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AN INTRODUCTION TO THE PREPARATION AND IDENTIFICATION OF ORGANIC COMPOUNDS

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AN INTRODUCTION TO THE PREPARATION AND IDENTIFICATION OF ORGANIC COMPOUNDS

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PREFACE

In designing a laboratory course for elementary organic chemistry and preparing a manual of directions, one should first have in mind the reasons for requiring the student to take laboratory work.

One of the reasons is that it is very important to tie the abstract chemistry learned in the classroom to something objective. With all the talk of tautomers, optical and geometrical isomers, strain theory, complicated syntheses, etc., a young student is quite apt to get lost in the maze of paper chemistry and forget that, after all, organic chemistry deals with real compounds and real reactions. It is the realities of the laboratory which should keep the course as a whole in its proper balance.

Aside from these considerations, it appears that there are two important functions of the laboratory course: first, to teach as much laboratory technique as possible and, second, to familiarize the student with as many reactions as may conveniently be covered. A number of years ago it was apparent to the authors that their laboratory course was not so effective in either one of these functions as it might be, and an attempt was made to remedy the situation. This laboratory manual is the result of that attempt. As the course is now designed, the student makes only half as many preparations as formerly, the remaining time being devoted to a form of qualitative organic analysis.

The results have been very gratifying. In the first place, the students take a much greater interest in the qualitative work than in a continuation of preparative work, this being a very important factor in the teaching of any subject. From the teacher's viewpoint, they learn much more. In identifying a number of unknown substances and preparing derivatives from them, a student is brought into contact with many more reactions than would have been possible had he spent the same amount of time in making routine preparations; in this respect the aim of the laboratory course is more nearly fulfilled.

In the second place, the student learns another technique in addition to that ordinarily acquired. The preparative work in the first half of the course is chosen with regard to the operations involved rather than the reactions illustrated. Each student performs preparations involving crystallizations, distillations, steam distillations, ether extractions, etc.; the better students are assigned work involving more difficult operations, such as vacuum distillations. In the second half of the course, instead of being required to go through a somewhat monotonous repetition of these same operations, the student acquires an entirely different technique, that of handling small quantities of materials. In identifying his unknown, the student performs a series of test-tube reactions with a much more definite object in view than the routine testing of properties, which makes up a part of some laboratory courses. After he has made a tentative identification of the substance, the preparation of a suitable derivative follows, starting with from one-tenth of a gram to two grams of material. Handling these small quantities without too much loss of material and time teaches a student much that he would miss were he to continue with the usual routine. Even the determination of a melting point takes on much greater significance and develops better technique when the answer is unknown or of diagnostic importance.

One of the difficulties in any organic laboratory course is that the classroom work is apt to lag far behind the laboratory. The study of aromatic chemistry is generally relegated to the latter third or fourth of the course, though the preparation and handling of aromatic substances are introduced much earlier than this in the laboratory. To counteract this situation, we have attacked the problem from two different angles. In the first place, we started some years ago teaching aliphatic and aromatic chemistry together, our order of presentation being paraffins, olefins, acetylenes, benzene, naphthalene, etc. Once we had made the change, we found that it had other manifest advantages: the students got a better appreciation of the relations existing between aliphatic and aromatic compounds, and there was much time saved in eliminating needless repetition.

The second attempt made to bridge the gap between classroom and laboratory was to include in the laboratory manual a preliminary discussion of the chemistry involved in the reactions being studied. This idea is not new, for it was one of the outstanding features of the well-known manual of Gattermann and Wieland. In the present manual this scheme has been followed throughout—in the special tests (page 137) and in the preparation of derivatives (page 164), as well as in the section on preparations. We now feel that the student is not at such a loss in the laboratory as he was formerly.

The preparations included in the first section of the manual were chosen largely from the standard ones used in many laboratory courses. They include several sequences, some expressly so, such as benzilic acid from benzaldehyde, and others which are listed as separate experiments, such as nitrobenzene, aniline, acetanilide, and *p*-nitroaniline. Experiments which we believe to be new for teaching purposes are the preparation of resacetophenone and its subsequent reduction to ethylresorcinol by means of the Clemmensen reaction, and the preparation of indigo in one laboratory period, starting with benzaldehyde.

The preparation of *p*-bromophenacyl bromide is assigned to the better students and gives very satisfactory results. Its importance lies in the fact that the material is needed in the second half of the course as a reagent for identifying acids and some of their derivatives.

The unique feature of the book is the inclusion of qualitative organic analysis arranged in such a way that the elementary student can handle it. This was accomplished by selecting a list of between three and four hundred of the most common and easily available organic compounds and arranging a set of tests and a key for the student to use as a guide in the identification of a substance. As far as possible chemical rather than physical properties were used for diagnostic purposes, although the use of melting and boiling points and water solubility could not be conveniently avoided.

At first an attempt was made to classify the compounds on the basis of chemical reactions that are characteristic of the classes to which the substances belong. This had to be given up, however, owing to the large number of compounds which behaved in an anomalous fashion. For instance, some primary amines do not give an easily recognizable carbylamine reaction (benzidine, nitroanilines), and some unsaturated compounds do not add bromine readily in chloroform solution (maleic and fumaric acids). The result of the occurrence of these discrepancies was the adoption of the present key, in which compounds of different classes appear together and in which many compounds occupy apparently anomalous positions. However, in requiring students to write equations, where possible, for all tests performed, the instructor is able to bring out certain features of organic chemistry which would otherwise be missed.

The student is called upon to make his own choice of a derivative. These are listed in such a way that, when he knows to which class of compounds the unknown belongs, he can turn to the appropriate section of the book and make a choice which will give him the greatest chance to differentiate the compound from closely allied substances. In so doing he cannot help acquainting himself with a certain amount of chemistry.

The students are required to standardize a thermometer during the first laboratory period, and throughout the course all observed melting and boiling points are to be corrected accordingly. All melting and boiling points listed in the manual have been checked wherever possible with the International Critical Tables and with Kamm's "Qualitative Organic Analysis." Where discrepancies were found, the original literature was consulted and a choice made. It is frequently impossible to tell whether a given value has been corrected or not, so that some questionable values have certainly been included in the book. In this connection, it is pertinent to lodge a vigorous protest against the prevalent practice of cluttering up chemical literature with "uncorrected" melting and boiling points—figures without any great significance, which could just as well have been corrected and presented in the literature as reliable data.

The change from the old type of laboratory work is not difficult for the instructor. *No new apparatus is needed.* Unknowns can be accumulated slowly over a period of years, several dozen being all that are necesary for a beginning. An appendix in this volume contains a list of the solutions and reagents needed. Several of the reagents would appear to be expensive were it not taken into consideration that very small amounts of them are needed. The expensive reagent used in largest amount, *p*-bromophenacyl bromide, can be prepared by the students themselves, as mentioned above.

While the authors have checked in the laboratory nearly every individual test, and in other ways have tried to insure the accuracy of the material published, no one realizes better than they the possibility of mistakes remaining in the manuscript. They will consider it a courtesy to be informed of any errors found, and any suggestions for improvement will be welcomed.

It is impossible to make adequate acknowledgment of all the material appearing in this book. One consciously or subconsciously picks up ideas from whatever one reads, ideas which are later drawn upon, the source having been lost track of in the meantime. In particular the authors can single out four works which have been of inestimable value, namely: Mulliken's "Identification of Pure Organic Compounds," Kamm's "Qualitative Organic Analysis," Clarke's "Handbook of Organic Analysis," and Gattermann's and Wieland's "Laboratory Methods of Organic Chemistry." In addition thanks are due to Professor J. J. Donleavy for criticisms of the manuscript, and to Mr. I. F. Walker for valuable technical assistance.

To Professor Arthur J. Hill the authors wish to express their sincere appreciation for his unlimited backing and encouragement, without which it would have been impossible to proceed.

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PART I

THE PREPARATION OF ORGANIC COMPOUNDS

CHAPTER I

INTRODUCTION

Laboratory work in organic chemistry is in many ways quite unlike that done in other fields of the science of chemistry. Whereas in physical or analytical chemistry, one is concerned largely with making accurate measurements and in drawing conclusions from them, in organic chemistry most of the work has to do with the methods of preparing carbon compounds and with the study of their properties.

In a large part, this difference in emphasis is due to the inherent nature of carbon compounds and organic chemical reactions. Whereas the number of inorganic compounds is comparatively small, organic substances can be made in almost limitless numbers, several hundred thousand having already been prepared and described. Furthermore, their reactions differ in several notable respects from those of inorganic substances. Two of these differences will be discussed briefly.

a. Rate of Reaction.—A large portion of the familiar inorganic reactions proceed almost instantaneously. On the other hand, organic reactions are in general slow, requiring hours, weeks, or even months for completion, although some proceed very quickly. The main reason for these slow rates is the non-ionic character of most of the reactions.

b. Side Reactions.—When inorganic substances react, in most cases they react in one way only, giving a quantitative relationship which can be described by a suitable equation. This is usually *not* the case with organic reactions. When organic substances are caused to react, it is generally found that they will react in two or more different fashions, and in addition, as a result of the slow rate of organic reactions in general, the various reaction products can frequently react with the original substances or with each other. Accordingly, when an equation is written for A reacting with B to produce C, it is merely a description of *one* of the reactions which takes place, not a description of the only reaction. The desired reaction can then be rated as good or bad in proportion to its predominance over the others. In a case of this type, that reaction of special interest is referred to as "the reaction," and all others taking place simultaneously as "side reactions." Owing to the frequency and importance of side reactions, a large part of organic laboratory technique is concerned with the isolation and purification of substances.

The laboratory work as covered in this outline is of two different types. The first part will be concerned with the preparation and purification of organic substances, or the synthetic side of the subject. The remainder is given over to the identification of unknown compounds, these being confined to a selected group of substances.

Certain regulations governing the laboratory work, together with some suggestions for the prevention of accidents and manipulation of apparatus, are given in the following paragraphs.

Prevention of Accidents.—Accidents in an undergraduate laboratory are frequent and sometimes serious. It cannot be overemphasized that these accidents are all preventable, and that a large majority of them result either from careless neglect of the few simple safety rules listed below or from failure to follow directions explicitly. After a student has acquired considerable experience in organic laboratory technique and familiarity with the reagents used, it is permissible for him to devise some of his own experimental procedures, but it is absolutely essential that an elementary student follow with great care the directions given him.

Distillations should never be performed in closed systems, nor should such systems ever be heated. A more or less serious explosion may result from neglect of this rule.

Inflammable volatile solvents, including ether, petroleum ether, carbon disulfide, acetone, alcohol, and benzene, should never be handled in the neighborhood of an open flame. Distillations of such liquids should be carried out with care in the manner described in the next chapter. A very common student failure is to boil alcohol in an open beaker over a free flame. Any such operation must be carried out in a flask attached to a reflux condenser.

Great care must be exercised in inserting glass tubing, thermometers, distilling-flask side-arms, etc., into cork or rubber stoppers. Entrance is made much easier by first moistening the glass and stopper with water or alcohol. The glass should then be held within 1 inch, *not* 6 *inches*, of the point of insertion. If both stopper and glass are wrapped in two or three thicknesses of towel, an accident is very rare. It is usually best to use a twisting motion rather than a straight push in inserting the tube, as well as in removing it. The latter operation, in the case of a rubber stopper, is facilitated if it is possible to introduce some water or alcohol between the glass and stopper by pulling the rubber away from the tube somewhat. In removing a stopper a straight pull on the glass is essential, and, if it is tightly stuck, it is better to cut the stopper off with a knife rather than risk a break.

Corks and rubber stoppers should be bored to the proper size before any attempt to insert glass apparatus is made.

Many of the reagents used in the organic laboratory may cause serious accidents if improperly or carelessly handled. The student should be familiar with the precautions to be used in this connection and the remedies to be applied in case of accident.

Bromine causes painful burns if it comes in contact with the skin. It is also very irritating to the mucous membranes. Noxious gases and vapors such as hydrogen chloride, chlorine, hydrogen sulfide, and others should be used only under an efficient hood. Poisonous compounds should be handled with great care, particularly such highly toxic substances as sodium and potassium cyanides. (These salts react slowly with moist air and liberate hydrogen cyanide so that any operation with them involving exposure to the air, such as pulverizing, must be done under a hood.) In addition it should be remembered that many organic substances are very irritating to the skin, so that care should always be taken to prevent contact of the skin with any chemicals. It might be added that a pair of hands smeared up with chemicals is invariably a sign of poor laboratory technique.

It is frequently necessary to employ metallic sodium in organic laboratory work. Since sodium reacts with great violence with water and sometimes spontaneously ignites in the air, it must be handled with extreme caution. It should never be exposed unnecessarily to the air, but should be kept under benzene until it has to be handled, as in cutting or transferring to a reaction mixture. Reactions involving sodium should never be heated on a water bath, an oil or sand bath being used instead. All sodium residues must be carefully destroyed by the addition of alcohol, or put in a suitable container designated for that purpose. Even the smallest pieces of the metal must never be thrown into the sink or waste bucket.

Ethyl ether is gradually oxidized on prolonged exposure to the air to yield *highly explosive peroxides.* Explosive decomposition of these peroxides is most likely to occur near the end of the evaporation of ether containing them. The peroxides can be destroyed by shaking the ether with weakly acid ferrous sulfate solution.

Treatment of Accidents.—In case of a fire involving a burning reagent, any inflammable material which is endangered should be removed. If the fire is small it can sometimes be smothered with a towel. Otherwise a fire extinguisher should be used. *Water must never be used.* If there is any danger that the container holding the burning liquid may break and throw the liquid around it is first of all important to stay at a safe distance. A fire extinguisher can be effectively operated from a considerable distance. If a pyrene or other carbon tetrachloride fire extinguisher has been used, the laboratory should be well aired out afterward to remove any phosgene which may have been formed.

Burning clothing should be smothered by a blanket or laboratory coat. Obviously, running will only tend to fan the flames.

Burns caused by fire should be treated by immediate application of tannic acid solution. If they are at all serious, medical attention should be obtained.

Burns caused by chemicals should be treated according to the type of reagent causing the burn. Acid and alkali burns should be washed freely with water and then with 5 per cent sodium bicarbonate or very dilute acetic acid, respectively. Bromine burns should be washed copiously with water followed by 5 per cent sodium bicarbonate.

Cuts should be disinfected and bandaged. If there is any chance that glass has remained in the cut or if the wound is large enough to require sutures, medical attention should be obtained. If an artery has been cut, a tourniquet or other appropriate first aid device must be used and a doctor consulted immediately.

If the eyes have been injured by some chemical, they should be washed out liberally with water, followed by 5 per cent sodium bicarbonate or boric acid, depending on the nature of the injuring chemical.

Arrangement of Apparatus.—All apparatus should be set up in a neat and stable fashion. Makeshift contrivances lead to accidents and loss of time. A stack of books, beakers, etc., is a poor foundation upon which to rest the result of hours of work. Such arrangements are needless if one remembers that a condenser clamp is in essence a universal joint.

In boring cork or rubber stoppers, it seems obvious that the stopper should not be held against the palm of the hand. Neither should it be placed on the stone table top, as one such treatment will ruin the edge of the borer for future use. Corks and rubber stoppers should be bored half way through from each end, so that it is unnecessary for the borer to come in contact with a hard surface at any time. A perfectly clean hole can only be obtained with a sharp borer. The boring of rubber stoppers is greatly facilitated if the borer is kept lubricated with alcohol. The hole should be slightly smaller than the object to be introduced. In the case of corks, the hole should be smoothed up with a round file.

It is not necessary to use vaseline to make stoppers tight if they have been bored to fit the apparatus correctly. All glass tubing should be heated over a fishtail burner before an attempt is made to bend it. Glass tubing held over an ordinary Bunsen burner is heated too locally, with the result that the bending materially reduces the tube size and makes fragile spots in the apparatus.

Order and Plan of Work.—The desk top and drawers should be kept clean and orderly. Glass and paper should be kept out of the sink for obvious reasons. It has been found best to clean apparatus immediately after use, and to place it in the desk, upside down in the case of beakers and flasks. Thus the apparatus is both clean and dry when required. When it is necessary to dry apparatus quickly, it should be rinsed out several times with acetone and dried with a stream of air. The same result can be obtained by rinsing first with alcohol and then with ether. The reason for the intermediate alcohol washing is that water is not sufficiently soluble in ether to make the latter solvent effective alone.

An essential aspect of organic laboratory practice is the careful planning of the work. In setting the required amount of work this feature has been considered. It is not necessary to loaf a whole period while a reaction mixture boils for 2 hours. It is generally advisable to have two or three experiments going at once to make the most effective use of available time. In order to do this the student must know what he is going to do before he enters the laboratory. It is thus important that the student seriously study the manual just as he studies a textbook. This practice will very effectively prevent him from getting the "lost" feeling which is so easily acquired when first entering the organic laboratory.

Laboratory Notebook.—One of the most important features of any laboratory work is the proper recording of notes. These should be kept in a permanent notebook. The following outline includes the essential points which should be covered in writing up notes on the preparation and purification of a substance:

1. Name and structural formula of the substance prepared.
2. Equation for the reaction by which it is formed.
3. A list of the available physical properties of the compound. This includes melting or boiling point, solubility in water, etc.
4. A short explanation of each of the important manipulative details in the directions.

This much of the write-up should be completed before starting the experiment.

5. Answers to all questions asked at the end of each set of directions, except for those questions which involve material not yet covered in the classroom.
6. Calculation of percentage yield.

The percentage yield given by a reaction is the chief criterion by which it is judged as being "good" or "bad." It is defined as the per cent of the theoretical yield actually obtained. Reactions differ enormously in this respect, ranging from several per cent up to the so-called "quantitative" yield. What is looked upon as a good percentage yield in one experiment might be regarded as very poor in another. A very closely allied consideration is the state of purity of the preparation, because the yield decreases with increasing purity due to inescapable losses in manipulation. (Grades on experiments are based on both the quality and quantity of material prepared, as well as the quality and completeness of the notebook write-up.)

An example of the calculation of theoretical yield is given below, the reaction selected being the oxidation of naphthalene to phthalic acid by means of potassium permanganate. Assume that the directions stipulate the use of 10 g. of naphthalene and 70 g. of potassium permanganate. The equations, *which must always be balanced,* are in this case:

$$C_{10}H_8 + 6KMnO_4 \longrightarrow C_6H_4(COOK)_2 + 2K_2CO_3 + 6MnO_2 + 2H_2O$$

$$C_6H_4(COOK)_2 + H_2SO_4 \longrightarrow C_6H_4(COOH)_2 + K_2SO_4$$

The first step in the calculation of any theoretical yield is to determine which reagent limits the amount of product obtainable. In this case, 10 divided by 128, the molecular weight of naphthalene, gives 0.078, the fraction of the amount indicated by the equation. Similarly 70 divided by 6×158 gives the fractional amount of permanganate, 0.074. It is obvious from these figures that the naphthalene is present in excess, so that it is impossible to get more than 0.074 the amount of phthalic acid indicated, or $0.074 \times 166 = 12.3$ g. This latter figure is the theoretical yield.

The preparation, when completed, should be turned in to the instructor. Solids should be contained in wide-mouth cork or glass-stoppered bottles, liquids in narrow-mouth glass-stoppered bottles. The bottles should be labeled with the student's name and desk number, and the name and *observed* melting or boiling point of the product. For the determination of these properties, consult the next chapter. The student should record in his notebook the physical properties of his preparation which he observed himself, the actual yield in grams, and the percentage yield.

CHAPTER II

IMPORTANT LABORATORY OPERATIONS

In the preparation and purification of organic substances, and also in their identification, there are certain important procedures that are used very frequently. Satisfactory laboratory results are impossible unless the student becomes thoroughly familiar with these working methods.

DISTILLATION

Distillation consists in the vaporization of a substance, either liquid or solid, and the condensation of the vapor in a vessel other than the one used for the vaporization. (If the condensed vapors are returned directly to the vaporization vessel, the substance is said to be refluxing.) In the case of a solid substance, if the material passes directly from the solid state to the vapor state and back again without intermediate liquefaction, the process is spoken of as sublimation.

Distillation is most frequently employed as a method of purification, particularly of liquid substances. It is evident that the compound being purified in this manner must be stable at the temperature of vaporization. Also, as a matter of convenience, in order that the distillation may be a sufficiently rapid process, it is desirable to have the temperature of vaporization coincide with the boiling point of the mixture being distilled. The fulfillment of these conditions offers no difficulties with substances that are stable at their boiling points under atmospheric pressure. In many other cases, these conditions can be fulfilled by such simple expedients as lowering the pressure over the substance to be distilled, or by mixing its vapor with steam (distillation under reduced pressure and steam distillation).

Distillation under Atmospheric Pressure.—The procedure for this operation is very simple. A distilling flask, of such size that the bulb will be one-half to two-thirds filled with liquid, is fitted with a *clean* cork carrying a tightly fitting thermometer (Fig. 1). Only in exceptional cases is it advisable to use rubber stoppers in ordinary distillations. The bulb of the thermometer should extend into the flask to a point 1 or 2 cm. below the side-arm. The side-arm is connected by means of a tightly fitting cork to a dry condenser and extends as far as possible into the condenser. If the material to be distilled boils at a temperature higher than 150 to 160° an air condenser should be used; with substances boiling below this temperature, a water condenser is necessary.

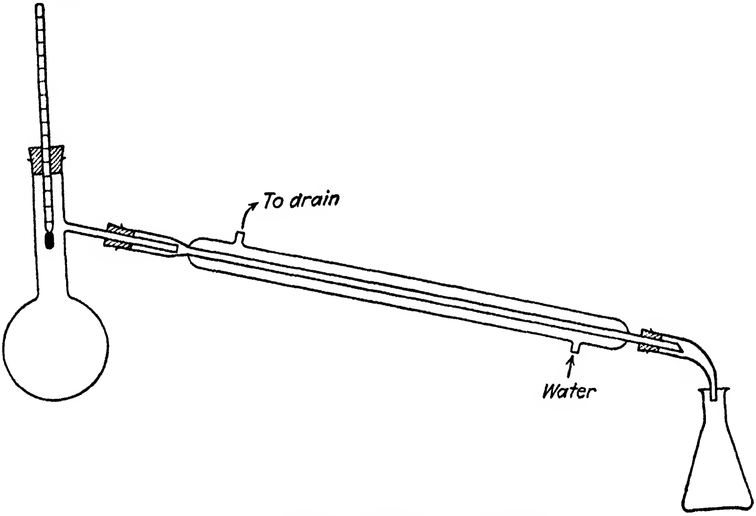

FIG. 1.—Simple distillation apparatus.

