distinction from glucose). It may also be distinguished from glucose by the facts that it is not sweet, it is much less soluble, and it is not so strong a reducing agent.

Osazones

Mulliken has based a scheme for the identification of pure sugars on the time of formation of their osazones :

Place 0·1 gm. of each of the following sugars, 0·2 gm. of phenylhydrazine hydrochloride, 0·3 gm. of sodium acetate, and 2 c.cs. of water in small test tubes ; cork loosely to prevent evaporation and heat in a boiling water bath. Shake the tubes occasionally without removing from the bath. Note the time required for the separation of precipitates.

Sugar	Time
Fructose - - -	2 min.
Glucose - - -	4 to 5 min.
Sucrose - - -	30 min. (due to slight inversion).
Lactose - - -	No precipitate in hot solution.

Starch

The appearance of different kinds of starch under the microscope is characteristic. Starch is insoluble in cold water, but when heated in water the granules swell up and burst giving an opalescent solution.

1. Heat a small quantity in a dry tube. Water and combustible gases are evolved and an odour like that of burnt sugar is emitted.

2. Heat a small portion with conc. sulphuric acid. Carbon dioxide and sulphur dioxide are evolved with charring.

3. Mix 1 gm. into a paste with 5 c.cs. cold water and pour into 50 c.cs. of boiling water. Treat portions of the solution as follows :

(*a*) To a cold portion add iodine solution (iodine dissolved in potassium iodide solution) ; a deep blue coloration is produced. Boil the solution and note the disappearance of the colour, which reappears, though more feebly, on cooling.

(*b*) To the major portion add 2 c.cs. of dilute sulphuric acid and boil gently under reflux. At intervals of 5 minutes withdraw a portion, cool, and test with iodine solution. The blue coloration due to starch gradually disappears. An intermediate stage (dextrin) occurs when a port wine coloration is obtained with iodine.

Glycosides

The natural glycosides are complex compounds of the sugars (generally glucose) with organic compounds. On hydrolysis with alkalis, mineral acids, or with ferments they yield a sugar and one or more other organic compounds.

Salicin (from willow bark) on hydrolysis yields glucose and saligenin (*o*-hydroxybenzylalcohol) :

$$\underset{\text{salicin}}{C_{13}H_{18}O_7} + H_2O \longrightarrow \underset{\text{glucose}}{C_6H_{12}O_6} + \underset{\text{saligenin}}{C_6H_4(OH)CH_2OH}.$$

Salicin is met with as colourless, glistening, crystalline plates, or as a white powder. It is moderately soluble in water, less soluble in alcohol, and insoluble in ether ; M.P. 200°.

1. Treat salicin with conc. sulphuric acid. Deep red colour in the cold.

2. Dissolve salicin in hot water, add a little conc. hydrochloric acid, boil, cool and filter off the saligenin ; neutralise filtrate, add Fehling's solution, and warm. Reduction due to glucose.

3. Warm with dilute sulphuric acid and potassium dichromate. Odour of salicylaldehyde similar to meadow sweet.

4. Heat on a porcelain lid. Odour of burnt sugar.

Amygdalin (the glycoside of bitter almonds) is a white crystalline compound, soluble in water, readily hydrolysed on heating with dilute sulphuric acid to benzaldehyde, hydrocyanic acid and glucose.

$$C_{20}H_{27}O_{11}N + 2H_2O \longrightarrow C_6H_5CHO + HCN + 2C_6H_{12}O_6.$$

1. Heat amygdalin with dilute sulphuric acid under reflux for a short time. Remove benzaldehyde and hydrocyanic acid by steam distillation. Test for benzaldehyde (phenylhydrazone test) and hydrocyanic acid (Prussian blue test) in distillate, and for glucose (osazone test) in residue.

2. Treat with conc. sulphuric acid. Deep red colour in the cold.

INDEX

INDEX

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