(A water condenser having a spiral or bulbed inner tube is useful in the distillation of compounds with very low boiling points.) The condenser is joined by means of a clean cork to an adapter which leads into the vessel used for collecting the distillate. The condenser should extend far enough into the adapter so that the liquid drops freely from the end. There is never any need for having the receiver rest on anything but the desk top, the whole apparatus being set up so that the adapter is at the proper height. Ordinarily the receiver for the main portion of the distillate should be a clean, dry, weighed bottle. In some cases the receiver must be of a special form, as in the distillation of acetyl chloride, when the distillate must be protected from atmospheric moisture. When such cases arise, special instructions will be given in the directions for the preparation of the substance.

Substances that boil below 80° should be heated in a water bath which is maintained at a temperature about 20° above the boiling point of the liquid to be distilled. Higher boiling compounds may be heated on a wire gauze or a perforated asbestos plate with a small gas flame, or in a bath of oil (an oil having a sufficiently high flash point should be used) or of a low-melting alloy, such as Wood's metal. In all cases, the heating should be adjusted so that the distillate collects at the rate of 1 drop or less per second, thus avoiding superheating as much as possible. It is usually advisable to introduce two or three pieces of porous plate 3 to 4 mm. in diameter into the distilling flask as a further precaution against excessive superheating. If the distillation is interrupted, it will be necessary to introduce fresh porous plate after allowing the superheated liquid to cool for a brief time.

In the simple distillation of a substance of known boiling point, the distillate is collected (conveniently in an Erlenmeyer flask) until the temperature of distillation, as observed on a *calibrated* thermometer, reaches a point 2 or 3° below the true boiling point. The receiver is then replaced by a clean, weighed bottle, and the distillation continued until a temperature 2 or 3° above the boiling point of the substance is reached. Usually the distillate so obtained is sufficiently pure for ordinary purposes. In some cases where a purer product is desired, or some impurities which are harder to remove are present, a distillate boiling over a range of 6 to 8° may be collected, and this distillate redistilled, the final product being collected over a range of 2 to 3° symmetrical about the true boiling point. Occasionally a more elaborate procedure known as *fractionation* is required. This operation will be discussed in some detail below.

It should be clearly understood that the specifications as to temperatures given above cannot be considered as perfectly general rules, but that they frequently need revision to meet the requirements of the particular problem in hand. Thus if the desired substance is contaminated with a comparatively large amount of a very high boiling impurity, only a small fraction of the amount of substance actually present may be obtained by strict adherence to the above suggestions. In such a case, the first distillate should be collected until the temperature of the distilling vapors reaches a point as much as 10 or even 20° above the boiling point of the pure substance. This distillate may then be redistilled as directed above, since the high boiling impurity has now been largely removed.

Fractional Distillation.—It is important that the student realize that the procedure outlined above is in many cases quite inefficient in several respects. In a simple distillation we proceed in such a manner as to obtain a distillate as free as possible from impurities without recourse to more time-consuming operations. But to accomplish this end we have wasted all the material which was "carried over" by the lower boiling impurities, and all that was "held back" by the higher boiling material present in the original mixture. Furthermore, in many cases the method of simple distillation cannot give even a small amount of substance of satisfactory purity. This is usually true when impurities are present which boil within a few degrees of the substance to be purified. To surmount these difficulties, the process of fractionation is frequently employed. This process is much more widely used in industrial operations than in laboratory practice since efficient recovery of materials is so important a factor in the industrial field. The purification of alcohols and the fractionation of petroleum are important examples of the technical application of this process.

Fractionation consists essentially in the systematic redistillation of distillates (fractions) of increasing purity. The principle of the method will be made clear by a simple example. Figure 2 shows what are called the distillation curves for a simple binary mixture, the two components of which are mutually soluble in all proportions. It should be emphasized that many binary mixtures have distillation curves of an entirely different character, but it will be impossible to go into more complicated cases here. Reference may be made to works on the phase rule[1] and on fractional distillation[2] for more complete discussions. The boiling

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[1] Findlay, Alexander, "The Phase Rule and Its Applications," Longmans, Green & Company, 1931.

[2] Robinson, C. S., "The Elements of Fractional Distillation," McGraw-Hill Book Company, Inc., 1930.

point of pure A is at 60° and that of pure B at 87°. The "liquid curve" shows the boiling point of various mixtures of A and B. Thus a mixture containing 50 per cent A will start to boil at 67° (point P_1 in the figure). This does not mean that the whole mixture will distill at this temperature. Obviously, the lower boiling A will distill off more rapidly than B, so that after distillation starts, the residue will become richer in B and hence its boiling point will gradually increase. This is equivalent to saying that the vapor in equilibrium with the 50-50 mixture will contain more than 50 per cent A. If a horizontal line is drawn from P_1 to P_2 on the "vapor curve," the composition corresponding to P_2 is the composition of the vapor in equilibrium with the 50-50 liquid mixture at the latter's boiling point. In other words, if a *vapor* mixture of the composition corresponding to P_2 were cooled, the first condensation would occur at 67°. Thus if a small sample of the 50-50 mixture were distilled, the first distillate would be found to contain only about 13 per cent of B. Similarly, if this distillate were redistilled, the first small sample of material distilling would be found to contain only 2 per cent of B. It is evident that in this way a sample of material could be obtained which would be practically free from B.

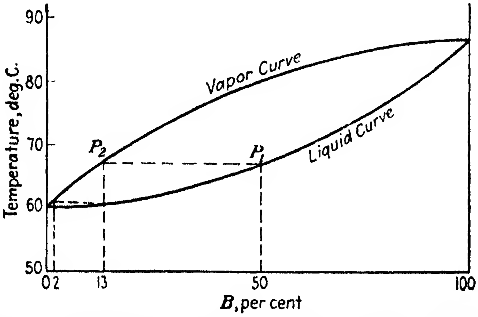

FIG. 2.—Distillation curves for a simple binary mixture.

In actual practice it is impractical to proceed in just this way, since the aim is not to obtain a very small sample of pure A, but to obtain in pure condition as much A and B as possible. To accomplish this, the original mixture is separated by distillation into several fractions of increasing average boiling point. The fractions are redistilled, and further separated into fractions. Neighboring fractions are combined and again distilled. The component A gradually accumulates in the low-boiling fractions and B in the high-boiling fractions. The specific procedure followed varies from case to case.

Fractionations can be carried out using an ordinary distilling flask, but in cases where the components do not have widely separated boiling points it is a very tedious process. A device known as a *fractionating column* very greatly simplifies the procedure. A fractionating column is essentially an apparatus for performing a large number of successive distillations without the necessity of actually collecting and redistilling the various fractions. Figure 3 is a simplified diagram of a fractionating column. Vapors from the distillation flask enter compartment I and are partially condensed there, the more volatile portion going on into compartment II, and so on. The material collected in I is richer in low-boiling material than the original mixture and therefore has a lower boiling point. Thus the vapors coming from the distillation flask are hot enough to make this material boil, in turn being partially condensed. Similarly the vapors from compartment I are hot enough to cause the distillation of material from compartment II into III, at the same time losing some of their heat and partially condensing out the higher boiling material. With an efficient column it is thus frequently possible to effect practically complete separation in one distillation in cases where fractionation with a simple distilling flask would require many redistillations.

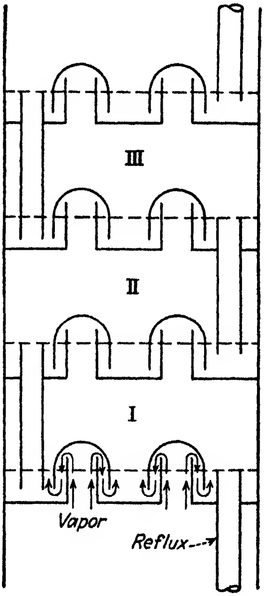

FIG. 3.—Fractionating column.

Figure 4 shows one of the types of fractionating column frequently used in laboratory work. Such a column is known as a *Hempel column.* It consists simply of a glass cylinder packed with glass beads or short pieces of glass tubing, each little interstice, in which liquid collects and through which vapor bubbles, serving as a small distillation flask. With high boiling liquids it is necessary to "lag" the column with a thermal insulator to prevent excessive condensation of vapors in the column.

It should be pointed out that there are some mixtures which cannot possibly be separated by fractionation, aside from the obvious case in which the components have the same boiling point. Thus a mixture containing about 5 per cent of water and 95 per cent of ethyl alcohol, a so-called *azeotropic* mixture, has a *constant* boiling point which is lower than that of either component; that is, such a mixture of alcohol and water would distill completely at one temperature. A perfectly efficient fractionation of 50 per cent ethyl alcohol would yield only pure water as the high-boiling product and this azeotropic mixture as the low-boiling product. A binary system of this type has distillation curves of a more complicated type than that illustrated in Fig. 2.

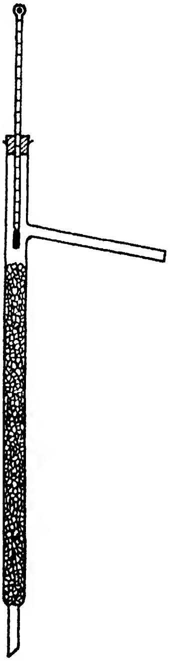

FIG. 4.—Hempel column.

Distillation of Solids.—In the distillation of substances which are solid at ordinary temperatures, the procedure is much the same as in the case of liquids, with a few minor changes. As a rule such substances boil at temperatures sufficiently high so that water condensers are unnecessary. Provision should be made in setting up the apparatus for the necessity of keeping the cooler parts, except for the receiver, free from solidified material. Thus it should be possible to apply heat, usually from the Bunsen burner, to any part of the condensing system. In the fractionation of solid substances it is necessary to have the column hot before the distillation starts, to prevent clogging by solid material.

Distillation under Reduced Pressure (Vacuum Distillation).—Many organic compounds decompose at temperatures lower than their normal boiling points, so that they cannot be distilled under atmospheric pressure. It is possible in many cases to lower the boiling point to a temperature at which decomposition does not take place by operating in a closed system under reduced pressure.

A simple apparatus for use in vacuum distillations is shown diagrammatically in Fig. 5. Tightly fitting rubber stoppers and tubes are to be used throughout. If the stoppers are too small they will be pulled into the flasks by the vacuum. The substance to be distilled is contained in a Claisen flask *A*, fitted with a tube with capillary opening *B* and a thermometer *C*. The capillary opening is made by drawing out one end of a piece of glass tubing to a diameter of 1 mm. and then further drawing out this section of the tube to a very fine capillary. The capillary is of the proper size if a very fine line of bubbles is formed on blowing into the open end while drawing the capillary through a small pool of water. The purpose of the capillary is to introduce a fine stream of bubbles into the liquid to prevent superheating and bumping. It is important that it be of the right size and that it extend clear to the bottom of the flask.

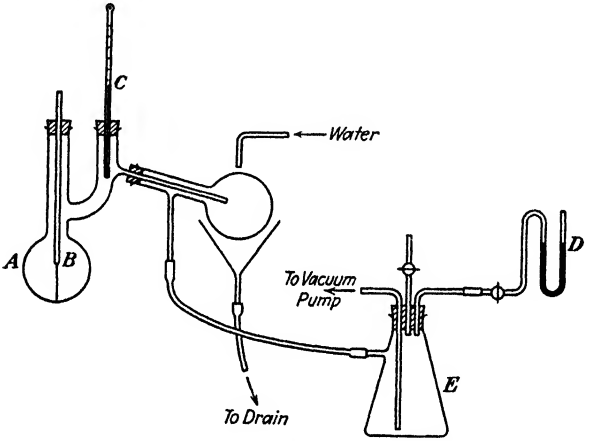

FIG. 5.—Vacuum distillation apparatus.

A satisfactory receiver, if the material to be distilled is not too volatile and if it is not necessary to collect several different fractions, is an ordinary distilling flask. This is connected to the side-arm of the Claisen flask by a rubber stopper; the side-arm of the Claisen flask should project into the bulb of the receiver so that complete condensation of the vapors can be accomplished.

The receiver is cooled in a stream of water, the waste water being collected in a funnel and carried to the drain by rubber tubing.

The side-arm of the receiver is connected by thick-walled tubing ("pressure tubing") to a mercury manometer *D* and a safety bottle *E*. The manometer is equipped with a stopcock so that it can be protected from condensing vapors during the distillation. This stopcock is to be opened only occasionally when it is desired to read the pressure. Great care must be exercised in opening the manometer to the atmospheric pressure because if the mercury is allowed to rise too rapidly it will break through the closed end of the manometer.

The safety bottle serves two important purposes. In the first place, it partially smooths out the more rapid fluctuations in the pressure of the system that arise both from irregularities in the rate of distillation and from changes in the efficiency of the evacuating water pump, resulting from variations in the laboratory water pressure. It is therefore advisable for the safety bottle to have a capacity of at least 500 cc. Furthermore, extreme fluctuations in the pressure of the water supply occasionally occur which result in water being sucked back into the apparatus from the suction pump. The safety bottle prevents contamination of the distillate from this cause. The safety bottle is fitted with three outlet tubes, one of which is connected to the suction pump by pressure tubing. This tube should reach to the bottom of the safety bottle so that if water is sucked into the bottle it will be withdrawn when evacuation again commences. Another of the outlet tubes is connected as shown to the rest of the apparatus, and the third, which may be closed by a glass stopcock or by a section of rubber tubing and a screw clamp, gives a convenient means of allowing the pressure in the system to rise. This tube should not be opened and the pressure inside the system allowed to rise, *until the manometer is shut off*, but it *must* be opened before the suction pump is turned off.

If the apparatus has been properly set up, no difficulty should be experienced in obtaining a pressure of 10 to 20 mm. of mercury, particularly when the water supply is comparatively cold. If a pressure of 20 mm. cannot be reached, it is necessary to go over the apparatus to eliminate leaks, making sure that the capillary tube is not too large, and checking up on all rubber stoppers and connections. One rather frequent cause of trouble is the use of such small glass tubing that the rubber tubing does not fit tightly over it. *It is never necessary or permissible to smear the apparatus over with vaseline in an attempt to eliminate leaks.*

If a comparatively volatile substance is to be distilled, a water condenser should be inserted between the Claisen flask and the receiver. If several fractions have to be collected, a different type of receiver will be more convenient. Several types have been designed which permit the collection of successive fractions without interruption of the distillation.[1]

In cases where the distillate solidifies on cooling, great care must be exercised to prevent the side-arm of the Claisen flask from becoming clogged up. If the distillation cannot be carried on rapidly enough to prevent the side-arm of the flask from becoming too cool, it may be necessary to interrupt the distillation at intervals to melt out the collected material.

The Claisen flask should be heated in an oil bath or, if care is used, on a wire gauze with a free flame moved back and forth rapidly beneath the gauze. It is perfectly feasible to use a fractionating column in a vacuum distillation.

If a pressure sufficiently low for distillation without decomposition cannot be obtained with a water pump, an oil pump may be used to obtain pressures as low as 1 to 5 mm. of mercury. Recently a technique has been developed for the distillation at low temperatures of very slightly volatile substances by the use of so-called *molecular stills*. These stills operate at the very low pressures (10^{-5} to 10^{-2} mm. of mercury) obtainable with diffusion pumps; they are designed so that the distance from the surface of the material being distilled to the condenser is less than the mean free path of the molecules at the temperature and pressure in the still.

It frequently happens that a substance is distilled at a pressure for which the boiling point is not given in the literature. In such cases it is helpful to know that for many organic substances at pressures in the neighborhood of 20 mm. a lowering of 10 mm. in the pressure causes a lowering of 10 to 15° in the boiling point. Another useful approximation is that the boiling points of sub-

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[1] L. GATTERMAN and H. WIELAND, "Laboratory Methods of Organic Chemistry," p. 20, The Macmillan Company, 1932.

stances having normal boiling points in the range 150 to 250° are lowered 100 to 120° by reduction of the pressure to 20 mm.

Steam Distillation.—Steam distillation is another method for accomplishing the distillation of a substance, solid or liquid, at a temperature below its boiling point under atmospheric pressure. It is necessary that the substance have an appreciable vapor pressure at 100° and that it be no more than slightly soluble in water.[1] The method consists essentially in removing the vapor of the substance from the distilling flask by flushing it out with steam. As soon as some of the vapor is removed in this manner, more of the substance will vaporize in the attempt to keep its partial pressure in the steam-vapor mixture constant.

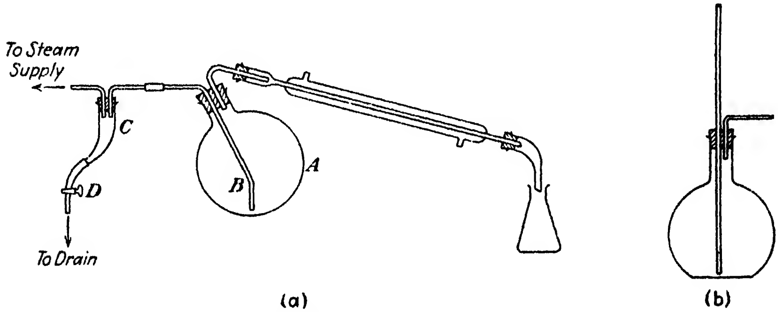

Fig. 6.—Apparatus for steam distillation.

The apparatus commonly used is illustrated in Fig. 6. The substance to be steam-distilled together with a small amount of hot water is placed in the flask *A*, which is fitted with an inlet tube *B* bent as illustrated and reaching to the bottom of the flask, and with an outlet tube leading (without a rubber connection) to a water condenser. The flask and tubes are placed as shown to minimize the danger of spattering material into the outlet during the rapid introduction of steam. If the laboratory is equipped

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[1] The term *steam distillation* is frequently loosely applied to the distillation of aqueous solutions of water-soluble volatile substances, such as acetic acid. The theory of such distillations is no different from that of the distillation of any homogeneous binary mixture. In cases where azeotropic mixtures (p. 16) are not formed, the boiling point of such a solution will lie between those of water and the substance in solution. On the other hand it will be shown that in a true steam distillation the temperature of distillation is lower than the boiling point of either component.

with steam outlets, a trap made from an adapter should be placed between the steam supply and the flask to catch the large amount of water usually present in the steam, thus preventing undue accumulation of water in the flask. *D* is a pinch clamp which is opened occasionally to allow the water in the trap *C* to run to the drain.

If no steam is available in the laboratory, the generator shown in Fig. 6*b* may be used. The generator flask (1 l. or more capacity) is fitted with a safety tube extending about 2 feet above the top of the flask. The addition of some pieces of porous plate will facilitate a steady flow of steam. If this generator is used, it is unnecessary to have a trap between it and the flask *A*.

During the distillation a small flame should be placed under the flask *A* to prevent too rapid accumulation of water. The distillation should be run as rapidly as possible, the only limits on the rate of distillation being the cooling capacity of the condensing system and the danger of splashing of material into the exit tube leading to the condenser. This latter danger can be minimized by having the end of the delivery tube flush with the stopper.

In the steam distillation of a substance solid at room temperature, it may be necessary to shut off the cooling water in the condenser to allow accumulated solid to be melted out in order to avoid an explosion. It should, however, be borne in mind that too sudden changes in temperature may break a soft-glass condenser.

Steam distillation is frequently used for purposes other than the distillation of a substance which cannot be distilled at atmospheric pressure. In the preparation of aniline (page 86), the preliminary purification of the product is accomplished by this method, even though aniline can be distilled at atmospheric pressure, because the only other means of isolating the aniline, namely, by extraction with ether (see page 39), would lead to the formation of emulsions difficult to "break" as a result of the alkali and tin compounds present. In the preparation of bromobenzene (page 62) steam distillation is used for the same reason, and also because it aids in the separation of the product from the main organic impurity, dibromobenzene, which is also soluble in ether. Another example of this application of the method occurs in the preparation of nitrophenols. In the nitration of phenol with dilute nitric acid the two main products are ortho and para nitrophenols. The former is much more "volatile with steam" than the latter, so that they may be separated by this method. Finally, steam distillation is frequently employed for the separation of impurities from a non-volatile product. Thus, in the preparation of triphenyl carbinol (page 101), the excess methyl benzoate and unreacted bromobenzene are removed from the non-volatile triphenyl carbinol in this way.

Consideration of the following numerical example will illustrate the fact that steam distillations are often surprisingly efficient, and will serve to clarify the above discussion. Table I gives the vapor pressures of aniline (B.P. 184°) and water at various temperatures. If we assume that water and aniline are mutually insoluble, which is not quite true, we may say that each exerts its vapor pressure independently of the other. We find by interpolation in the data given in the table that at 98.4° the pressure of the water vapor is 717 mm. and that of the aniline vapor is 43 mm., so that, if the atmospheric pressure is 760 mm., the mixture will boil at this temperature. According to Dalton's law, the molecular ratio of the two substances in the vapor phase is equal to the ratio of their partial pressures. Therefore, under equilibrium conditions, which are only more or less closely approached in actual distillations, we have, in the distillate collected, the ratio:

TABLE I

Temperature, °C.	Vapor pressure of water, mm. Hg	Vapor pressure of aniline, mm. Hg
80	355	18.0
90	526	29.2
100	760	45.7
110	1075	69.2

$$\frac{\text{Mols of aniline}}{\text{Mols of water}} = \frac{43}{717}$$

or, on introducing molecular weights,

$$\frac{\text{Weight of aniline}}{\text{Weight of water}} = \frac{43 \times 93}{717 \times 18} = 0.31$$

Thus the distillate contains

$$\frac{0.31 \times 100}{1.31} = 24 \text{ per cent}$$

of aniline by weight. Of course, the chief reason this result comes out so high is that water has such a low molecular weight. It should be pointed out that the failure to maintain equilibrium conditions in an actual distillation always tends to lower this figure. It would thus appear to be useless to increase the actual rate of distillation too much as this would result in a greater departure from the equilibrium conditions.

Sublimation.—This method of purification is comparatively unimportant so that it will be only very briefly mentioned. A simple apparatus (Fig. 7) for subliming a small amount of material consists in a porcelain evaporating dish covered with a piece of filter paper or cardboard perforated with a number of small holes. Over this rests an inverted funnel which acts as a condenser. The dish is heated with a very small flame. One of the modifications needed when larger amounts of material are to be sublimed is a water-cooled condenser. In such cases it is also desirable to replace the paper by a perforated porcelain plate.

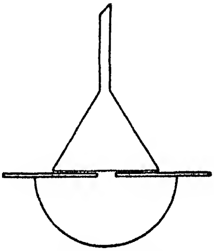

Fig. 7.—Sublimation apparatus.

Filtration

The subject of filtration is one which merits space in any discussion of laboratory methods as the procedure used depends very much upon the results desired. The common methods of filtration can be conveniently classified as filtration by gravity and filtration by suction.

The former method is the one with which the student is familiar from elementary chemistry. In organic laboratory practice this method is rarely used in cases where the precipitate is the desired product, the reason being that suction filtration offers a much quicker result with a more complete removal of the filtrate. If a small amount of precipitate is to be removed and discarded, gravity filtration should be used. The filtration can be carried out through a filter paper in the ordinary manner, or through a so-called "fluted" filter, which is one that has been so folded that the whole area of the paper is effective. (The laboratory assistant can illustrate the method of folding.) In certain cases the use of a fluted paper is not advantageous as it is difficult to wash it effectively. When it is desired to wash the precipitate, the filter paper should be folded in the orthodox manner.

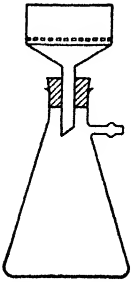

FIG. 8.—Büchner funnel and filter flask.

Filtration by suction can be carried out by means of any one of several devices, all of which utilize the same principle. Perhaps the commonest method involves the use of a Büchner funnel with a filter flask (Fig. 8). The Büchner funnel consists of a receptacle (generally porcelain) with a false bottom which is generously perforated. The stem of the funnel is fitted by means of a *rubber* stopper into the filter flask, the latter being connected with pressure tubing to the water suction pump. The filter paper, which should be small enough to lie flat on the false bottom of the funnel, is held in place by the vacuum. It should be moistened with the solvent being used, and the vacuum turned on, before starting the filtration. When finished, the vacuum should be broken before turning off the pump, as otherwise water will be sucked from the water mains back into the filter flask. Filtration by this method is ordinarily very rapid. The precipitate or crystals on the funnel may be washed with a small amount of solvent, and by allowing the pump to draw air through the product, it is easily dried. It is not advisable to use a Büchner funnel when a clear filtrate is desired, as when filtering off charcoal, because a small amount of the precipitate always finds its way underneath the paper. If it is desired to free a liquid of a large amount of precipitate, the precipitate can be filtered off and washed on a Büchner and the solution and washings later refiltered through a folded paper in the usual fashion.

A Hirsch funnel is in reality a modified Büchner, with sloping sides rather than straight ones, and designed to handle a smaller amount of precipitate. These funnels may be had tapering down to a size which accommodates a 3- to 4-mm. filter paper. A few milligrams of material may be easily handled in this way.

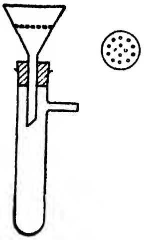

Fig. 9.—Side-arm test tube equipped with funnel and Witt plate.

A convenient substitute for the Büchner or Hirsch funnel is an ordinary glass funnel fitted with a Witt plate, which is a perforated porcelain plate 1 to 3 cm. in diameter which serves as a false bottom and upon which the filter paper can rest (Fig. 9). In this case the filter paper should have a diameter about 1 cm. larger than that of the Witt plate, and after being moistened with the solvent in use should be carefully fitted and folded into the funnel while the suction is applied. The proper use of the Witt plate is a little more troublesome than the use of the Büchner and Hirsch funnels. On the other hand, it is always possible to be assured of clean apparatus, whereas in the case of the porcelain funnels it is impossible to see whether or not they are clean under the false bottom.

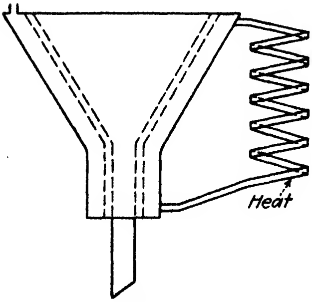

Fig. 10.—Hot-water funnel.

The filtration of hot saturated solutions is another matter which should be commented upon. The use of a Büchner or Hirsch funnel at this point is inadvisable, due to the fact that the lower temperature of the funnel causes crystals to be deposited in the small holes of the false bottom, and the funnel is completely plugged up in a very short time. A filtration of this kind is best carried out through fluted filter paper contained in a short-stemmed funnel that has previously been heated *cautiously* over a Bunsen burner to the temperature of the solution. This will minimize crystallization in the stem of the funnel. Another source of trouble at this stage, the crystallization of material before it has passed through the paper, can be largely avoided by placing a watch glass over the top of the funnel. This decreases the evaporation of the solvent with its attendant cooling. In cases where these precautions are insufficient, a device known as a hot-water funnel (Fig. 10) may be used. This is an ordinary glass funnel equipped with an outer jacket, usually of copper, through which water of any desired temperature may be circulated.

RECRYSTALLIZATION

By far the larger number of solid organic substances can be purified by a process known as *recrystallization,* which may be carried out in a number of different ways. In any case, the principle involved is the solution of the substance in a suitable solvent, followed by its reprecipitation by one of several methods; all or part of the impurities remaining dissolved in the mother liquor. In any of these methods losses are inevitable, in general, varying from insignificant ones in the case of a relatively insoluble compound, to very considerable losses in the case of a more soluble substance. The most commonly applicable methods will be described below.

Direct Recrystallization from a Solvent.—This method, which is that most commonly used, depends upon the fact that most substances are more soluble in a hot solvent than in a cold one. The substance to be purified is accordingly dissolved in a little more than just enough boiling solvent to effect solution. The hot solution is then filtered, if necessary, from any insoluble residue, and is cooled, the dissolved material crystallizing out. Most of the soluble impurities generally remain in solution, although frequently many recrystallizations are necessary to remove them completely. The yield of crystals can generally be increased by cooling the solvent below laboratory temperature by means of a suitable bath. Once the crystals have separated, they are best filtered off by suction. When they have been sucked as free as possible of mother liquor, they are washed with two or three small portions of cold solvent and then dried by allowing the vacuum pump to draw air through them while they remain on the funnel. *In performing a recrystallization in this manner, it is important, in case the solvent being used is inflammable, that the heating be done under a reflux condenser and the filtration carried out at a distance from a free flame.*

A device frequently resorted to for the quicker and more effective removal of soluble impurities is the use of some agent, such as norite, whose function it is to adsorb the impurities. This reagent is a chemically inert charcoal product which has been prepared in such a manner that it has a large surface-mass ratio. This is important because adsorption is a surface phenomenon. Although adsorption is much more complete at lower temperatures, it is customary to use norite at or near the boiling point of the solvent owing to the fact that equilibrium is reached so much more quickly at the higher temperature. The customary procedure is to add a small quantity of norite to the hot solution, in general about 0.25 to 0.5 g. per 100 cc. of solvent. Care must be taken that the solution is not superheated for, if norite is added to a superheated liquid (a freely boiling liquid is generally superheated), it causes an immediate and very vigorous boiling that usually results in the loss of a good deal of material. After addition of the norite, the solution is kept at or just under its boiling point for a suitable length of time, in general about 5 to 10 minutes, and the norite is then removed by filtration. Several such treatments with norite are frequently necessary. For hints about filtration see the previous section.

Some substances readily form highly supersaturated solutions. In such cases, recourse can be had to the process known as *seeding,* which consists in adding a few crystals of the substance to the solution. These *seeds* act as nuclei for crystal formation, which begins at once. Scratching the inside of the beaker with a sharp piece of glass will frequently have the same effect. It should be remembered that many organic substances precipitate from supersaturated solutions very slowly even after crystallization has been started. It is thus important never to discard a solution until one is certain no more crystallization will take place.

The choice of solvent is one of the most important points in a recrystallization, but no general rule can be given to cover this. A list of the common solvents which may be used for recrystallizing, in the approximate order in which they should be tried, follows: water, alcohol, benzene, glacial acetic acid, petroleum ether, chloroform, carbon tetrachloride, and ethyl acetate. Other solvents may be used in special cases. It is self-evident that one cannot use a solvent which will react with or decompose the solute. The temperature coefficient of solubility of a given solute varies enormously as we pass from one solvent to another, but the best solvents can generally be found only by the trial and error method, that is, by test tube experiments with small amounts of material.

Sometimes a mixture of two solvents, such as 50 per cent alcohol, will be found effective although neither of the solvents alone is useful. When a mixture of two solvents is used, they must generally be mutually soluble in all proportions. In choosing a mixture, one solvent is selected in which the solute has too great a solubility for effective recrystallization, and another in which it is only very slightly soluble. The general method of procedure is to dissolve the compound in the solvent in which it is soluble and then add the second solvent until the turbidity just disappears at the boiling temperature. The mixture is then allowed to cool.

Special Method for Recrystallizing Acids and Bases.—Most organic acids or bases can be recrystallized as described above, but there is in addition a special method which can be applied. This consists in taking advantage of the acidic or basic properties of these substances and dissolving them in water in the form of their salts, which are usually more soluble than the free acids or bases themselves. This is easily done, for instance in the case of acids (which include phenols), by dissolving the substance in dilute sodium hydroxide. An amine (organic base) is correspondingly treated with dilute hydrochloric acid. The solution can then be treated with norite if necessary, and filtered either hot or cold. The original substance is reprecipitated by neutralizing the inorganic base or acid which was added. If an acid is being recrystallized, acidification is generally carried out with hydrochloric or sulfuric acid. In the case of a base, ammonia will generally cause its precipitation although on occasion it may be necessary to use sodium hydroxide. Recrystallizations of this type may be carried out repeatedly until the substance has reached the desired state of purity.

Recrystallization by Evaporation of the Solvent.—It is occasionally difficult or impossible to find a solvent in which a substance has a high enough temperature coefficient of solubility to make an ordinary recrystallization feasible. In such a case two other methods are available, neither of which, however, is as satisfactory as the foregoing methods. The first of these alternate procedures is to dissolve the compound in some solvent, treat it with norite if desired, and then evaporate the solvent. This can be done either by evaporation in an open dish or by distillation *in vacuo* or at ordinary pressures. Crystals obtained in this way are much more apt to have inclusions or coatings of impurities. In the case of an inflammable solvent, precautions against fire must be taken.

Recrystallization by Precipitation with a Second Solvent.—This is perhaps the least satisfactory of all the methods of purification, as the crystals generally have inclusions of impurities, and common experience shows that it is in general a slow method for increasing the purity of a substance. This method consists in dissolving the material in a solvent, treating with norite if desired, and then filtering. A second solvent is then selected which is completely miscible with the first, but in which the compound to be purified is comparatively insoluble. By addition of the second solvent to the first, the solute is caused to precipitate or crystallize out. The commonest variation of this method is to dissolve the compound in alcohol and then precipitate it out by the addition of water. As a general rule, this method should be used only as a last resort.

Determination of Boiling and Melting Points

Valuable criteria of the purity of an organic substance are furnished by its boiling and melting points. These two physical properties are also of prime importance in the identification of organic compounds. As mentioned in the discussion of fractionation, a mixture of two mutually soluble substances will in general have a boiling point different from that of either pure component. Furthermore, a pure liquid will distill entirely at a constant temperature (except for superheating effects) while an impure substance will not. Thus the "distillation range" of a particular sample of a liquid gives a qualitative indication of its purity A sample of bromobenzene distilling in the range 152 to 162° will be less pure than a sample collected from 156 to 158°, if both samples are distilled under identical conditions.

In a similar manner, it is found that much information concerning the purity of a solid substance can be obtained from a determination of its melting point. In the vast majority of cases the presence of small amounts of impurities lowers the melting point of a solid substance, usually by several degrees. Furthermore, a pure substance usually melts over a smaller range than an impure one. A perfectly pure substance, if it melts without decomposition and if provisions are made for efficient equalization of temperature throughout the melting mass, would melt at a constant temperature. This degree of purity is, however, frequently difficult to obtain.

It is evident that considerable attention should be given to the determination of these important physical properties. The following paragraphs describe methods for their determination which will yield results sufficiently reliable for most organic work.

Calibration of a Thermometer and Determination of Boiling Points.—Because thermometers whose accuracy is guaranteed by the manufacturers are expensive, it is best to use an unguaranteed thermometer and to calibrate it by the method outlined below. *It cannot be too strongly emphasized that an uncalibrated thermometer should never be used for the determination of boiling or melting points.*

There are two serious sources of error in the ordinary thermometer. In the first place, the bore of the capillary tube holding the mercury is usually not quite uniform in diameter, though the scale is always uniform. It is thus possible for the thermometer to read correctly at some temperatures but not at others. In the second place, even if the capillary is perfectly uniform and the scale correctly placed, the thermometer will not record the temperature correctly unless the whole of the mercury column is immersed in the material whose temperature is being measured. In other words, thermometers are commonly designed for "complete immersion." It is obviously impractical to have this condition fulfilled, so that we must consider the so-called *exposed stem correction.* The part of the mercury column not immersed in the material under examination will be exposed to the cooler laboratory air and will therefore be somewhat contracted. For the present purposes, where we wish only to measure temperatures to the nearest degree, the exposed stem correction needed to allow for this effect is given with sufficient accuracy by the expression

$$+0.000154S(t - t_0) \text{ degrees}$$

where S is the exposed portion of the mercury column measured in degrees; t is the observed temperature; t_0 is the average temperature of the exposed stem; and 0.000154 is the apparent coefficient of expansion of mercury in glass. The magnitude of this correction, which has to be added to the observed temperature, is illustrated in Fig. 11, where the stem corrections have been plotted against observed temperatures for the case of a thermometer immersed to the 10° mark, the rest of the stem being exposed to an average temperature of 25°. It is evident that the exposed stem effect becomes important above 100° under these typical conditions.

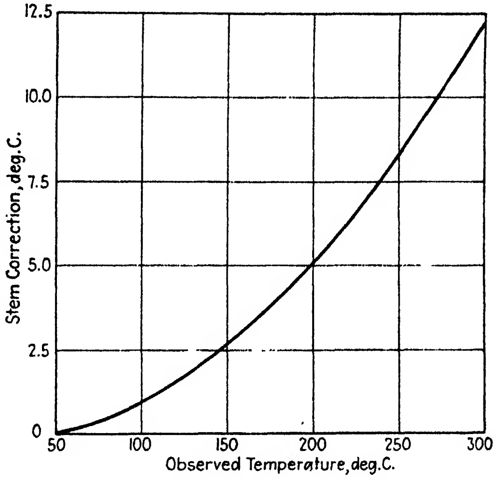

Fig. 11.—Variation of stem correction with observed temperature. (Exposed stem temperature = 25°; thermometer immersed to the 10° mark.)

It will be seen that the stem correction is taken care of in the method of calibration described below, so that it need not be considered in each temperature observation. It is present to the same extent in the calibration of the thermometer as in the use of it. It can be shown that this holds true, within the limits of accuracy desired here, even if there is considerable variation in the depth of immersion of the thermometer during the calibration and the subsequent measurements, or if the room temperature changes within reasonable limits (compare Problem 8, page 50). It is sufficient to keep the depth of immersion in all temperature measurements within ± 15 to 20° of the depth at the time of calibration.

A thermometer can be calibrated with sufficient accuracy by observing the boiling points of several pure liquids whose true boiling points are known. The boiling point of a substance varies with the atmospheric pressure, so that if this is very different from 760 mm. a correction should be applied. It has been found that the boiling points of most pure liquids increase by approximately 0.0001 of the absolute boiling point for each millimeter increase in barometric pressure; thus

$$\text{B.P.}_{\text{corr.}} = \text{B.P.}_{\text{obs.}} + 0.0001[273 + \text{B.P.}_{\text{obs.}}] \times [760 - \text{observed pressure}]$$

where $\text{B.P.}_{\text{corr.}}$ is the boiling point at 760 mm. pressure and $\text{B.P.}_{\text{obs.}}$ is the observed boiling point. It can be seen that this correction will not be very important if the barometric pressure is within 10 to 15 mm. of standard pressure.

It should be mentioned that other sources of error must be considered in more accurate temperature measurements.

Method.—A 50-cc. distilling flask is fitted with a thermometer and condenser, using cork stoppers, and 15 cc. of chloroform and several small pieces of porous plate are introduced. The flask is supported over an asbestos board having a 2-cm. hole drilled through the center. The thermometer should be so adjusted that the bulb is just below the side-arm of the flask. In future distillations and in the determination of melting points, care should be taken that the portion of the thermometer extending below the vapor ring in a distillation, or below the surface of a melting-point bath, is always nearly the same. In this manner, the stem correction for the thermometer is cancelled out as described above.

The chloroform is heated to boiling with a small flame and distilled at the rate of 1 drop per second. The thermometer is observed carefully and when the mercury becomes stationary the temperature is recorded. This is the observed boiling point.

After the flask is washed and dried, the process is repeated with each of the liquids listed in Table II. For liquids boiling above 160°, an air condenser should be used.

TABLE II

Substance	Boiling Point at 760 Mm.
Chloroform	61
Water	100
Chlorobenzene	132
Aniline	184
Nitrobenzene	211
p-Phenetidine	254

The observed boiling points (corrected to 760 mm. if necessary) are subtracted from the true boiling points given in the table above, to give the correction (which may be plus or minus) corresponding to each of the observed temperatures. These corrections are plotted against the *observed temperatures* on a sheet of cross-section paper. The calibration curve thus obtained is to be kept for future reference. In the determination of the boiling point of an unknown substance, one distills slowly, as directed above. The true boiling point (again including the effect of change of barometric pressure if necessary) is the algebraic sum of the observed temperature and the corresponding correction as read from the calibration curve.

The calibration of the thermometer may also be accomplished by determining the melting points of several pure solid substances of known melting point by the method described in the following paragraphs.

Determination of Melting Points.—The melting point of a substance is defined as the temperature at which the solid form of the substance is in equilibrium with the liquid form. The melting point is not appreciably affected by changes of pressure.

The melting point is determined by immersing a sample of material contained in a thin-walled capillary tube in a bath of a suitable liquid and observing the bath temperature at which fusion of the sample takes place. A convenient bath is afforded by a 100-cc. round-bottomed flask filled about two-thirds full with concentrated sulfuric acid. Another type of bath frequently employed is the so-called *Thiele tube*. The tube is filled to a level a little above the upper branch of the side-arm, and the side-arm is heated with a small flame. The warm liquid rising in the side-arm sets up convection currents that aid somewhat in stirring the bath. The same effect is obtained in the simple round-bottomed flask by the rising currents of warm liquid near the wall of the flask. Both these types of bath are rendered much more reliable by providing them with additional means for stirring. In the case of the round-bottomed flask, an air-driven screw stirrer may be used. A Thiele bath may be effectively stirred by introducing a small stream of air bubbles into the lower branch of the side-arm. These melting-point baths are illustrated in Fig. 12.

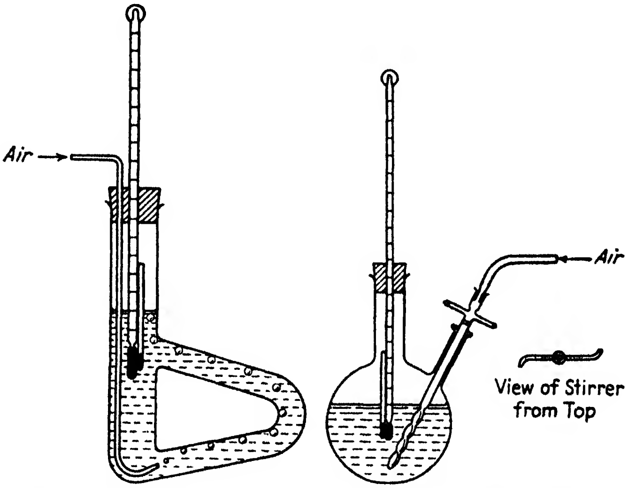

FIG. 12.—Melting-point baths equipped with stirring devices.

Melting-point baths filled with concentrated sulfuric acid may be heated to a temperature of about 250°. Above this temperature, the acid will fume objectionably unless some potassium sulfate is dissolved in it. *Caution must obviously be used in heating a bath of concentrated acid. Serious accidents may occur if the container cracks. A hot bath should not be cooled under the tap.* If the bath becomes discolored, it may be restored by the addition of a few small crystals of sodium nitrate. A cork and *standardized* thermometer are fitted in the neck of the flask so that the thermometer is immersed to about the same depth as it was during calibration. The cork should be cut out so that the capillary and scale of the thermometer are visible.

A capillary tube of 1-mm. internal diameter is made by drawing out a piece of glass tubing (or a test tube if a blast lamp is available). The capillary is cut into 10-cm. lengths and the wider end of each length is sealed up. Sufficient of the *thoroughly dried*[1] material to fill the capillary tube to a depth of 5 mm. is introduced. This can be accomplished by pushing the open end of the tube into some of the substance and then tapping the tube in a vertical position on the desk. If tapping fails to dislodge the material in the open end, this end may be lightly rubbed along a file. Sometimes even this procedure is unsuccessful; in such cases the tube may be placed, open end down, inside a slightly larger capillary.

The melting-point tube is attached to the thermometer by capillary attraction so that the sample is next to the thermometer bulb. The thermometer is immersed to the proper depth in the flask which is heated with a small flame. The temperature can be raised at the rate of several degrees per minute until 15° below the melting point of the substance, when the rate should be cut down to 2 or 3° per minute. (In case a substance of unknown melting point is being tested, it is advisable to run a quick preliminary determination to get a rough idea of the melting point.) The temperatures at which melting starts and at which the whole sample has just liquefied are carefully observed. These two temperatures define the melting range, and should both be recorded. Obviously if the bath is being heated so rapidly that insufficient time is allowed for the transfer of heat through the walls of the capillary, the observed melting point will be higher than the true melting point.

Mixed Melting Points.—Frequently it happens that an unknown solid substance may be one of several compounds whose melting points are close together. If samples of these compounds are available, the identity of the unknown substance can be established by the determination of *mixed melting points.* Briefly, the principle involved is that two samples of material,

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[1] The presence of even a small amount of a solvent may lower the melting point by many degrees.

each having nearly the same melting point, are in all probability identical if the melting point of a mixture of the two shows no depression. If they are not identical, a depression of from 5 to 50° is noted in the mixed melting point[1] except in the case of certain compounds of high molecular weight and very similar chemical constitution, such as the sterols. Approximately equal amounts of unknown and reference substances should be mixed, and it is frequently advisable to insure intimate mixing by melting the mixture in the capillary tube and refreezing it before determining the mixed melting point.

WASHING AND DRYING OF LIQUIDS

Washing.—In the course of the isolation of a product from a reaction mixture, or in the purification of solvents, it is frequently necessary to "wash" a liquid with water or some other reagent, such as aqueous alkali or acid or concentrated sulfuric acid.

The liquid to be washed is placed in a separatory funnel the capacity of which is 50 to 100 per cent greater than the volume of the liquid. Care must be taken that the stopcock and stopper of the funnel fit perfectly and that they are lubricated with a *very thin* layer of vaseline or stopcock grease. The washing reagent is then added. As shown below in the discussion of the operation of extraction, it is usually better to use two or three small portions of reagent rather than one large portion. In general, each portion of reagent should be about one-tenth to one-fifth the volume of the liquid to be washed.

While the stopper is held in place with one hand, the funnel is inverted. *If a volatile liquid is being used, the stopcock is immediately opened to allow the excess pressure in the funnel to escape.* After closing the stopcock, the funnel is shaken once or twice, still in an inverted position, and the stopcock again opened for a second. This process is repeated as long as any considerable pressure develops in the funnel on shaking; the funnel is finally shaken vigorously for a minute or two, replaced in the stand, and

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[1] Explanations of these generalizations, based on the phase rule, may be found in Alexander Findlay, "The Phase Rule and Its Applications," Longmans, Green & Company, 1931.

the stopper immediately removed or placed in such a position that any excess pressure can readily escape. It is a wise precaution to tie the stopper to the funnel with a piece of string, so that it will not be broken if it is pushed out.

After the two liquids have separated in the funnel, the lower layer is run into a flask of suitable size. If the lower layer is the one that is to be retained, care is taken that none of the upper layer is allowed to run out, while, if the upper layer is to be saved, a very small amount of it is allowed to run out to make sure that all the lower layer has been removed, and the upper layer is then poured out through the top of the funnel. It is advisable to allow plenty of time for complete separation of the liquids, and to withdraw the lower layer slowly to allow time for the liquid to drain from the sides of the funnel. If after withdrawal of the lower layer, the funnel is again shaken, the remainder of the heavy layer is consolidated in the bottom.

A great deal of time and effort is wasted by beginners who carelessly discard the wrong layer. It is therefore wise to make perfectly sure of the layer to be retained by performing a suitable test. For example, if a liquid immiscible with water is being washed with a water-soluble reagent, one should be sure that the layer discarded is miscible with water.

Emulsion Formation.—It occasionally happens that in the shaking operation an emulsion is formed which is difficult to "break." This is particularly apt to be the case if alkali is present. In many cases it is only necessary to wait for some time to elapse before attempting to draw off the lower layer. Frequently the addition of an electrolyte such as sodium chloride in rather large amount will hasten the separation of the layers In other cases, particularly when a very volatile liquid, such as ether, is present, it is helpful to apply weak suction from the water pump to the top of the funnel.

Reagents.—It is obvious that any reagent used in washing a liquid must be practically immiscible with the liquid. In most cases in organic work, a water-insoluble organic solvent, or a solution of an organic compound in such a solvent, has to be washed; consequently water or aqueous reagents are generally used, the commonest being dilute sulfuric or hydrochloric acid and dilute sodium or potassium hydroxide or carbonate. Dilute acids are used to remove acid-soluble substances such as amines (removed in the form of salts). Washing with an acid is always followed, unless circumstances prohibit, by washing with dilute alkali or alkali carbonate to remove the acid, and finally by washing with water. Dilute alkali is used to remove alkali-soluble substances such as phenols or acids, both organic and inorganic. Washing with this reagent is always followed by washing with water.

Drying.—The removal of water from organic solvents or solutions is usually accomplished by the addition of an anhydrous, insoluble inorganic salt which readily forms hydrates. The two commonest reagents are anhydrous calcium chloride and sodium sulfate. Calcium chloride should never be used when alcohols or amines are present, since it forms complex compounds with these substances. Solid potassium or sodium hydroxides are sometimes employed to dry alkali-stable substances in which they are insoluble, such as pyridine and other amines.

It is important never to use more of a drying reagent than necessary, in order to keep losses by absorption down to a minimum. A small amount of the reagent should be added, and the mixture shaken from time to time. If the reagent appears to become hydrated, more should be added. For most purposes, it may be assumed that drying is sufficiently complete after two hours, or less, if the mixture is repeatedly shaken.

In general, the drying agent has to be removed by filtration before the solution is distilled. This is due to the fact that salt hydrates have the property of decomposing with the evolution of all or part of their water of crystallization at perfectly definite temperatures. In the case of $Na_2SO_4 \cdot 10H_2O$, this temperature is 33°. Thus, if sodium sulfate were used for drying a solution and were not filtered off before distillation, at a temperature of 33° it would give back all the water it had taken from the solution plus any it might have had before use. As a result, sodium sulfate must always be removed. In the case of calcium chloride, the mixture should not be heated above 75° without removal of the drying agent. To avoid losses due to excessive absorption of the solution by the drying agent, the latter should be washed with dry solvent, the washings being combined with the filtrate.

Directions are given in a later section (page 42) for the more complete drying and purification of certain solvents.

EXTRACTION WITH VOLATILE SOLVENTS

One of the most convenient and frequently used methods of isolating an organic substance from an aqueous mixture, particularly if inorganic salts are present, is by extraction with an appropriate volatile solvent which is immiscible with water, such as ether or benzene. After extraction, the organic solution is washed with suitable reagents and dried, and the solvent removed by distillation as described below (page 41).

Extraction.—The extraction is performed in the manner described on page 36 under the washing of liquids. The number and volumes of successive portions of extracting solvent to be used depend on several factors. As a general rule, if the substance to be extracted is not too soluble in water, two or three portions of solvent each amounting to about one-fifth the volume of solution to be extracted are sufficient. In some cases only one portion is needed. Consideration of specific examples will clarify this point.

If a small amount of a solute is distributed between two liquid phases which are in equilibrium with each other, it is found that the concentrations in the two phases are such that:

$$\frac{\text{Concentration in phase A}}{\text{Concentration in phase B}} = \text{constant} = k$$

regardless, within limits, of how the total amount of solute or relative amounts of solvents are varied. This constant is known as the distribution coefficient, and, of course, has a different value for each pair of solvents and each solute. For a given solvent pair and solute, the coefficient also varies with the temperature. If the two solvents are completely immiscible, the constant k is equal to the ratio of the solubilities of the solute in the two pure solvents.

Suppose we have a solution of 5 g. of acetic acid in 100 cc. of water. The distribution coefficient of acetic acid between ether and water at 25° is about 0.5; that is, at equilibrium, the concentration of acetic acid in the ether layer is approximately half that in the aqueous layer. If 100 cc. of ether is added and the mixture brought to equilibrium by vigorous shaking, a certain amount, say x g., of the acetic acid will be removed from the water layer. The concentration of the acetic acid, expressed in grams per 100 cc. of solvent, in the ether layer will be x and that in the water layer will be $5 - x$. Therefore, according to the distribution law given above,

$$\frac{x}{5 - x} = 0.5$$

so that $x = 1.67$. This one extraction will thus remove

$$\frac{1.67 \times 100}{5} = 33 \text{ per cent}$$

of the acetic acid from the aqueous solution.

If in place of this one extraction with 100 cc. of ether, two successive extractions with 50-cc. portions of ether are performed, the acetic acid will be somewhat more completely removed. After the first extraction, the concentration in the ether layer will be $x/50$ g. per cc., or $2x$ g. per 100 cc., and that in the water layer will be $5 - x$. Therefore, since

$$\frac{2x}{5 - x} = 0.5, \qquad x = 1.0$$

20 per cent of the acetic acid is removed. After the second extraction the concentrations will be $2y$ and $4 - y$, respectively, if y g. are removed from the aqueous layer. Therefore, since

$$\frac{2y}{4 - y} = 0.5, \qquad y = 0.8$$

we see that these two extractions will remove a total of 36 per cent of the acetic acid.

By similar calculations, it can be shown that five successive extractions with 20-cc. portions of ether would remove 38 per cent of the acetic acid. It is thus apparent that in this particularly unfavorable case a large number of extractions would be required to accomplish anything approaching complete removal of the acid.

In the case of the extraction of *n*-butyric acid from water by means of ether (distribution coefficient = 5 at 25°), it is easily shown that, for a solution in 100 cc. of water, one portion of 60 cc. of ether removes 75 per cent of the acid while three successive portions of 20 cc. remove 88 per cent. A more extreme case is afforded by the extraction of aniline from water by benzene (distribution coefficient = approximately 15). In this case, a single extraction with a quarter volume of benzene will remove 79 per cent of the aniline, and a single extraction with a half volume of benzene will remove 88 per cent of the aniline, while extractions with two successive quarter volumes will remove a total of 96 per cent. Thus in this particular case it would be wasteful of time and solvent to use more than two extractions.

It should be emphasized that the above calculations are only approximate in nature, and are introduced simply to illustrate certain of the general rules of extraction.

Solvents.—The solvents commonly employed in extractions from aqueous solutions or suspensions are ether, benzene, toluene, petroleum ether (a low-boiling fraction of petroleum), chloroform, carbon tetrachloride, and carbon disulfide.

Treatment of the Extract.—If any inorganic or organic impurities which can be removed by washing with suitable reagents are present, the non-aqueous extract is washed and then dried over a suitable drying agent (see remarks on page 38). When thoroughly dry, the solvent may be removed by distillation. Since in most cases the organic solvent is volatile and inflammable, precautions have to be taken in this operation, particularly with ether, petroleum ether, and carbon disulfide.

Distillation of Volatile Inflammable Solvents.—A distilling flask (or Claisen flask, if the residue after removal of the solvent is to be vacuum distilled) is fitted with a dropping funnel in a tightly fitting cork (Fig. 13). The flask should have a capacity of about twice the estimated volume of the residue to be left after removal of the solvent. In the distillation of an inflammable solvent, the receiver is a filter flask fitted to the condenser with a cork and having a rubber tube leading from the side-arm to the floor to remove uncondensed vapors (heavier than air) from the vicinity of any flames. A few pieces of porous plate are placed in the flask, which is heated in a water bath, or better on a steam bath. The solution to be distilled is placed in the dropping funnel and allowed to run into the flask at such a rate that the flask does not become more than half full. If a water bath is used, the flame should be removed to a safe distance before the solution is poured into the dropping funnel.

It should be remembered that distillation on the water bath will not as a rule remove all of the volatile solvent, as explained on page 13. The remainder may be removed by cautious distillation using a wire gauze and a free flame. In this operation, however, it is frequently necessary to proceed with caution as the residue left after evaporation of the solvent may be more or less decomposed if the temperature rises too high.

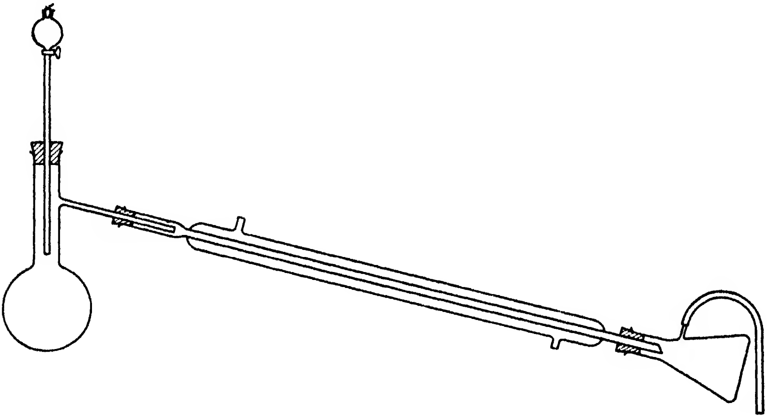

Fig. 13.—Distillation of volatile inflammable liquids.

Purification of Solvents

In the following paragraphs will be given methods for obtaining solvents which are reasonably pure. If purity of a higher degree is desired, advanced works on organic laboratory methods should be consulted.

Absolute Ethyl Alcohol.—One liter of 95 per cent ethyl alcohol and 200 g. of quicklime are placed in a 1500-cc. flask which is equipped with a reflux condenser. Atmospheric moisture is excluded by fitting a calcium chloride tube into the top of the condenser. The material is then refluxed for two hours and the apparatus rearranged for distillation from a boiling water bath. Care should be taken to protect the alcohol from moisture during this change. A convenient receiver consists of a 1-l. distilling or filter flask, to the side-arm of which is attached a calcium chloride tube. The first 10 cc. of distillate is discarded because it has removed the moisture from the air which was in the apparatus. The alcohol so obtained is termed *absolute*, although in reality it still contains 0.5 to 1 per cent of water.

If it is desired to remove the remainder of the water, recourse must be had to some other method. Metallic sodium is frequently used for the complete dehydration of solvents, but it cannot be used alone in the case of alcohol since the sodium hydroxide formed by its action is partially converted to water and sodium ethoxide by reaction with the alcohol:

$$NaOH + C_2H_5OH \rightleftharpoons C_2H_5ONa + H_2O$$

However, if excess sodium is used and the sodium hydroxide is removed, alcohol of a high degree of purity can be obtained. The alkali is conveniently removed by causing it to react with an ethyl ester of such a high boiling point that the purified alcohol can be removed from an excess of the ester by distillation. For this purpose diëthyl phthalate is usually employed.

$$C_6H_4(COOC_2H_5)_2 + 2NaOH \longrightarrow C_6H_4(COONa)_2 + 2C_2H_5OH$$

One liter of so-called *absolute alcohol* is placed in a 2-l. flask equipped with a reflux condenser, which should have a calcium chloride tube to give protection from moisture. Seven grams of clean sodium cut in small pieces is dissolved (**Caution!**) in the alcohol, followed by 30 g. of diethyl phthalate. After refluxing for 1 hour, the alcohol is removed by distillation. If proper precautions are taken for constant exclusion of moisture, the water content should not be more than 0.05 per cent. *As absolute alcohol is extremely hygroscopic, it must be kept in a tightly sealed bottle.*

Absolute Ether.—The common impurities in commercial ether are water, alcohol, and in samples which have been exposed to air for some time, ether peroxides. These latter are very explosive when concentrated by evaporation of the ether, but can be destroyed by washing the ether with a solution of ferrous sulfate containing a small amount of sulfuric acid. In fresh samples of ether the peroxides can be ignored.

For the removal of alcohol and water, the ether is first treated with anhydrous calcium chloride which forms an addition compound with alcohol as well as water. This treatment should be continued for several days, with as frequent shaking as possible. The calcium chloride is then removed by filtration and the remaining impurities are removed by the addition of sodium, which should be cut into small pieces if it is not available in the form of wire. As soon as the evolution of hydrogen has ceased, the ether can be distilled from a water bath and stored in a bottle over fresh sodium. It is, of course, necessary to protect the ether from atmospheric moisture at all stages.

Benzene.—For ordinary purposes in an elementary laboratory, it is sufficient to dry benzene over sodium, followed by distillation as in the case of ether. The dried benzene is stored over fresh sodium. It should be mentioned, however, that this does not serve to remove thiophene, which is usually a contaminant but which is not objectionable in most cases. Benzene of high purity is obtained by washing thoroughly with concentrated sulfuric acid and then with alkali followed by water. The benzene is then dried in the manner described for ether, first with calcium chloride and then with sodium.

Acetone.—Acetone is refluxed with successive small portions of potassium permanganate until the violet color of the permanganate persists. It is then dried over anhydrous potassium carbonate and distilled, precautions being taken to exclude moisture.

Chloroform and Carbon Tetrachloride.—These two solvents *cannot* be dried over sodium, owing to their reaction with this reagent. Ordinary impurities can be removed by washing with concentrated sulfuric acid in a separatory funnel, followed by washings with alkali and water. They are then dried over calcium chloride. If more complete removal of water is desired, they are dried over phosphorus pentoxide and distilled in the absence of moisture.

PREPARATION AND PURIFICATION OF GASES

Hydrogen Chloride.—Anhydrous hydrogen chloride is frequently used in organic reactions, as in the preparation of esters and the formation of hydrochlorides of amines. The most convenient preparation of the gas on a laboratory scale is by the dehydration of concentrated hydrochloric acid with sulfuric acid or by the action of sulfuric acid on sodium chloride.

If a comparatively small amount of the gas is required, it may be formed in a generator of the type illustrated in Fig. 14. A filter flask, fitted with a dropping funnel, is connected with a wash bottle which carries a safety tube and contains concentrated sulfuric acid. The wash bottle is in turn connected with a safety bottle to prevent the sucking back of the organic reaction mixture into the wash bottle should the flow of gas become too slow. Rubber stoppers are used throughout the apparatus, and any connections of rubber tubing should be as short as possible since the tubing will be ruined for any other purpose. A layer of sodium chloride about 1 cm. thick is placed in the generating flask which is one-third filled with concentrated hydrochloric acid. Concentrated sulfuric acid is added from the dropping funnel at a rate sufficient to maintain a steady flow of gas. No trouble will be experienced in adding the sulfuric acid, if a rubber connection is made between the top of the dropping funnel and a T-tube placed between the generating flask and the wash bottle. This connection serves to equalize the pressure above and below the acid in the funnel. The hydrogen chloride is dehydrated by being passed through the concentrated sulfuric acid contained in the wash bottle.

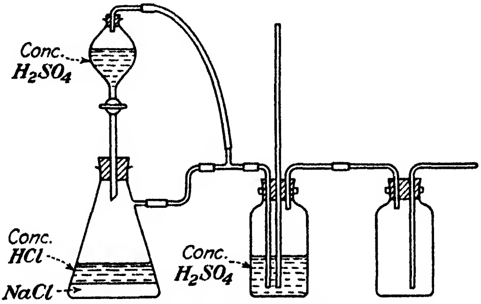

FIG. 14.—Hydrogen chloride generator.

Several points should be borne in mind. If the hydrogen chloride must be quite anhydrous it will be advisable to pass it through two wash bottles connected in series (the second one need have no safety tube). Or the simple type of bottle illustrated may be replaced with a bottle designed to insure more prolonged and intimate contact of the gas with the sulfuric acid. Efficient drying can be accomplished only if the stream of gas is not too rapid. If the total depth of sulfuric acid through which the gas has to go is more than 6 or 7 cm., it may be advisable to wire in place those rubber stoppers subjected to the largest pressure differences.

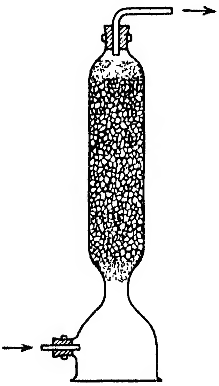
FIG. 15.—Drying tower.

The purified hydrogen chloride is usually to be absorbed in some organic solvent, such as alcohol or ether, in which it is highly soluble. It is therefore necessary to be certain that the evolution of gas does not become so slow as to allow organic liquid to be sucked back, and *to disconnect the absorption flask before the flow of gas is shut off*. These remarks should be kept in mind in connection with the use of the other gases considered below.

All experiments involving the use of hydrogen chloride should be performed in the hood.

Ammonia.—Ammonia is prepared on a laboratory scale by distillation from concentrated ammonium hydroxide. The distillation is performed from a round-bottomed flask fitted with an efficient reflux condenser. A tube leads from the top of the condenser to a drying tower of the type shown in Fig. 15, which is loosely packed with soda lime for removing water. At each end of the column of soda lime there should be a layer of glass wool, the upper one serving as a filter and the lower one as a support for the soda lime. The ammonia is led from the drying tower to a safety bottle, arranged so that any liquid sucked back from the mixture being treated with the gas will eventually be returned to the mixture. Work with ammonia should always be performed under the hood.

Carbon Dioxide.—This gas may be generated in small quantities in an apparatus of the type illustrated in Fig. 14. Some small lumps of marble are placed in the generating flask and dilute hydrochloric acid (1:1) is added from the dropping funnel. The gas may be freed from hydrogen chloride and dried by passing it first through water and then through concentrated sulfuric acid. If the carbon dioxide is to be used for quantitative analytical purposes, further precautions must be taken.[1]

A Kipp generator (Fig. 16) is a very convenient source of carbon dioxide. Carbon dioxide for use in forming acids from Grignard reagents is frequently employed in the form of "dry ice."

Hydrogen Sulfide.—This gas can be prepared in the generator in Fig. 14 by the action of dilute hydrochloric acid on ferrous sulfide. It should be washed by passage through water. A Kipp generator is more convenient if available. All work with hydrogen sulfide is to be done under the hood.

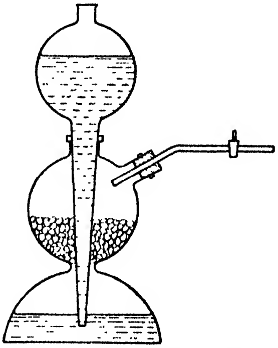

FIG. 16.—Kipp generator.

Chlorine, Sulfur Dioxide, Oxygen, Hydrogen, Nitrogen.—These gases are most conveniently obtained from cylinders of the compressed or liquefied substance. *Cylinders of compressed or liquefied gases should always be handled with care.* The above-mentioned gases can all be dried sufficiently for most purposes by passage through concentrated sulfuric acid. For special purposes it is frequently necessary to purify the gas by a more or less elaborate purification "train." For discussion of these procedures, reference should be made to more advanced laboratory manuals, or to such standard works as Houben-Weyl, "Die Methoden der organischen Chemie," or to the original literature in certain cases.

In using a gas from a cylinder it is advisable, particularly in the cases of very soluble gases, to put a trap of generous capacity between the tank and the rest of the apparatus to prevent entrance of any foreign material into the tank. Furthermore, if there is likely to be any considerable resistance to the passage of the gas, safety valves, such as a long upright glass

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[1] FISHER, H. L., "Laboratory Manual of Organic Chemistry," pp. 302–308, John Wiley & Sons, Inc., 1931.

tube reaching below the surface of the liquid in the wash bottle, should be provided. For gases under high pressure a reducing valve or a "micro" control valve is necessary. Finally, it is always necessary to provide traps to prevent sucking back of foreign liquid material into any wash bottles used in the purification train. Chlorine and sulfur dioxide should be used only under an efficient fume hood.

Cleaning and Drying Apparatus

A few suggestions on this subject will be helpful. There are two good reasons for always cleaning apparatus as soon as possible after use. If this practice is followed, the apparatus will usually have a chance to dry before it is needed again, and it will also be clean if needed in an unexpected emergency. Much time is wasted by students who look at the directions for their next experiment and find that a flask which has been standing dirty for a week is needed in the first operation. There is usually plenty of time to clean up one's apparatus during a filtration or a short refluxing period. Another reason is that a more intelligent selection of an efficient cleaning agent may be made if the nature of the deposit in the apparatus is known. For example, in the preparation of *p*-nitrobenzoic acid by the oxidation of *p*-nitrotoluene with permanganate (page 73), a brown stain of manganese dioxide is left in the flask. This stain would be difficult to remove with soap and water, but it is easily removed with concentrated hydrochloric acid.

In the absence of any preference based on the nature of the contamination to be removed, the first cleansing agent to be tried is soap, hot water and a brush. If this is ineffective, various solvents may be used, the commonest being alcohol, ether, acetone, aqueous acids or alkalies, or concentrated sulfuric acid. Finally oxidizing agents may be tried. For this purpose a hot solution of crude sodium dichromate in crude concentrated sulfuric acid is very satisfactory. This mixture is commonly called "cleaning solution." There are very few contaminations likely to be present in apparatus used for organic work that are not removed by this agent. It is frequently helpful, in cleaning a flask with concentrated sulfuric acid or cleaning solution, to add a teaspoonful or so of dry sand, followed by shaking. This effectively scours out the dirt. Care should be taken that the sand be discarded into the waste jar, not the sink. If much apparatus has to be cleaned, it is convenient to have a bath of the cleaning solution contained in a large porcelain evaporating dish. It should be remembered that the action of this cleansing agent is not generally instantaneous. Obviously, great care should be exercised in handling this solution. When cooled it may be kept for future use in a tightly stoppered container.

Occasionally it is desirable to dry a piece of apparatus rapidly. This is readily accomplished by rinsing the clean apparatus with two or three small portions of acetone, and removing the acetone by a stream of air from the compressed air outlet. The acetone rinsings may be replaced by a rinsing or two with alcohol to remove the water, followed by a rinsing with ether to remove the alcohol.

WASH BOTTLE

A wash bottle (Fig. 17) should be made at the first laboratory period, and used consistently. If it is made with a capacity of 500 cc., it can be used for solvents other than water.

Except when performing qualitative tests for the elements present in organic compounds, or in quantitative procedures, it is usually unnecessary to use distilled water, ordinary tap water sufficing.

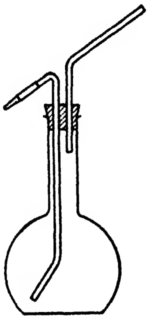


FIG. 17.—Wash bottle.

Problems

1. In each of the following cases indicate whether the boiling point of the mixture will be lower than that of the more volatile component or between the boiling points of the two components. The third mixture is the only one in which an azeotropic mixture is formed. Give reasons for your answers.

Toluene and benzene (mutually soluble)
Aniline and water (mutually insoluble)
Ethyl alcohol and water (mutually soluble)

2. Under equilibrium conditions, the steam distillation of a certain substance insoluble in water took place at 90° and yielded a distillate containing 75 per cent by weight of the substance. The barometric pressure was 755 mm. Calculate the molecular weight of the substance. (The vapor pressure of water at 90° is 526 mm.)

3. Ether boils at 35°. Explain the fact that it is impossible, on a boiling water bath, to remove all the ether from a mixture of ether and a substance boiling at 200° which is soluble in it in all proportions. Under what circumstances of solubility would it be possible to remove all the ether on a boiling water bath?

4. Suppose a very large quantity of a mixture containing 90 per cent B is available (distillation curves in Fig. 2). It is desired to obtain a small amount of relatively pure A. Approximately how many successive distillations would be required to obtain this sample, if in each distillation only a small fraction of the preceding distillate is collected? Explain.

5. The distribution coefficients between ether and water of ortho- and para-nitroanilines are, respectively, 62 and 10. Suppose a solution of equal amounts of these two substances in 100 cc. of water were extracted with 100 cc. of ether and the ether removed by distillation. Which nitroaniline would be present in the residue in larger amount, and what percentage would it be of the total residue? Assume the solubilities of each of the isomers to be unaffected by the presence of the other.

6. Salicylic acid has a distribution coefficient between ether and water of approximately 50. How much ether would have to be used to remove 95 per cent of the salicylic acid from 100 cc. of an aqueous solution in one extraction? How much acid would be extracted with an equal volume of ether?

7. Perform the calculations referred to (pages 39–41) in connection with the extraction of acetic acid, butyric acid, and aniline from water.

8. Suppose a thermometer has been calibrated for temperatures in the neighborhood of 250° with the stem immersed to the 0° mark. What would be the approximate error introduced in measuring an unknown melting point in this neighborhood with the thermometer immersed to the 20° mark? Would likely changes in the room temperature (10° at the most) affect the accuracy of such measurements appreciably?

CHAPTER III

PREPARATION OF ORGANIC COMPOUNDS

INTRODUCTION

Much of the laboratory work in organic chemistry, both in courses in the subject and in original research, has to do with the preparation and purification of organic compounds. Though the variety of known organic compounds is very great, and the variety of as yet unknown substances which can be prepared by known reactions and methods is vastly greater, nevertheless a surprisingly small number of laboratory techniques is needed in the preparation of the large majority of substances. The preparations outlined in this chapter have as a major purpose the illustration of the more important of these techniques. These preparations are somewhat time consuming, so that only a fraction of them can usually be included in any course. For this reason they are to be considered rather as illustrations of organic laboratory methods than as illustrations of organic reactions. It is therefore permissible to include in a student's assignment those preparations which involve reactions that have not been studied in class, if by so doing a given method is more effectively or efficiently presented. Short theoretical discussions are introduced before each preparation to prevent the student from losing the real connection between the theoretical and laboratory sides of the subject while performing a preparation involving as yet unstudied chemistry. It is very important that the student study these discussions carefully, and supplement his study by reference to the textbook whenever possible.

Directions for organic preparations are most conveniently presented in a form which bears an unfortunate resemblance to the familiar household cookbook. However, there are usually very good reasons for each of the details in a preparation, and it is highly important for the student to discover these reasons, first by serious study on his own part and, if this is unsuccessful, by discussion with the laboratory assistant or instructor. It cannot be too strongly stated that if the preparative work in organic chemistry degenerates into so-called "cookbook" chemistry, no one is to blame but the student himself.

In practical organic work, it is frequently necessary to perform a series of reactions in which the product of one reaction is the starting material in the next. In such series of reactions, it is obviously essential to obtain as good a yield of each product involved as possible. To develop in the student a reliance on his own results, a few simple series of reactions are included in the preparations described.

It is of interest to note that many of the preparations given are really laboratory-scale duplicates of reactions of major importance in the industrial field. It will be instructive for chemical engineering students to compare details of the laboratory preparations with the same processes as carried out in the chemical industry, considering such points as the relative efficiencies, and the modifications desirable in large scale production. A means of direct correlation with the engineering courses is thus obtained.

It is obvious that one can, in general, expect good results in a preparation only if reagents of reasonable purity are employed. Such reagents are assumed throughout in the following preparations. Where reagents of doubtful purity are to be employed, they should be subjected to a suitable method of purification before the reaction is started. In this connection it is worth while observing that, in many cases, although impurities may be present which will not interfere with the desired reaction, nevertheless they may render purification of the final product more difficult.

The yields given at the end of each experiment represent what an average student should obtain.

Preparation 1. Benzene

One of the classical methods in organic chemistry for the elimination of the carboxyl group of an acid is to heat the substance or its sodium salt with soda lime which is a mixture of calcium oxide and sodium hydroxide. The reaction may be represented by the equation:

$$\mathrm{R\boxed{COONa + NaO}H \xrightarrow{\Delta} RH + Na_2CO_3}$$

The reaction is characteristic of both aliphatic and aromatic acids. The following preparation is frequently used when it is desired to obtain benzene which is completely free of thiophene, the common contaminant of benzene obtained from coal tar.

Procedure.—Ten grams of sodium benzoate is intimately ground with 20 g. of soda lime, and the mixture is placed in a 25- by 150-mm. Pyrex test tube and covered with unground soda lime. The tube is then clamped in a horizontal position and fitted with a delivery tube that leads to a test tube resting in a beakerful of cracked ice. This serves as a condenser.

The tube is now heated strongly with a Bunsen flame, beginning near the top in order to have the soda lime hot before vapors start to pass over it. The heating is gradually extended down the tube until it has all been heated to a dull redness. During this time about equal amounts of water and benzene condense in the receiver, along with various impurities. The benzene is purified by adding to it several crystals of potassium permanganate and distilling carefully, condensing the vapors in a test tube in the same manner as before. The benzene is separated from the water and dried with a piece or two of anhydrous calcium chloride. The yield of pure benzene should be 3 to 4 cc.

Questions

1. What by-product should be obtained when sodium or calcium benzoate is heated?

2. What purpose did the potassium permanganate serve, and how? From this what would you judge as to the stability of benzene to strong oxidizing agents?

3. Write equations for the reactions occurring between benzene and each of the following reagents: (*a*) Bromine and a catalyst; (*b*) concentrated nitric and sulfuric acids; (*c*) fuming sulfuric acid.

Preparation 2. Acetylene

Acetylene is one of the most important industrial raw materials. It is used in the form of "Prestolite," a solution under pressure in acetone, for oxyacetylene welding, but more important still is its use as the starting material in the production of acetaldehyde, acetic acid, ethyl acetate, synthetic rubber, and a host of other industrial chemicals. The acetylene, so used, is all produced from water and calcium carbide, which is in turn produced from lime and coke. The reactions are represented by the equations:

$$CaO + 3C \longrightarrow CaC_2 + CO$$
$$CaC_2 + 2H_2O \longrightarrow C_2H_2 + Ca(OH)_2$$

Procedure.—Ten grams of calcium carbide is placed in a distilling flask which is clamped in an upright position and is equipped with a dropping funnel and a glass delivery tube leading into a pan of water or a pneumatic trough. It is necessary for the following experiments to collect three bottles of the acetylene by downward displacement of water. These bottles should be fitted with glass plates to serve as covers. One bottle of gas should be discarded before the samples to be used below are collected. When arrangements have been completed for the collection of the gas, water is added dropwise through the separatory funnel, the reaction proceeding very rapidly. When the three bottles of gas have been collected, the flask is *taken to the hood* and washed out carefully with water. The following experiments can then be performed on the samples of acetylene:

1. *Bromine and Acetylene.*—Two drops of bromine are added to a bottle of acetylene. The bottle is then covered and shaken until the bromine color disappears. If too much bromine has been added, it can be decolorized by the addition of a little 5 per cent sodium hydroxide. Note the odor and appearance of the product formed in this reaction.

2. *Potassium Permanganate and Acetylene.*—To another bottle of the gas is added 5 cc. of a very dilute solution of potassium permanganate. Note the color change and formation of a precipitate.

3. *Cuprous Chloride and Acetylene.*—Cuprous chloride is prepared by boiling a mixture of 5 g. each of copper oxide and metallic copper in a 1:1 solution of hydrochloric acid. This is done in a flask with a funnel in its neck to prevent access of air.

After the solution has become a straw-yellow in color, it is cooled under the tap, decanted, and made ammoniacal. Five cubic centimeters of this solution is added to a bottle of acetylene. Note the color of the voluminous precipitate formed. This reaction is a test for the group $—C{\equiv}CH$, two of these groups being present in acetylene. Acetylenes of this type also react with ammoniacal silver nitrate, with the production of a white precipitate. These acetylides are dangerously explosive when dry, and the precipitate should therefore be discarded into the sink.

Questions

1. Why is the first bottle of gas discarded?
2. Write all the equations for the reactions in the three tests performed on acetylene.
3. Write equations for the reactions of acetylene with: (*a*) Hydrogen bromide; (*b*) silver nitrate; (*c*) sulfuric acid and mercury salts; (*d*) hydrogen and a catalyst.
4. Illustrate by equations several of the important commercial syntheses in which acetylene serves as the starting material.
5. Calculate the volume of acetylene collected over water at 25° and 750 mm. pressure which should be obtained from 10 g. of calcium carbide. The vapor pressure of water at 25° is 23.8 mm.

Preparation 3. Ethyl Bromide

A common reagent for the conversion of an alcohol into an alkyl halide is the corresponding halogen acid. This preparation illustrates a convenient method of obtaining the halogen acid, namely, its generation *in situ* from sodium halide and sulfuric acid. The net result can be represented by the equation,

$$C_2H_5OH + NaBr + H_2SO_4 \longrightarrow C_2H_5Br + NaHSO_4 + H_2O$$

As ethyl bromide is very volatile, care has to be exercised that it is not exposed unnecessarily to chances for evaporation.

Procedure.—Ninety grams of 95 per cent ethyl alcohol is placed in a 2-l. round-bottomed flask and 110 cc. of concentrated sulfuric acid is cautiously added with constant shaking and cooling. Fifty grams of cracked ice and 90 g. of sodium bromide are then added and the mixture is thoroughly shaken. The flask is connected tightly (*with a rubber stopper*) to a condenser equipped with an adapter tube which should dip under the surface of a beakerful of ice water (Fig. 18). The flask is placed in a sand bath which is heated with a large Bunsen flame. The ethyl bromide distills over rapidly and collects as an oily layer in the bottom of the receiver. The distillation is continued as long as any water-insoluble material passes over.

The oil is separated from the water by means of a separatory funnel and washed (see page 36) once with water, once with dilute sodium carbonate, and again with water. In these washings it is well, in drawing off the ethyl bromide, to place the tip of the funnel under the surface of the next solution to be used for washing. After washing, the ethyl bromide is drawn off into a distilling flask, 5 g. of anhydrous calcium chloride is added, and the mixture is occasionally shaken during a period of 1 hour. The ethyl bromide is then distilled from a water bath whose temperature should not exceed 60°. The fraction boiling between 38 and 42° is collected. Ethyl bromide boils at 39°. About 65 to 70 g. of product should be obtained.

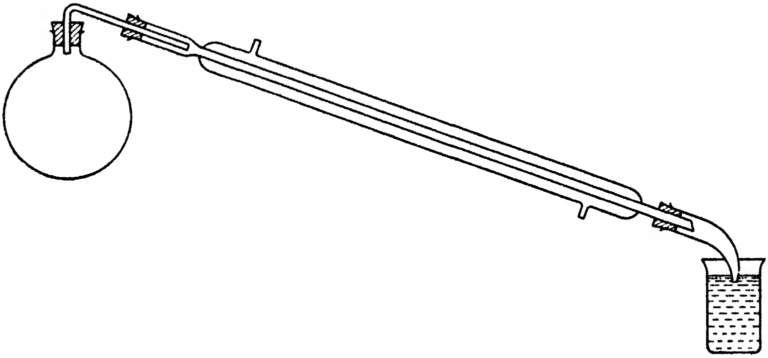


Fig. 18.—Apparatus for ethyl bromide.

Questions

1. What does the washing with sodium carbonate remove? How did these products arise?

2. Occasionally the ethyl bromide distills over with a reddish color. Suggest what this color is due to and give an explanation of the origin of the substance causing the color.

3. Suggest a reason for the fact that ethyl iodide cannot be prepared by this method, with sodium iodide replacing the bromide.

4. Write equations for the reactions of ethyl bromide with each of the following reagents: (*a*) Aqueous sodium hydroxide; (*b*) alcoholic sodium hydroxide; (*c*) ammonia; (*d*) magnesium; (*e*) sodium; (*f*) methyl magnesium bromide; (*g*) sodium acetate; (*h*) sodium ethoxide; (*i*) sodium cyanide.

5. How could ethyl bromide be converted into each of the propyl bromides?

Preparation 4. n-Butyl Bromide

This preparation illustrates the same general reaction as the preceding one; the formation of an alkyl halide from an alcohol and a halogen acid. In this case, however, the hydrogen bromide is obtained by the reduction of bromine with sulfur dioxide.

Procedure.—**(Caution! Read the remarks on pages 5 and 6 about the handling of bromine.)** Seventy-five grams of crushed ice and 70 g. (22 cc.) of bromine are placed in a flask immersed in an ice bath, and sulfur dioxide is passed into the mixture until the bromine color just disappears **(Hood!)**. To this solution is added 50 g. of *n*-butyl alcohol, and then 36 g. (20 cc.) of concentrated sulfuric acid in small portions with shaking. The mixture is refluxed (see Fig. 19) for 2 hours **(Hood!)**, and the butyl bromide is then removed by distillation, the distillation being continued as long as water-insoluble material passes over. The non-aqueous layer in the distillate is separated, washed with dilute sodium carbonate **(Caution!)**, and finally with water. The bromide is dried over calcium chloride and, after removal of the drying agent, purified by distillation. *n*-Butyl bromide boils at 102°. The yield should be 65 to 70 g.

Questions

1. Could an alkyl iodide be prepared by this method? Explain.

2. In the preparation of ethyl bromide it was unnecessary to remove the drying agent before the final distillation, while in the present case this must be done. What is the explanation of this difference?

3. Write equations for the reactions of *n*-butyl bromide with each of the following reagents: (*a*) Aqueous sodium hydroxide; (*b*) alcoholic sodium hydroxide; (*c*) ammonia; (*d*) magnesium; (*e*) sodium; (*f*) methyl magnesium bromide; (*g*) sodium acetate; (*h*) sodium ethoxide; (*i*) sodium cyanide.

Preparation 5. Methyl Iodide

The two preceding preparations involve the conversion of an alcohol to an alkyl halide by the action of a halogen acid. This method is not usually applicable to the preparation of alkyl iodides, since these substances are easily reduced to hydrocarbons by hydrogen iodide. Alkyl iodides are generally prepared by the action of phosphorus and iodine on alcohols. It is probable that the inorganic reagents react to form a phosphorus iodide, which then reacts with the alcohol in the same manner as phosphorus chlorides or bromides.

Procedure.—Methyl iodide boils at 44°, so that *special care must be taken to avoid loss by volatilization.* Forty-two grams of methyl alcohol and 12 g. of red phosphorus are placed in a flask connected to an efficient reflux condenser (see Fig. 19); while the flask is cooled in an ice bath, 120 g. of iodine is added in small portions during a period of 45 minutes. The mixture is allowed to stand for 24 hours or longer, and the methyl iodide is then removed by slow distillation from a water bath. The end of the condenser should be fitted with an adapter which reaches below the surface of some ice water contained in a beaker. The methyl iodide is separated from the aqueous layer and is washed with *cold* dilute sodium hydroxide solution. It is advisable, in performing the washing, to allow the iodide to run from the separatory funnel directly into the next portion of washing reagent to be used, with the end of the funnel dipping below the surface of the reagent. Sufficient alkali should be used to destroy any iodine color present in the methyl iodide. The methyl iodide is then dried over calcium chloride and purified by distillation from a water bath heated to 50°. It is unnecessary to remove the drying agent before the distillation. The yield should be 90 to 95 g.

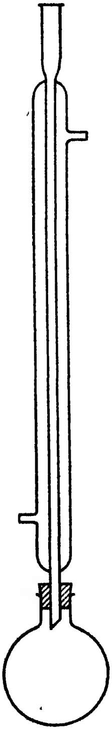


FIG 19.—Apparatus for refluxing.

Questions

1. Explain in detail the removal of the iodine from the product by means of sodium hydroxide.

2. Why is it unnecessary to remove the drying agent from the methyl iodide before distillation of the latter?

3. Write equations for the reactions of methyl iodide with each of the following reagents: (*a*) Aqueous sodium hydroxide; (*b*) sodium cyanide;

(*c*) sodium acetate; (*d*) sodium ethoxide; (*e*) ammonia; (*f*) sodium; (*g*) magnesium; (*h*) methyl magnesium iodide.

Preparation 6. Ethylene Dibromide

The first step in this preparation is the dehydration of ethyl alcohol by means of sulfuric acid to yield ethylene; it is probable that ethyl acid sulfate is an intermediate product:

$$C_2H_5OH + H_2SO_4 \longrightarrow C_2H_5OSO_3H + H_2O$$

$$C_2H_5OSO_3H \xrightarrow{\Delta} C_2H_4 + H_2SO_4$$

It is evident that the sulfuric acid is not used up in the reaction. However, after it has become somewhat diluted by the water formed in the first reaction it is no longer effective as a dehydrator. If the intermediate ethyl acid sulfate is heated with excess alcohol, ethyl ether is formed instead of ethylene (compare Preparation 8). The dehydration can also be accomplished by means of phosphoric acid.

The ethylene is passed into bromine with which it readily reacts to form ethylene dibromide:

$$C_2H_4 + Br_2 \longrightarrow C_2H_4Br_2$$

(Compare the reaction of acetylene with bromine, page 54.)

Procedure.—(Caution! Read the remarks on pages 5 and 6 about the handling of bromine.) A 500-cc. distilling flask is fitted with a two-hole rubber stopper carrying a thermometer and a dropping funnel (Fig. 20). The thermometer should extend below the surface of the mixture of acid and alcohol to be introduced into the flask. The stem of the dropping funnel is connected, by means of a short rubber connection, to a glass tube, the lower end of which is drawn out to an opening 1 or 2 mm. in diameter, which reaches below the surface of the contents of the flask. The side-arm of the distilling flask is connected with an empty safety bottle immersed in an ice bath, in which ether and unchanged alcohol will condense. The gas is led from the safety bottle to a wash bottle containing dilute sodium hydroxide solution to remove carbon dioxide and sulfur dioxide. The wash bottle is equipped with a safety tube about 2 feet long which extends about one-half inch below the surface of the alkali. The washed ethylene is then absorbed in 30 g. of bromine and 5 g. of water contained in a 25- by 150-mm. test tube immersed in an ice bath. It is advisable to lead the escaping gas into dilute sodium hydroxide to absorb the bromine which is carried over and any hydrogen bromide formed in side reactions.

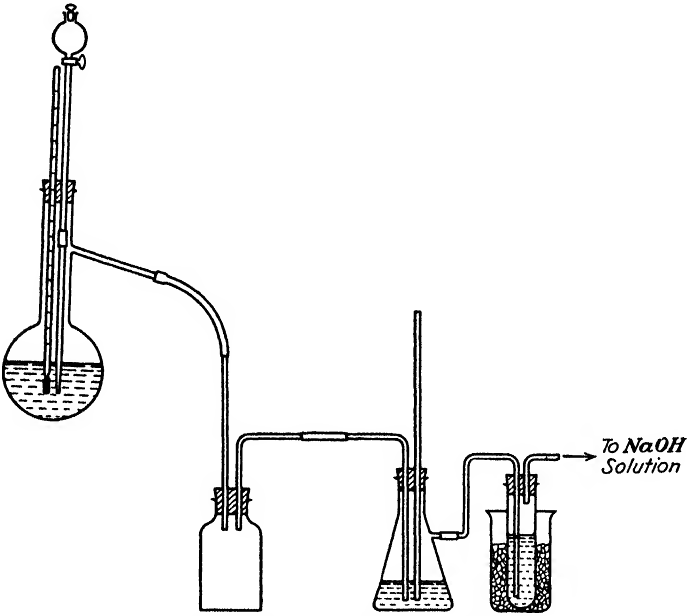


FIG. 20. -Apparatus for ethylene dibromide.

A mixture of 25 g. of ethyl alcohol and 150 g. (*not* cc.) of concentrated sulfuric acid is placed in the generating flask. In preparing this mixture the acid should be added to the alcohol slowly with shaking and cooling. The mixture is then slowly heated to 170°, at which temperature the ethylene is evolved. After the evolution of gas has become steady, a mixture of 1 part of alcohol and 2 parts *by weight* of concentrated sulfuric acid is added slowly through the dropping funnel, to maintain a constant flow of ethylene. If the flow of gas is too rapid, the removal of sulfur dioxide and carbon dioxide from the ethylene will not be complete. This procedure is continued until the bromine is decolorized. Time will be saved if the ice bath surrounding the absorption tube is removed after half an hour or so; if there is evidence of appreciable volatilization of the bromine, the ice bath must be replaced for a while longer. When the decolorization of the bromine is complete, the test tube is disconnected from the apparatus and the crude ethylene dibromide treated as described below.

Before the flow of gas is stopped two further experiments are to be performed. (1) Ethylene is bubbled through a dilute solution of potassium permanganate in 5 per cent aqueous sodium hydroxide for a few minutes. (2) Ethylene is bubbled through cold concentrated sulfuric acid. Explanations should be given for the observed results in each case.

The crude ethylene dibromide is washed twice with dilute sodium hydroxide and once with water. It is then dried with a small amount of anhydrous sodium sulfate. After an hour, the drying agent is removed by filtration and the dibromide is purified by distillation. The fraction coming over between 129 to 134° is collected. Ethylene dibromide boils at 132°. The yield should be 15 to 20 g.

Questions

1. Explain in detail the origin of the chief contaminants, namely, alcohol, ether, sulfur dioxide, and carbon dioxide, in the ethylene leaving the generating flask.

2. Why is it essential to free the ethylene from sulfur dioxide before it is passed into the bromine? Is there any need to remove the carbon dioxide?

3. Describe in detail a "purification train" which could be used to free methane from ethylene and hydrogen chloride.

4. Why is it necessary to cool the bromine in ice during the first part of the reaction? Explain why the ice may be removed after a good part of the bromine, though not all of it, has reacted.

5. What is the nature of the side reactions which may lead to the formation of hydrogen bromide?

6. Write equations for the reactions of ethylene with: (*a*) Concentrated sulfuric acid; (*b*) potassium permanganate; (*c*) ozone; (*d*) hydrogen bromide; (*e*) hypochlorous acid.

7. Indicate by equations how each of the following compounds can be prepared from ethylene dibromide: (*a*) Ethylene glycol; (*b*) glycol diacetate; (*c*) succinonitrile; (*d*) glycol diethyl ether; (*e*) diethyl succinate; (*f*) acetylene.

8. Discuss the chemical evidence for the structures assigned to ethylene dibromide and ethylidene dibromide.

Preparation 7. Bromobenzene

The halogenation of aromatic hydrocarbons is a very important reaction, both in the laboratory and in industry. It is the most frequently employed method for obtaining halogen substituted aromatic compounds. This is to be contrasted with the situation in the aliphatic series, where indirect methods are almost always used in the preparation of halides. In the industrial field the chlorination of benzene and toluene are of particular importance; chlorobenzene is used in the synthesis of phenol while the side-chain halogenated derivatives of toluene are converted to benzyl alcohol, benzaldehyde and many other substances.

The conditions employed in the halogenation of an aromatic hydrocarbon containing an alkyl side-chain very markedly affect the course of the reaction. If the reaction is carried out at ordinary temperatures in the presence of a catalyst such as iodine, iron, or amalgamated aluminum, the halogen attacks the hydrogen atoms in the benzene ring. If, on the other hand, the reaction is performed at an elevated temperature and no catalyst is present, the halogen attacks only the side-chain. Side-chain halogenation is also greatly accelerated by ultraviolet light. This latter set of conditions is employed in the preparation of benzyl chloride described on page 98.

Procedure.— **(Caution! Read the remarks on pages 5 and 6 about the handling of bromine.)** The catalyst is prepared by immersing 2 sq. cm. of aluminum foil in a solution of mercuric chloride for a few minutes. The aluminum is then removed and washed successively with water, alcohol, and benzene.

This aluminum-mercury couple is placed in 50 g. of sodium-dried benzene, which is contained in a 500-cc. flask equipped with a three-way tube and reflux condenser (see Fig. 21). A small dropping funnel is fitted into the top of the three-way tube. A large quantity of hydrogen bromide is evolved, so that it is necessary to arrange for its collection, as it is quite noxious. This is accomplished by connecting to the top of the condenser by glass tubing a funnel, which is supported just over the surface of some dilute sodium hydroxide contained in a beaker. Care must be taken that all corks used fit well.

Sixty grams of bromine is placed in the dropping funnel and dropped slowly into the benzene at such a rate that the bromine has all been added within an hour. In case there has been no obvious evolution of hydrogen bromide during the early stages of the reaction, the addition of the bromine should be stopped and a new aluminum-mercury couple added.

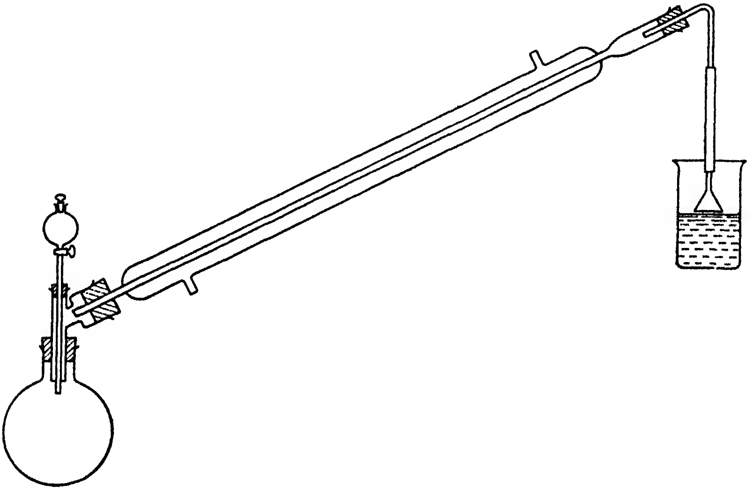


Fig. 21.—Apparatus for bromobenzene.

When the evolution of hydrogen bromide ceases, the reaction mixture is cooled and 100 cc. of dilute sodium hydroxide is added. The bromobenzene is then steam-distilled (see page 20). As soon as water-insoluble oil stops coming over, or when crystals of dibromobenzene begin to appear in the condenser, the distillation is stopped and the bromobenzene is separated from the water and dried with anhydrous calcium chloride. After the drying is completed, the calcium chloride is filtered off and the product distilled. The fraction boiling between 140 to 170° is collected and redistilled. In the second distillation the material boiling from 154 to 160° is collected. Bromobenzene boils at 156°. The yield should be about 30 g.

Questions

1. What product distills off before 140° is reached? Explain how this substance happens to be present. What comes over above 170°? Explain.

2. Suggest a method other than steam distillation for isolating the bromobenzene from the reaction mixture. Why is steam distillation preferable to this method?

3. Write equations for the reactions, if any, between bromobenzene and each of the following reagents: (*a*) Magnesium; (*b*) bromine; (*c*) concentrated nitric and sulfuric acids; (*d*) aqueous alkali; (*e*) ammonia.

4. How could bromobenzene be converted into (*a*) ethyl benzene and (*b*) ethyl benzoate? How could *m*-dibromobenzene be prepared?

Preparation 8. Diethyl Ether

The most important method for the preparation of simple aliphatic ethers is the dehydration of the corresponding alcohols, usually by means of concentrated sulfuric acid. The same reagent can in general be employed to effect more drastic dehydration to yield olefins, so that the experimental conditions have to be carefully regulated. (Compare with Preparation 6.)

Ethyl alcohol and sulfuric acid react at ordinary temperatures to form ethyl hydrogen sulfate:

$$C_2H_5OH + H_2SO_4 \longrightarrow C_2H_5OSO_2OH + H_2O$$

If this ester is heated to about 170° it undergoes decomposition with the formation of ethylene:

$$C_2H_5OSO_2OH \xrightarrow{\Delta} C_2H_4 + H_2SO_4$$

If, however, it is heated with an excess of alcohol, reaction takes place at about 140° to yield ether:

$$C_2H_5OSO_2OH + C_2H_5OH \xrightarrow{\Delta} C_2H_5OC_2H_5 + H_2SO_4$$

It is evident that the sulfuric acid is regenerated in the process. The reaction may therefore be developed into a "continuous process" which continues until the sulfuric acid becomes so diluted with water that it is no longer effective for the first reaction. This is the basis for the technical production of ether.

Procedure.—(**Caution!** Ether is very volatile and inflammable.) Fifty cubic centimeters of concentrated sulfuric acid is added with shaking and cooling to an equal volume of alcohol contained in a distilling flask. The flask is fitted with a thermometer extending below the surface of the liquid and with a dropping funnel, to the end of which is attached a glass tube leading below the surface of the liquid in the flask. The distilling flask is connected with an efficient condenser arranged for distillation (see Fig. 22). The receiver should be similar to that described on page 41, with a rubber tube leading to the floor, and it should be covered with ice. Rubber stoppers should be used throughout.

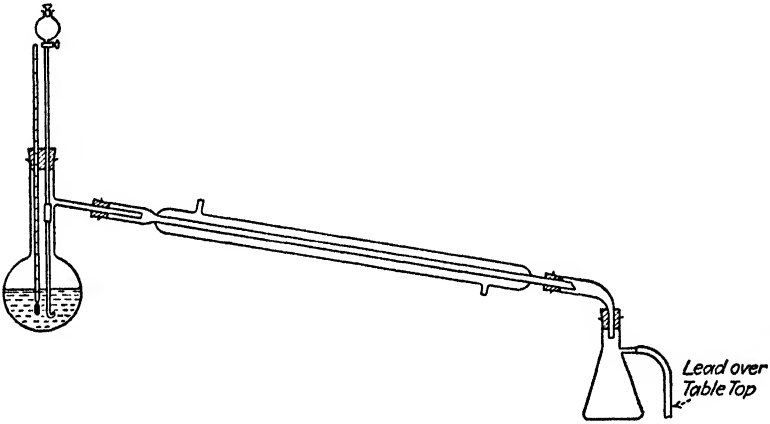


Fig. 22.—Apparatus for diethyl ethyl.

The flask is heated on a wire gauze over a small flame until the thermometer registers 140 to 145°. While this temperature is maintained 100 cc. of alcohol is added from the dropping funnel at the same rate as that at which the ether distills over. Toward the end of the reaction it may be necessary to raise the temperature somewhat. When the reaction is complete, the distillate is washed successively with dilute sodium hydroxide and saturated sodium chloride. The ether is dried over powdered calcium chloride in a flask, fitted with a calcium chloride tube. If the product is contaminated with much alcohol, it may be necessary to use a comparatively large amount of the drying agent. The ether is finally decanted from the drying agent and distilled on a water bath the temperature of which does not exceed 45°. Ether boils at 35°. About 35 g. of ether should be obtained.

Questions

1. What are the main causes of the rather low yield obtained in this experiment?

2. Suggest another method for the manufacture of diethyl ether. Why is it not used commercially?

3. What are the most important uses of ether?

4. What is the purpose of the washing with sodium hydroxide? Why is this followed by washing with sodium chloride solution?

5. Write equations for the reactions, if any, of diethyl ether with each of the following reagents: (*a*) Concentrated sulfuric acid; (*b*) concentrated sodium hydroxide; (*c*) hydriodic acid; (*d*) phosphorus pentachloride; (*e*) chlorine; (*f*) oxidizing agents; (*g*) reducing agents; (*h*) metallic sodium.

Preparation 9. Phenetole

This preparation of phenetole, $C_6H_5OC_2H_5$, is an example of the Williamson method for the preparation of ethers. This method is particularly well adapted to the preparation of mixed ethers. The method consists essentially in the reaction between the sodium salt of an alcohol or a phenol and an alkyl halide or sulfate. In the present case, the phenol is dissolved in aqueous alkali and treated with diethyl sulfate:

$$C_6H_5OH + NaOH \longrightarrow C_6H_5ONa + H_2O$$

$$C_6H_5ONa + (C_2H_5)_2SO_4 + NaOH \longrightarrow C_6H_5OC_2H_5 + C_2H_5OH + Na_2SO_4$$

Diethyl sulfate constitutes a much cheaper source of ethyl groups than ethyl bromide or iodide, which may also be used in this reaction. With the latter reagents the reaction is performed under anhydrous conditions.

Procedure.—Thirty grams of phenol is dissolved in 130 cc. of 10 per cent sodium hydroxide. Fifty-five cubic centimeters of diethyl sulfate and 250 cc. of 10 per cent sodium hydroxide are added from separate containers in small portions with constant shaking. The addition should require about 30 minutes and should be so regulated that both reagents are added at the same fractional rate. The mixture is then heated under a reflux condenser with frequent shaking on a boiling water bath for an hour (the solution should be alkaline at the end of this time). The phenetole is extracted from the reaction mixture with ether and the ether solution dried over anhydrous sodium sulfate. After removal of the ether (see page 41), the phenetole is purified by distillation. It boils at 176°. The yield should be nearly quantitative.

Questions

1. Could diphenyl ether be prepared by the Williamson method? Explain.

2. Compare the amounts of sodium hydroxide and diethyl sulfate used in the preparation with those theoretically required. Suggest a reason for using these amounts.

3. Write equations for the reactions, if any, between phenetole and each of the following reagents: (*a*) Hydriodic acid; (*b*) concentrated sulfuric acid; (*c*) concentrated sulfuric and nitric acids; (*d*) sodium hydroxide.

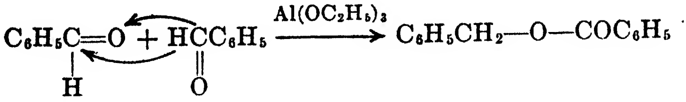
Preparation 10. Benzyl Alcohol and Benzoic Acid

This preparation is an example of the interesting property of aromatic aldehydes (and formaldehyde) of undergoing intermolecular oxidation and reduction in the presence of alkali. The reaction is known as the *Cannizzaro reaction* and in the present case is represented by the equation:

$$2C_6H_5CHO + KOH \longrightarrow C_6H_5CH_2OH + C_6H_5COOK$$

Half of the aldehyde is reduced while half of it is oxidized.

The reaction proceeds through the intermediate stage of ester formation, as is indicated by the fact that an anhydrous reagent, such as aluminum ethoxide, gives only the ester, benzyl benzoate, as the product. In such a case the reaction may be looked upon as an addition of one molecule of aldehyde to another:



$$C_6H_5\underset{\overset{|}{H}}{C}{=}O + H\underset{\overset{\|}{O}}{C}C_6H_5 \xrightarrow{Al(OC_2H_5)_3} C_6H_5CH_2—O—COC_6H_5$$

In the presence of aqueous alkali the ester is saponified.

The Cannizzaro reaction with an anhydrous reagent may also be applied in the aliphatic series. Thus ethyl acetate is made on a commercial scale from acetaldehyde and aluminum ethoxide.

With aliphatic aldehydes (except formaldehyde) aqueous alkali causes aldol condensation or resinification.

Procedure.—Twenty-seven grams of potassium hydroxide, dissolved in 25 cc. of water, is added to 30 g. of benzaldehyde. The mixture is shaken until an emulsion forms, and is then set aside for 24 hours in a stoppered flask. At the end of this time enough water is added to dissolve the potassium benzoate and the benzyl alcohol is extracted with ether, *the aqueous solution being saved.* The ether solution is dried over sodium sulfate, and, after removal of the ether (see page 41), the alcohol is purified by distillation. It boils at 206°.

The aqueous alkaline solution of potassium benzoate is warmed in a beaker on a water bath (**Caution!**) to remove dissolved ether, and is then acidified with dilute hydrochloric acid and thoroughly cooled. The precipitated benzoic acid is filtered off and recrystallized from water. Benzoic acid melts at 122°. The yield of each product should be about 12 g.

Questions

1. Theoretically, the two products in this reaction should be formed in equimolecular amounts. If this was not actually the case, suggest an explanation for the discrepancy between fact and theory.

2. Compare the types of addition which evidently take place in the Cannizzaro reaction and in the benzoin condensation (see page 95). Is the reaction of formaldehyde with dilute alkali to form hexoses similar to the former or the latter reaction?

3. Write equations representing the reactions of benzyl alcohol with each of the following reagents: (*a*) Sodium; (*b*) potassium permanganate; (*c*) benzoic acid and hydrogen chloride; (*d*) phosphorus and iodine.

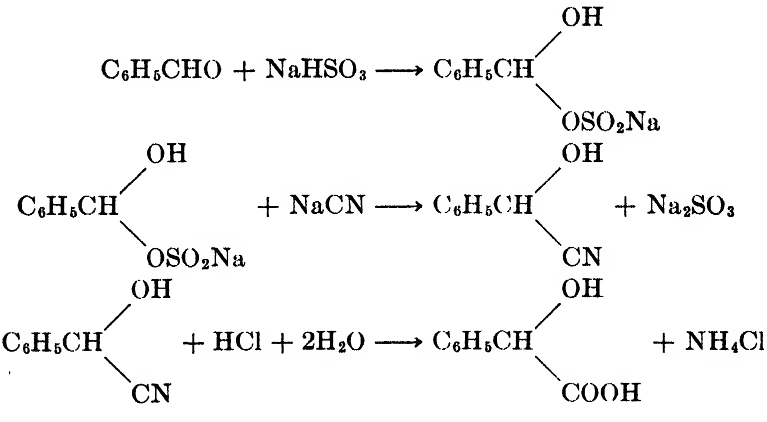
4. Indicate by equations how benzoic acid reacts with each of the following reagents: (*a*) Sodium hydroxide; (*b*) phosphorus pentachloride; (*c*) methyl alcohol and hydrogen chloride; (*d*) chlorine; (*e*) concentrated nitric and sulfuric acids.

Preparation 11. Mandelic Acid

One of the standard procedures for the synthesis of an α-hydroxy acid is what is known as the cyanohydrin method. This consists in the addition of hydrocyanic acid to an aldehyde or a ketone, followed by the subsequent hydrolysis of the cyanohydrin so formed. To avoid the use of hydrocyanic acid, which is very volatile and extremely poisonous and which should thus be handled only by experienced laboratory workers, the cyanohydrin is prepared in this experiment by the treatment of the sodium bisulfite addition compound of the aldehyde with a solution of sodium cyanide. Although this reagent is also very poisonous if taken internally, it is reasonably safe to handle if care is taken that it does not come into contact with the skin or with any acid. In the latter case hydrocyanic acid will be liberated.

A cyanide group can be hydrolyzed to a carboxyl by concentrated acids or alkalies. In this experiment concentrated hydrochloric acid is the reagent selected. The cyanohydrin should be hydrolyzed as quickly as possible after its formation to avoid its spontaneous decomposition.

The equations expressing the various stages in the preparation of mandelic acid follow:



$$C_6H_5CHO + NaHSO_3 \longrightarrow C_6H_5CH\begin{matrix}OH\\ OSO_2Na\end{matrix}$$

$$C_6H_5CH\begin{matrix}OH\\ OSO_2Na\end{matrix} + NaCN \longrightarrow C_6H_5CH\begin{matrix}OH\\ CN\end{matrix} + Na_2SO_3$$

$$C_6H_5CH\begin{matrix}OH\\ CN\end{matrix} + HCl + 2H_2O \longrightarrow C_6H_5CH\begin{matrix}OH\\ COOH\end{matrix} + NH_4Cl$$

Procedure.—**(Hood!)** Twenty-five grams each of sodium bisulfite and benzaldehyde are added to 75 cc. of water contained in a flask. The mixture is shaken vigorously until it appears that no more addition compound is crystallizing out, and the flask is then cooled under the tap. A solution of 15 g. of sodium cyanide (**Caution!** Highly toxic!) in 40 cc. of water is then added and the shaking is continued until the crystalline material has been replaced by an oil, the cyanohydrin. This is immediately separated with a separatory funnel and added to a flask containing 50 cc. of concentrated hydrochloric acid **(Hood!)**.

The flask is closed with a cork stopper, is vigorously shaken, and is allowed to stand overnight. The experiment must not be interrupted until this point is reached. The mixture is then heated in an evaporating dish on a water bath (**Hood!**) until the volume is reduced to about 20 to 30 cc. The solution is boiled with norite, filtered, and the filtrate cooled in an ice bath. The precipitated mandelic acid is filtered off, washed with 10 cc. of ice-cold water, thoroughly dried, and recrystallized from toluene. *dl*-Mandelic acid melts at 118°. The yield should be 15 to 20 g.

Questions

1. As a rule considerable benzaldehyde remains unreacted. At what stage in the procedure is it removed from the mandelic acid?

2. Why should the mandelonitrile be separated from the aqueous layer before the addition of the hydrochloric acid?

3. Why is *dl*-mandelic acid obtained rather than an optically active form?

4. Write equations for the reactions, if any, between mandelic acid and each of the following reagents: (*a*) Sodium bicarbonate; (*b*) acetic anhydride; (*c*) methyl alcohol and hydrogen chloride; (*d*) phosphorus trichloride; (*e*) dilute potassium permanganate; (*f*) concentrated potassium permanganate.

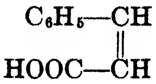
Preparation 12. Cinnamic Acid

Aldehydes condense with compounds containing methyl or methylene groups which are rendered "active" by their position next to a carbonyl, carboxyl, or acid anhydride group. Thus benzaldehyde reacts with acetone in the presence of alkali to give dibenzylidene acetone:

$$2C_6H_5CHO + CH_3COCH_3 \longrightarrow$$
$$C_6H_5CH{=}CH{-}CO{-}CH{=}CHC_6H_5 + 2H_2O$$

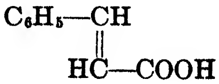
In the reactions of benzaldehyde with acid anhydrides higher temperatures are required, and an alkali salt such as sodium acetate is used as condensing agent. The reaction is known as *Perkin's synthesis*.

Cinnamic acid exists in two geometrically isomeric forms, which may be represented by the structures



$$\begin{array}{r}C_6H_5{-}CH\\ \|\;\;\\ HOOC{-}CH\end{array}$$

and



$$\begin{array}{l}C_6H_5{-}CH\\ \;\;\;\;\;\;\;\|\\ \;\;\;\;\;HC{-}COOH\end{array}$$

The first formula represents the cis-form, commonly called allocinnamic acid, while the second represents the trans-form. Ordinary cinnamic acid is the latter form.

Procedure.— A mixture of 20 g. of benzaldehyde, 30 g. of acetic anhydride, and 10 g. of sodium acetate (fused just before use according to the directions given on page 78) is boiled under a reflux condenser in an oil bath for 8 hours. The top of the condenser should be fitted with a calcium chloride tube. The mixture is then cooled and diluted with 4 to 5 volumes of water and the excess benzaldehyde is removed by distillation with steam. The residue is made alkaline with dilute sodium hydroxide, is boiled for a few minutes with norite, and is filtered through a fluted filter paper. The filtrate is acidified with hydrochloric acid and allowed to cool. The precipitated cinnamic acid is purified by recrystallization from water. The pure substance melts at 133°. The yield should be about 15 g.

Questions

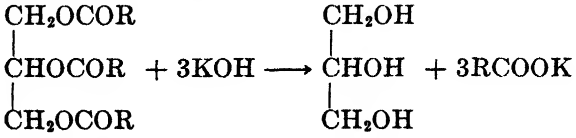
1. Outline by equations a method for the preparation of phenyl propiolic acid, $C_6H_5C\equiv C{-}COOH$. Which form of cinnamic acid would you expect to be formed by the addition of two atoms of hydrogen to the triple bond of this substance? Why?

2. Write the equations for another method of preparing cinnamic acid. Compare its convenience with the one described here.

3. Indicate by equations the reactions of cinnamic acid with each of the following reagents: (*a*) Bromine; (*b*) sodium carbonate; (*c*) ethyl alcohol and hydrogen chloride; (*d*) hydrogen and a catalyst; (*e*) potassium permanganate.

Preparation 13. Palmitic Acid

This reaction illustrates the saponification of a fat or glyceride, which proceeds according to the following equation:



$$\begin{array}{l} CH_2OCOR \\ | \\ CHOCOR \end{array} \!\!\! \begin{array}{l} \\ \\ + 3KOH \longrightarrow \end{array} \begin{array}{l} CH_2OH \\ | \\ CHOH \end{array} \begin{array}{l} \\ \\ + 3RCOOK \end{array}$$

$$\begin{array}{l} CH_2OCOR \\ | \\ CHOCOR \\ | \\ CH_2OCOR \end{array} + 3KOH \longrightarrow \begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array} + 3RCOOK$$

giving one mol of glycerine and three of soap. The R groups may be the same, but in naturally occurring fats there are always several different radicals present. However, in palm oil there is enough predominance of $C_{15}H_{31}$ groups to make it possible to isolate reasonably pure palmitic acid, contaminated chiefly with stearic acid, $C_{17}H_{35}COOH$. The main difficulty encountered in this preparation is the purification of the product.

Procedure.—Fifty grams of palm oil and 30 g. of potassium hydroxide are weighed into a flask, 200 cc. of 70 per cent ethyl alcohol is added and the material boiled under a reflux condenser for 3 hours. It is then transferred to an evaporating dish and evaporated nearly to dryness on a steam bath. The residue is taken up in 1 l. of hot water. The fatty acids, chiefly palmitic, are liberated from the soap by acidification with dilute sulfuric acid. At the elevated temperature they appear as an oil. The mixture is set aside and allowed to cool *without disturbance*, so that the fatty acids float to the top and solidify as a solid cake. This cake is removed, dried as much as possible with filter paper, remelted in a dry beaker, and again allowed to cool, thus separating a further quantity of water. This cake, after drying with filter paper, is spread in a thin layer on a folded newspaper and pressed between layers of paper for 48 hours, the upper layer being changed occasionally. The paper absorbs a large part of the liquid oleic acid present.

The solid fatty acids are scraped off the paper and recrystallized twice from 150-cc. portions of acetone (*inflammable*) and once from 100 cc. of alcohol, norite being used each time. It is necessary to cool the solutions in an ice bath before filtering. The yield should be 10 to 15 g. of product melting at 61 to 62°. Pure palmitic acid melts at 64°.

Questions

1. Why is alcoholic rather than aqueous potassium hydroxide used for the saponification?

2. Calculate the saponification equivalent of glyceryl tripalmitate (see page 131).

3. Palm oil contains a small amount of unsaponifiable material. Where is this eliminated in the preparation? What becomes of the glycerine?

4. Why is the alcohol evaporated before liberation of the acids from their soaps?

5. Why is it necessary to remove the water from the fatty acid cake so completely before the cake is pressed out on the newspaper?

6. Write equations for the reactions, if any, occurring between palmitic acid and the following reagents: (*a*) Sodium bicarbonate; (*b*) sodium hydroxide; (*c*) bromine; (*d*) methyl alcohol and hydrogen chloride; (*e*) phosphorus pentachloride.

Preparation 14. *p*-Nitrobenzoic Acid

This reaction illustrates one of the typical properties of aromatic compounds, the oxidation of side-chains to carboxyl groups. A great many reagents can be used for this purpose, some of the most important being potassium permanganate in alkaline solution, potassium dichromate and sulfuric acid, and nitric acid. The commercially employed catalytic oxidation by air of naphthalene to phthalic acid is another reaction of this type.

Procedure.—Fifty grams of potassium permanganate and 20 g. of sodium hydroxide are dissolved in 1 l. of water contained in a 2-l. flask arranged for refluxing. Twenty grams of *p*-nitrotoluene is then added and the mixture kept at the boiling temperature until the purple color of the permanganate is entirely replaced by a brown precipitate of manganese dioxide. During the boiling the mixture will probably "bump" very badly because of the precipitate of manganese dioxide, so the condenser and flask must be firmly supported. The bumping may be relieved to some extent by the addition of small pieces of porous plate as "bumping stones," and by the use of a small smoky flame. The bumping will be aggravated if the refluxing is interrupted before the reaction is complete.

After the purple, and occasionally a succeeding green color, have disappeared, the manganese dioxide is filtered from the cooled solution on a Büchner funnel and washed with water. The filtrate is then acidified with dilute sulfuric acid. The *p*-nitrobenzoic acid separates as pale yellow crystals which are filtered off by suction and thoroughly washed with cold water. The product is purified by being redissolved in dilute sodium hydroxide, treated with one-half gram of norite, and heated to boiling for 10 minutes. The solution is then filtered while hot through a fluted paper. The filtrate is cooled, acidified, and the precipitate filtered off, washed with water, and dried. The yield should be about 15 g. *p*-Nitrobenzoic acid melts at 242°.

Questions

1. Ordinarily in an organic reaction the inorganic substances are used in excess. Suggest a reason why the reverse is the case in this reaction.

2. What are the crystals which appear in the condenser during the refluxing, and by what mechanism did they arrive there?

3. Balance the equation for this oxidation assuming that potassium dichromate and sulfuric acid had replaced the permanganate. Suggest any changes in the procedure which this change in oxidizing agent would necessitate.

4. Balance the equations for the following oxidation reactions (water may be added to either side of the equations if necessary):

(*a*) $C_6H_{11}OH$ (cyclohexanol) + $HNO_3 \longrightarrow$ $C_4H_8(COOH)_2$ (adipic acid) + NO_2

(*b*) $C_6H_4(CH_3)_2 + K_2Cr_2O_7 + H_2SO_4 \longrightarrow C_6H_4(COOH)_2 + Cr_2(SO_4)_3 + K_2SO_4$

(*c*) $CH_3CH{=}C(CH_3)_2 + KMnO_4 \longrightarrow CH_3COOK + (CH_3)_2CO + MnO_2 + KOH$

5. Write equations for the reactions of *p*-nitrobenzoic acid with each of the following reagents: (*a*) Aqueous sodium bicarbonate; (*b*) tin and hydrochloric acid; (*c*) ethyl alcohol and hydrogen chloride; (*d*) phosphorus pentachloride.

Preparation 15. Ethyl Acetate

This preparation is one of the simplest demonstrations of the process known as *esterification*, the loss of water between a carboxyl group and an alcoholic hydroxyl group. The best known catalyst for this reaction is the hydrogen ion, generally furnished by the addition of hydrochloric or sulfuric acid.

$$CH_3COOH + C_2H_5OH \rightleftharpoons CH_3COOC_2H_5 + H_2O$$

As indicated by the equation, this reaction is reversible and therefore reaches a state of equilibrium. If one mol each of acetic acid and ethyl alcohol are allowed to react, equilibrium is established when about six-tenths of a mol of the ester has been formed. In the absence of a catalyst and at room temperature, this equilibrium condition is not reached for several days.

Procedure.—Sixty cubic centimeters each of glacial acetic acid and ethyl alcohol are mixed, treated with 4 cc. of concentrated sulfuric acid, and gently refluxed for 30 minutes. The reaction product is then distilled until the thermometer registers 100°. A 1-cc. sample of distillate is collected and treated with 1 cc. of water. If two liquid phases can be detected, the distillation is continued until a repetition of this test gives a negative result.

The distillate in the flask is mixed with 30 cc. of water and solid sodium bicarbonate is added, a little at a time with vigorous shaking, until the *ester* reacts neutral to moist litmus paper. The upper layer is separated, washed once with 30 cc. of water, separated again, and dried with 10 g. of anhydrous calcium chloride. It is then filtered from the drying agent and purified by distillation. Ethyl acetate boils at 77°. The yield is about 45 g.

Questions

1. Using the approximate figures given in the introductory paragraphs, calculate the mass-law constant of the reaction.

2. Explain just how the unreacted alcohol and acid are removed during the purification.

3. What steps can be taken to shift the equilibrium so as to increase the yield of ethyl acetate? To decrease it?

4. Why is sodium bicarbonate used in purifying the ester rather than sodium hydroxide?

5. Would increasing the concentration of hydrogen ion affect the yield of ethyl acetate?

6. As stated above, the reaction between ethyl alcohol and acetic acid is reversible. Explain why it is nevertheless possible to wash ethyl acetate with water without any appreciable loss.

7. Write equations for the reactions of ethyl acetate with each of the following substances: (*a*) Aqueous alkali; (*b*) concentrated ammonium hydroxide; (*c*) sodium and ethyl alcohol.

Preparation 16. Methyl Benzoate

This preparation is an example of a simple esterification process. For the general considerations of the esterification process, read page 74. The only essential difference in procedure in this case is the length of time necessary to complete the reaction, benzoic acid being less reactive than acetic.

Procedure.—Sixty-one grams of benzoic acid is refluxed for 4 hours with 200 cc. of methyl alcohol containing 5 cc. of concentrated sulfuric acid. The excess alcohol is then removed on a water bath and the residual liquid is cooled, poured into 500 cc. of water, and the ester removed by two extractions with ether, using 200- and 100-cc. portions. The combined ether extracts are washed with dilute sodium carbonate solution. As carbon dioxide is evolved, it is necessary to use care in the handling of the separatory funnel. The ether extract is dried over sodium sulfate, the ether is removed in the usual manner (see page 41), and the methyl benzoate is purified by distillation. Methyl benzoate boils at 198°. The yield should be 45 to 50 g.

Questions

1. What is the purpose of the sulfuric acid? Of the large excess of methyl alcohol?
2. Why could not the reaction mixture be purified by a direct distillation, without the intermediate steps?
3. Many comparatively strong acids may be esterified without the addition of a catalyst. Thus methyl alcohol and formic acid yield methyl formate on being heated together. Suggest an explanation of this fact.
4. Adapt Questions 2, 3, 4, 5, and 6 on page 75 to the present case and answer them.
5. Write equations for the reactions, if any, occurring between methyl benzoate and each of the following reagents: (*a*) Sodium hydroxide; (*b*) concentrated ammonium hydroxide; (*c*) sodium and alcohol; (*d*) concentrated nitric and sulfuric acids.

Preparation 17. Acetyl Chloride

The common method of preparing organic acid chlorides can be stated in rather general terms as consisting in the action of the acid chloride of an inorganic acid upon an organic acid. A number of these inorganic acid chlorides are available, the more important being phosphorus trichloride (PCl_3), phosphorus pentachloride (PCl_5), sulfuryl chloride (SO_2Cl_2), thionyl chloride ($SOCl_2$), and silicon tetrachloride ($SiCl_4$). The yields in the various reactions vary from nearly quantitative to very low ones depending upon the inorganic reagent used and, what is of greater importance, the nature of the organic acid. For instance, some organic acids are very easily dehydrated to anhydrides, and as all the above mentioned reagents are good dehydrating agents, this property frequently causes a very annoying side reaction.

Owing to the fact that acid chlorides react so readily with water, they should at all times be protected from atmospheric moisture when being used in a reaction, and exposure during transfer from one piece of apparatus to another should be as brief as possible. In fact *acetyl chloride reacts with explosive violence, so great caution must be exercised in preventing the access of water to this substance.*

The equation for the reaction by which acetyl chloride is formed in this preparation is:

$$3CH_3COOH + PCl_3 \longrightarrow 3CH_3COCl + H_3PO_3$$

It is to be noticed that this equation calls for the evolution of no hydrogen chloride, yet a great deal is actually obtained. It is formed by a number of side reactions, a typical one being

$$3CH_3COOH + PCl_3 \longrightarrow P(OCOCH_3)_3 + 3HCl$$

The organic compound represented here is a mixed acid anhydride of acetic and phosphorous acids.

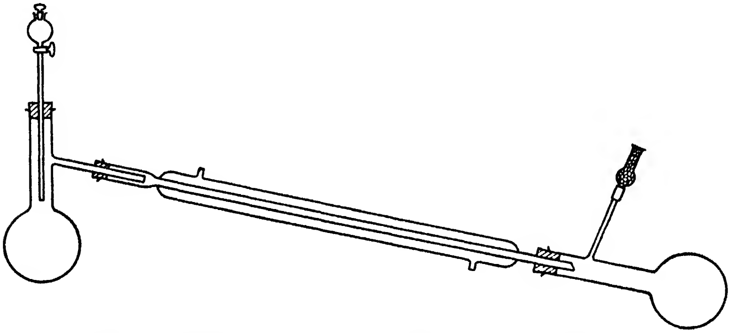


FIG. 23.—Apparatus for acetyl chloride and acetic anhydride.

Procedure.—The apparatus consists in a 250-cc. distilling flask equipped with a dropping funnel, and arranged with a condenser for distillation (see Fig. 23). The receiver is another similar flask, the side-arm of which is connected through a calcium chloride tube to a funnel. The wide mouth of the latter is supported *just above* the surface of some water contained in a beaker. *A violent explosion may result if water is sucked back from this beaker into the receiver during the collection of the acetyl chloride.* The absorption arrangement is made necessary by the copious evolution of hydrogen chloride. Glass tubing with short rubber connections and cork stoppers are to be used throughout.

The bulb of the distilling flask, which contains 75 g. of glacial acetic acid, is completely immersed in a pan of cold water and 60 g. of phosphorus trichloride is added slowly from the dropping funnel. After all the chloride has been added, the water bath is heated to 50° until the evolution of hydrogen chloride slackens and the liquid in the flask separates into two layers. The water bath is then heated to boiling and the acetyl chloride distilled. It is redistilled from the flask used as a receiver, the fraction boiling from 50 to 55° being collected. Acetyl chloride boils at 52°. The yield should be 40 to 50 g.

Questions

1. What are the acids corresponding to the inorganic acid chlorides mentioned in the first paragraph above?

2. Assuming that water reacts much more readily with phosphorus trichloride than acetic acid does, calculate the effect on the yield of using 95 per cent acetic acid (5 per cent water by weight) instead of 100 per cent acid.

3. Write equations for the reaction of acetyl chloride with: (*a*) Isopropyl alcohol; (*b*) methylamine; (*c*) diethylamine; (*d*) sodium acetate; (*e*) sodium hydroxide.

Preparation 18. Acetic Anhydride

One of the most common methods for the preparation of acid anhydrides is the reaction of a sodium salt of an acid with an acid chloride; it is evident that "mixed" anhydrides can be formed by this method:

$$\mathrm{RCOONa + R'COCl \longrightarrow RCO{-}O{-}OCR' + NaCl}$$

Certain acids form anhydrides so readily that direct dehydration of the acid may be used. Thus, dibasic acids such as succinic or phthalic acids, may be dehydrated by heating or by treatment with acetic anhydride, acetyl chloride, or other dehydrating agents.

Procedure.—The sodium acetate used in this experiment must be freshly fused just before it is to be used. Sixty grams of "anhydrous" sodium acetate is heated just to the melting point for several minutes in a porcelain casserole. The molten mass is then allowed to cool with stirring, to prevent the formation of a solid cake. As soon as possible the material is transferred to a mortar and finely pulverized. It is kept until needed in a tightly stoppered container.

Fifty grams of this fused sodium acetate is placed in a distilling flask which is fitted with a dropping funnel and is connected to a condenser. As a receiver another distilling flask is employed, its side-arm being connected to a calcium chloride tube (see Fig. 23, page 77). The first flask is placed in a bath of cold water, and 40 g. of acetyl chloride is added slowly through the dropping funnel at such a rate that no unreacted acetyl chloride distills over. After about half the acetyl chloride has been added, the flask should be temporarily disconnected from the condenser and, while it is still in the water bath, shaken at first cautiously and finally vigorously. This process should be repeated after all the acetyl chloride has been added. If any liquid has distilled during the addition, it is returned to the flask.

The dropping funnel is replaced by a cork and the liquid in the flask distilled with a small flame which is kept moving to prevent local superheating. Two grams of fused sodium acetate is added to the distillate which is then redistilled, the material boiling between 135 and 140° being collected. Acetic anhydride boils at 139°. The yield should be about 35 g.

Questions

1. Assume that the reaction of acetyl chloride with water is very much more rapid than its reaction with sodium acetate. Calculate the theoretical yield in this preparation if the sodium acetate contains 5 per cent of water.
2. Write equations for the reactions of acetic anhydride with each of the following reagents: (*a*) Water; (*b*) ammonia; (*c*) ethyl alcohol; (*d*) aniline.

Preparation 19. Acetamide

This experiment illustrates one of the commonest methods for the preparation of acid amides—the action of ammonia on an ester. The reaction is frequently spoken of as *ammonolysis*, by analogy with the term *hydrolysis* applied to the similar reaction with water. In this reaction primary and secondary amines may be used in place of ammonia, substituted amides being formed.

Procedure.—Fifty grams of ethyl acetate and 100 cc. of concentrated ammonium hydroxide are allowed to stand in a closed vessel until the mixture becomes homogeneous. The reaction product is distilled, a water condenser being used until the temperature of the distilling vapors reaches 160° (**Hood!**). The water condenser is replaced by an air condenser and the material distilling between 160 and 225° is collected. The acetamide which crystallizes in the condenser may be removed by gentle warming. After decantation of any liquid the distillate is redistilled, the product being collected between 218 and 225°. Final purification is effected in the following manner: The distillate is heated *just* to its melting point. *All flames within* 10 *ft. are extinguished,* and, while the material is vigorously stirred, ether is added. The ether will vaporize rapidly at first, but soon the acetamide will cool and solidify. Enough ether is to be used so that there is considerable liquid present when the process is finished. The acetamide is filtered by suction and dried as soon as possible on the filter. It should be preserved in a well-stoppered bottle. Acetamide melts at 81° and boils at 222°. The yield should be 15 to 20 g.

Questions

1. Write the equations involved in three other methods for the preparation of acetamide.

2. Indicate by equations two important synthetic procedures for which acid amides form the starting point.

3. If acetamide is heated with aniline, acetanilide is formed:

$$CH_3CONH_2 + C_6H_5NH_2 \xrightarrow{\Delta} CH_3CONHC_6H_5 + NH_3$$

No observable reaction takes place at ordinary temperatures. Suggest an explanation of these facts.

4. Explain why the reaction mixture is allowed to stand until it becomes homogeneous.

5. Show by means of equations how acetamide reacts with each of the following reagents: (*a*) Hot dilute hydrochloric acid; (*b*) hot dilute sodium hydroxide; (*c*) nitrous acid.

Preparation 20. Acetanilide

The acetylation of an amine is a frequent laboratory and commercial operation. Such common medicinals as aspirin and phenacetin are prepared by methods which involve acetylation. In addition, acetylation is a good method for protecting an amine group before performing a reaction such as bromination or nitration, as is illustrated in the preparation of *p*-nitroacetanilide (page 85). The three acetylating agents commonly used are acetic acid, acetic anhydride, and acetyl chloride. In certain cases ketene, $CH_2{=}C{=}O$, is used as a vigorous acetylating agent. Ketene is essentially an anhydride of acetic acid;

it is usually prepared by the pyrolysis of acetone, methane being formed at the same time.

Procedure.—To 40 g. of aniline is added, cautiously with shaking, 50 g. of acetic anhydride. The product is poured into 1 l. of water and the mixture is heated to boiling. After the addition of sufficient additional water to complete the solution of the product at the boiling temperature (note that acetanilide melts under boiling water, so that sufficient water must be added to dissolve all the oil thus formed), norite is added and the boiling is continued for 5 minutes. The norite is then filtered from the hot mixture on a large fluted filter and the acetanilide, which separates from the filtrate on cooling, is filtered off and dried. Acetanilide melts at 114°. The yield should be 45 to 50 g.

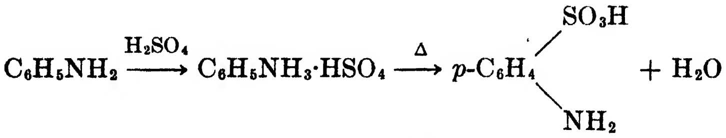
Questions

1. Indicate by equations a method for the preparation of each of the medicinals mentioned in the introductory paragraph.

2. Write equations for the reactions, if any, of acetanilide with each of the following reagents: (*a*) Concentrated nitric acid; (*b*) cold dilute hydrochloric acid; (*c*) hot concentrated hydrochloric acid; (*d*) hot dilute sodium hydroxide; (*e*) nitrous and hydrochloric acids.

Preparation 21. Sulfanilic Acid

The method described below differs from the process used in the technical production of sulfanilic acid mainly in that, in the latter, only one mol of acid is used per mol of aniline. In the method used here a considerable excess of sulfuric acid is used. In this sulfonation the usual difficulties experienced in the isolation of the sulfonated product (see page 106) are not encountered because the product is only slightly soluble in water. The steps in the reaction are represented by the following equations:



$$C_6H_5NH_2 \xrightarrow{H_2SO_4} C_6H_5NH_3\cdot HSO_4 \xrightarrow{\Delta} p\text{-}C_6H_4\begin{matrix} SO_3H \\ NH_2 \end{matrix} + H_2O$$

Procedure.—Twenty-five grams of aniline is *cautiously* added to 45 cc. of concentrated sulfuric acid contained in a small round-bottomed flask. The mixture is heated in an oil bath at 165 to 175° for 4 to 5 hours. A convenient test for the completion of the reaction is made by withdrawing a drop of the hot mixture on a glass rod and mixing it with some dilute sodium hydroxide on a watch glass. If no oil separates, the sulfonation is complete. The cooled reaction mixture is poured with stirring into 300 cc. of cold water and the precipitated sulfanilic acid is removed by filtration and washed with cold water. It is then dissolved in excess sodium carbonate solution and the solution is decolorized by boiling with norite. The hot solution is filtered, acidified with hydrochloric acid and allowed to cool. The sulfanilic acid is filtered off, recrystallized from water if necessary, and dried in the air. The product crystallizes with water of crystallization which is gradually lost on drying in the air. Sulfanilic acid has no sharp melting point; it decomposes at about 280 to 300°. The yield of anhydrous sulfanilic acid should be about 20 g.

Questions

1. Explain the significance of the test for the completion of the reaction.
2. Explain the fact that hydrochloric acid precipitates *free* sulfanilic acid from a solution of its sodium salt even though the molecule contains an amine group.
3. Write equations for the reactions, if any, which take place when sulfanilic acid is treated with each of the following reagents: (*a*) Nitrous and hydrochloric acids; (*b*) sodium carbonate; (*c*) phosphorus pentachloride.

Preparation 22. Nitrobenzene

One of the most important reactions of aromatic substances is the replacement of a nuclear hydrogen atom by a nitro group under the influence of nitric acid. The chief commercial importance of the resulting nitro compounds arises from their reduction to amines.

The fundamental reagent for nitration is nitric acid. The concentration of the acid used, the temperature of the reaction, and whether or not the nitric acid is mixed with sulfuric acid depend on the substance to be nitrated and on how many nitro groups it is desired to introduce. Thus the mononitration of phenol is accomplished by dilute nitric acid at 25°, while in the mononitration of benzene a mixture of concentrated nitric and sulfuric acids is used and the mixture is heated to 60°. As a contrast to these relatively easy nitrations, the preparation of 3,5-dinitrobenzoic acid from benzoic acid requires prolonged treatment with a mixture of fuming nitric and sulfuric acids.

The chief function of the sulfuric acid used in nitrations is to take up the water formed during the nitration. In this connection it is interesting to note that concentrated nitric acid is primarily a nitrating agent, while dilute nitric acid usually functions as an oxidizing agent. Thus benzaldehyde is readily oxidized by the latter reagent to benzoic acid, while with concentrated nitric acid *m*-nitrobenzaldehyde is formed.

Procedure.—Eighty cubic centimeters of concentrated sulfuric acid is added, cautiously and with cooling, to 70 cc. of concentrated nitric acid. To this mixture 50 g. of benzene is added in small portions with shaking. The temperature of the mixture is not allowed to rise above 60°. After all the benzene has been added, the shaking is continued for about 30 minutes while the temperature is kept at 60°. The mixture is then cooled, and the lower acid layer removed. The nitrobenzene (which is heavier than water) is washed once with water, once with 10 per cent sodium hydroxide, and finally with water. It is dried over calcium chloride and purified by distillation. The product which passes over between 205 and 215° is redistilled, the fraction boiling between 209 and 212° being collected in the second distillation. *In neither distillation is the temperature to be carried above* 215°, *or the distillation to be continued until the flask is dry.* Nitrobenzene boils at 211°. The yield should be about 40 g.

Questions

1. Explain the origin of the brown fumes evolved during the nitration.
2. What is the reason for not carrying the distillations of the nitrobenzene too far?
3. Write equations for the reactions of nitrobenzene with: (*a*) Tin and hydrochloric acid; (*b*) chlorine; (*c*) nitric and sulfuric acids.

Preparation 23. *m*-Dinitrobenzene

The nitration of benzene can be readily controlled to yield either mono- or dinitrobenzene as desired. By comparison with the preceding preparation, it is seen that dinitration is accomplished by using a larger amount of nitric and sulfuric acids relative to the benzene used, and by heating the reaction mixture to 120 instead of 60°. The introduction of a third nitro group into benzene is very difficult. Trinitrobenzene can be prepared by boiling dinitrobenzene with fuming nitric acid for several days.

Procedure.—Seventy-five cubic centimeters of concentrated sulfuric acid is cautiously added with cooling to an equal volume of concentrated nitric acid. To the cooled mixture, contained in a 1-l. flask, 30 g. of benzene is added in small portions with vigorous shaking. The flask is cooled somewhat between additions of the benzene to prevent the reaction from becoming too violent. After the addition of the benzene is complete, the mixture is shaken vigorously for several minutes. One hundred and fifty cubic centimeters of concentrated sulfuric acid is then added in small portions with agitation, but without cooling. A thermometer is introduced *into the mixture* which is then heated in an oil bath to 120° for 5 minutes. A few drops of the liquid is removed on a stirring rod and added to a test tube filled with cold water. If the nitration is complete the dinitrobenzene will separate as a hard, pale yellow solid. If the nitration is not complete, an oil will be formed, and the heating must be continued.

The reaction mixture is finally cooled to about 80° and poured, with stirring, into 2 l. of cold water. The dinitrobenzene that separates is filtered by suction and washed thoroughly with water. It is purified by recrystallization from dilute alcohol. The dinitrobenzene is added to a mixture of 250 cc. of alcohol and 50 cc. of water, and some norite is added. After refluxing for 5 minutes, the mixture is filtered through a fluted paper on a large funnel which has been previously warmed, and the filtrate is cooled. The dinitrobenzene is filtered off, washed with a little cold 50 per cent alcohol, and then abundantly with water, and dried. *m*-Dinitrobenzene melts at 90°. The yield should be 50 to 60 g. of pale yellow material.

Questions

1. What are the source and formula of the brown fumes evolved during the nitration?

2. Why is the test, described above, a satisfactory test for completion of the reaction?

3. Write equations for the reactions, if any, of each of the following reagents with *m*-dinitrobenzene: (*a*) Tin and hydrochloric acid; (*b*) ammonium sulfide; (*c*) chlorine.

Preparation 24. *p*-Nitroaniline

In the nitration or halogenation of aromatic primary amines, difficulties are frequently encountered because of the sensitivity of the amine group to these reagents unless the amine group is first "blocked." Furthermore, the blocking of the amine group very markedly cuts down the ease of substitution, which is desirable when it is wished to obtain mono-substituted products. Thus, if acetanilide is treated with a solution of bromine in acetic acid, *p*-bromoacetanilide is formed, while the reaction between aniline and bromine water leads directly to the formation of tribromoaniline.

The blocking of the amine group is conveniently accomplished by forming the acetyl derivative with acetic anhydride or acetic acid. Another method frequently used is the formation of the benzylidene derivative ("Schiff's base") with benzaldehyde.

Read the discussion of nitration included in Preparation 22, page 82.

Procedure.—Thirty grams of acetanilide, prepared as described on page 80, is dissolved by heating in 30 cc. of glacial acetic acid. The solution is cooled until crystallization starts and is then poured slowly into 43 cc. of concentrated sulfuric acid. The mixture is cooled to 0° and a solution of 11 cc. of concentrated nitric acid in 13 cc. of concentrated sulfuric acid is added in small portions with stirring, while the temperature is kept below 10°. After all the mixed acid has been added, the reaction mixture is allowed to stand for 1 hour at room temperature. It is then poured into 500 cc. of cold water and the precipitated *p*-nitroacetanilide is filtered off and washed with water. It may be purified by recrystallization from alcohol, though this is not necessary if the free nitroaniline is the desired product. Pure *p*-nitroacetanilide melts at 214°.

***p*-Nitroaniline.**—*p*-Nitroacetanilide is hydrolyzed by being boiled for 30 minutes with ten times its weight of dilute hydrochloric acid (1:1). The mixture is then cooled and diluted with an equal amount of water. (No precipitate should be present at this point in the procedure if the hydrolysis is complete.) The free base is precipitated by the addition of an excess of ammonium hydroxide; it is filtered off, washed with a small amount of cold water, and recrystallized from water, about 1500 cc. of solvent being used. *p*-Nitroaniline melts at 148°. The yield should be about 15 g.

Questions

1. How does *p*-nitroacetanilide react with hot aqueous alkali? Why would this reaction be less convenient than the similar reaction actually used in the preparation?

2. Indicate by equations the reactions of *p*-nitroaniline with each of the following reagents: (*a*) Acetyl chloride; (*b*) dilute sulfuric acid; (*c*) chloroform and potassium hydroxide; (*d*) tin and hydrochloric acid; (*e*) nitrous and hydrochloric acids; (*f*) ethyl bromide.

Preparation 25. Aniline

The commonest method for the preparation of aromatic primary amines is the reduction of nitro compounds. The reducing agent used is of considerable importance since a wide variety of products other than amines may be obtained by the choice of suitable reagents.

On a commercial scale, the reduction of nitrobenzene to aniline is accomplished by the use of iron, hydrochloric acid, and steam, only a small fraction of the hydrochloric acid theoretically necessary actually being used. On a laboratory scale, convenient though more expensive reagents, tin and hydrochloric acid, are used.

The reduction evidently involves the formation of one or more intermediate compounds. Thus, if an insufficient quantity of tin is used, the formation of the red colored azobenzene, $C_6H_5—N=N—C_6H_5$, can be observed.

In most reduction reactions where the substance being reduced and the reducing agent occupy different phases, it has been postulated that the reduction is accomplished by hydrogen in an especially active form—"nascent hydrogen"—produced, in the present case, by interaction of the tin and hydrochloric acid. The concept of nascent hydrogen is introduced because it is well known that ordinary gaseous hydrogen is without effect under similar circumstances.

Procedure.—Ninety grams of granulated tin and 50 g. of nitrobenzene are placed in a round-bottomed flask attached to a reflux air condenser. To this mixture is added 230 cc. of concentrated hydrochloric acid in small portions as follows: About one-tenth of the acid is added and the mixture shaken gently until a violent reaction starts. The flask is immediately placed in a bath of cold water until the reaction moderates. Successive small portions of acid are then added in the same manner until about one-half has been added, after which the addition can be performed more rapidly. The mixture is finally heated on a boiling water bath for 30 minutes.

At this point of the procedure the aniline exists as the double salt $(C_6H_5NH_2{\cdot}HCl)_2SnCl_4$. To obtain the free base the cooled reaction mixture is diluted with 100 cc. of water and is then made alkaline with a solution of 150 g. of crude sodium hydroxide in 200 cc. of water. Care should be taken during the addition of the alkali to avoid loss of aniline by volatilization. The aniline is obtained from the mixture by steam distillation, the distillation being interrupted as soon as no more aniline distills over. (*Note:* In order to answer Question 1, it will be necessary to estimate the total volume of steam distillate.) The distillate is extracted twice with ether and the combined ether solutions are dried over anhydrous sodium sulfate. After removal of the ether (see page 41), the aniline is purified by distillation. Aniline boils at 184°.

Questions

1. From the total weight of steam distillate collected (assume the over-all density is 1.0), and the yield of aniline obtained, calculate the percentage of aniline by weight in the distillate. Compare this figure with the theoretical value calculated from the data on page 22. Explain the difference.

3. Suggest another method for isolating the aniline from the reaction mixture, and compare its suitability with the method actually used.

4. Write equations for the action, if any, of each of the following reagents on aniline: (*a*) Hydrochloric acid; (*b*) sodium hydroxide; (*c*) nitrous and hydrochloric acids; (*d*) chloroform and potassium hydroxide; (*e*) benzaldehyde; (*f*) carbon disulfide; (*g*) acetyl chloride; (*h*) acetic anhydride; (*i*) methyl iodide; (*j*) concentrated sulfuric acid; (*k*) bromine water.

Preparation 26. *m*-Nitroaniline

m-Nitroaniline, an important dye intermediate, is always prepared by the partial reduction of *m*-dinitrobenzene. The reduction can be accomplished by the ordinary reagents for the reduction of nitro compounds, such as tin and hydrochloric acid, but in such cases the reaction must be very carefully controlled to prevent the formation of *m*-phenylenediamine. Fortunately, there are two reagents which seem to be specific for the partial reduction of dinitro compounds, ammonium sulfide and sodium polysulfide. The latter is the reagent which is used in the commercial preparation of *m*-nitroaniline.

Procedure.—Twenty grams of sulfur is added to a solution of 75 g. of crystalline sodium sulfide in 300 cc. of hot water. To this solution is slowly added 50 g. of *m*-dinitrobenzene at such a rate that the mixture is kept gently boiling by the heat of the reaction. When the addition is complete, the boiling is continued for 30 minutes more. The mixture is then thoroughly chilled and the sulfur and *m*-nitroaniline filtered off and washed with water. This solid mixture is added to 500 cc. of boiling 5 per cent hydrochloric acid, treated with norite, and filtered by gravity; the *m*-nitroaniline is precipitated from the filtrate by addition of excess ammonium hydroxide. The product so obtained is filtered off and recrystallized again in the same manner. The purified *m*-nitroaniline is finally washed with water and dried. *m*-Nitroaniline melts at 112°. The yield should be about 10 g. Considerable unchanged dinitrobenzene can be recovered from the acid-insoluble material.

Preparation 27. Iodobenzene

The preparation of organic iodides by direct replacement of hydrogen by iodine is in general difficult, so that indirect methods are necessary. One of the most convenient methods for the preparation of aromatic iodides involves the replacement of an amine group by iodine:

$$C_6H_5NH_2 \xrightarrow{HNO_2 + HCl} C_6H_5N_2Cl \xrightarrow{KI} C_6H_5I + N_2 + KCl$$

The nitrous acid required in the first step is usually obtained *in situ* from sodium nitrite and hydrochloric acid.

In the diazotization of an aromatic amine three precautions are to be observed:

1. The reaction mixture must be kept cold since the diazonium salt reacts with water even at room temperature to form a phenol. Furthermore, nitrous acid itself is unstable.

2. An excess of mineral acid must be present to prevent the diazonium salt from reacting with unchanged amine with the formation of a diazoamino compound:

$$C_6H_5N_2Cl + C_6H_5NH_2 \xrightarrow[\text{solution}]{\text{neutral}} C_6H_5N{=}N{-}NHC_6H_5$$

3. An excess of nitrous acid is usually avoided. In the present case, excess nitrous acid would oxidize some of the potassium iodide used in the second step. However, it is obviously necessary to add enough nitrous acid to react with all the amine present. A convenient procedure is to test the reaction mixture after each addition of nitrite solution when the diazotization is nearly completed. This is done with strips of filter paper impregnated with potassium iodide and starch. When a faintly positive test is obtained at the end of 3 minutes after the last addition of sodium nitrite, enough nitrous acid has been added.

Procedure.—The phenyl diazonium chloride is prepared by dissolving 20 g. of aniline in 100 cc. of water to which 50 cc. of concentrated hydrochloric acid has been added. After cooling to a temperature lower than 5°, a cold solution of 17 g. of sodium nitrite in 75 cc. of water is added slowly with continuous stirring, the temperature being held below 5°. A few pieces of ice may be added directly to the mixture to keep the temperature down. After the lapse of 3 minutes, the solution is tested with starch-iodide paper; if no blue color is observed, a small additional amount of nitrite is added and the test is again performed after 3 minutes. This procedure is continued until a slight excess of nitrite is present.

To this solution of phenyl diazonium chloride is added a solution of 40 g. of potassium iodide in an equal weight of water and the mixture is allowed to stand for several hours. (The experiment must not be interrupted until the potassium iodide has been added.) The mixture is then heated on a boiling water bath until the evolution of nitrogen ceases. After the solution has been made strongly alkaline with sodium hydroxide, the iodobenzene is removed by steam distillation. The product is separated from the water, dried with a few pieces of calcium chloride, decanted, and distilled, an air condenser being used. Iodobenzene boils at 189°. The yield should be about 35 g. of nearly colorless product.

Questions

1. Why is it necessary to wait for 3 minutes after addition of the nitrite before testing for nitrous acid with starch-iodide paper?

2. Why is the solution made strongly alkaline before steam distillation? Write equations for any reactions suggested by your explanation.

3. Write equations for all the reactions mentioned in connection with the precautions to be observed in diazotizing an aromatic amine.

4. Explain the chemistry of the test for nitrous acid by means of starch-iodide paper. Write equations wherever possible.

5. Describe in detail a method not involving steam distillation for the isolation of the iodobenzene from the reaction mixture. Which method would you expect to be most satisfactory? Why?

6. Write equations for the reactions, if any, occurring: (*A*) When phenyl diazonium chloride reacts with: (*a*) dimethyl aniline; (*b*) phenol; (*c*) sodium sulfite; (*d*) ethyl alcohol; (*e*) cuprous cyanide; (*B*) When iodobenzene reacts with: (*a*) nitric and sulfuric acids; (*b*) sodium hydroxide; (*c*) magnesium in dry ether; (*d*) ammonia.

Preparation 28. *m*-Chloronitrobenzene

A very important application of aromatic primary amines to synthetic purposes is their conversion into diazonium salts (see page 88), with subsequent replacement of the diazonium salt group by hydrogen, hydroxyl, halogen, or cyano groups. The reaction described below, which involves replacement of amino by halogen, is an example of the so-called *Sandmeyer's reaction,* which term also includes the replacement of amino by cyano.

Chloronitrobenzene may also be prepared by the action of chlorine on nitrobenzene in the presence of a carrier catalyst (iodine, ferric chloride, etc.).

Attention should be given to the precautions in diazotization discussed on page 88.

Procedure. *Cuprous Chloride.*—A solution of 110 g. of crystalline cupric sulfate and 40 g. of sodium chloride in 400 cc. of water is heated to 60 to 70° and a concentrated aqueous solution of the amount of sodium bisulfite theoretically required to reduce the copper is added. The precipitate of cuprous chloride is filtered off by suction, washed with water, and then suspended in a mixture of 200 cc. of water and 150 cc. of concentrated hydrochloric acid.

Diazotization.—A solution of 50 g. of *m*-nitroaniline in a mixture of 50 cc. of concentrated hydrochloric acid and 100 cc. of hot water is treated with an additional 110 cc. of concentrated hydrochloric acid. The solution is cooled rapidly with stirring. This mixture is diazotized at a temperature below 5° by the slow addition from a dropping funnel, with constant vigorous stirring, of a solution of 25 g. of sodium nitrite in 70 cc. of water.

The diazotized solution is added with stirring to the cuprous chloride suspension, the temperature being kept at 25 to 30°. After the evolution of nitrogen has subsided, the mixture is heated to 100° under a reflux condenser to complete the reaction. Finally the *m*-chloronitrobenzene is steam-distilled, care being taken to prevent the condenser from becoming stopped up with solid material. The product is purified by recrystallization from a small volume of alcohol. It melts at 44°. The yield should be about 35 g.

Questions

1. Calculate the volume of nitrogen, measured over water at 25°, which should be evolved in the reaction. The vapor pressure of water at 25° is 23.5 mm.

2. By what other reagent could the diazonium salt be converted into the chloride? What becomes of the copper in the course of the reaction as described above?

3. Why is it essential to stir vigorously during the diazotization?

4. Write equations showing how the following conversions could be accomplished: (*a*) Benzene to *m*-dibromobenzene; (*b*) benzene to phthalic acid.

5. Discuss the importance of the Sandmeyer reaction as compared with the apparently simpler method of direct halogenation.

6. Write equations for the reactions of *m*-nitrophenyl diazonium chloride with each of the following reagents: (*a*) Cuprous bromide; (*b*) cuprous cyanide; (*c*) heat; (*d*) potassium iodide; (*e*) ethyl alcohol.

7. Write equations for the reactions, if any, of *m*-chloronitrobenzene with: (*a*) Tin and hydrochloric acid; (*b*) aqueous alkali.

Preparation 29. Phenylhydrazine Hydrochloride

Phenylhydrazine is an important reagent used for the identification of carbonyl compounds and sugars and also in certain important synthetic procedures. Examples of its use in the formation of phenylhydrazones and osazones for identification purposes are given on pages 179 and 211.

The standard method for preparing derivatives of hydrazine, $NH_2 \cdot NH_2$, containing one aromatic group, is by the reduction of a diazonium salt. The reduction is sometimes accomplished by stannous chloride, but the reagent usually used is sulfurous acid. The probable course of the reaction in the formation of phenylhydrazine is illustrated in the following equations:

$$C_6H_5NH_2 \xrightarrow{HNO_2} C_6H_5N_2Cl \xrightarrow{Na_2SO_3} C_6H_5{-}N{=}N{-}SO_3Na$$

$$C_6H_5{-}N{=}N{-}SO_3Na \xrightarrow[(SO_2)]{\text{reduction}} C_6H_5{-}NH{-}NH{-}SO_3Na \xrightarrow{HCl} C_6H_5{-}NH{-}NH_2 \cdot HCl$$

The sulfite is itself oxidized to sulfate.

The discussion of diazotization on page 88 should be read before the experiment is performed.

Procedure.—Before diazotization of the aniline, a solution of sodium sulfite is to be prepared. Fifty-eight grams of anhydrous sodium bisulfite dissolved in 250 cc. of water is neutralized with 22 g. of sodium hydroxide dissolved in 50 cc. of water. If the solution is alkaline to phenolphthalein, just enough additional bisulfite is added to decolorize the indicator.

A solution of aniline hydrochloride is prepared by mixing 50 cc. of concentrated hydrochloric acid, 150 g. of ice, and 20 g. of aniline. To this solution is added with constant stirring a solution of 16.2 g. of sodium nitrite in as small an amount of water as possible. The temperature is to be kept below 5° by the use of an ice-salt bath. The addition of the nitrite should require about 20 minutes.

After the addition of the nitrite the solution is stirred for 10 minutes, and is then rapidly added with stirring to the sulfite solution. The mixture is made just neutral to litmus with 10 per cent sodium hydroxide and warmed to 60° for 30 to 40 minutes on a steam bath. It is then made acid to litmus with hydrochloric acid and warmed on a steam bath for 2 hours or longer. (The solution may be left overnight at this point.)

Any insoluble material present is filtered off and the filtrate is boiled with norite and refiltered.

Two hundred cubic centimeters of concentrated hydrochloric acid is carefully added to the hot filtrate, which is then cooled under running water and finally in an ice bath until the precipitation of the phenylhydrazine hydrochloride is complete. The crystals are filtered off by suction, washed with a small amount of cold dilute hydrochloric acid (1:1), and recrystallized from dilute hydrochloric acid (1:2). The yield should be about 15 g.

Questions

1. Describe in detail a method for obtaining pure phenylhydrazine from its hydrochloride. (Phenylhydrazine suffers partial decomposition when distilled under atmospheric pressure.)

2. Write equations for the reactions of phenylhydrazine with each of the following substances: (*a*) Hydrochloric acid; (*b*) strong reducing agents; (*c*) an aldehyde; (*d*) a ketone; (*e*) *d*-arabinose; (*f*) acetoacetic ester (see page 197).

Preparation 30. Glycine

One of the important methods of preparing α-amino acids is by the action of ammonia on halogenated acids. In the present preparation the reaction is represented by the equation:

$$Cl{\cdot}CH_2{\cdot}COOH \xrightarrow{NH_3} NH_2{\cdot}CH_2{\cdot}COONH_4 + NH_4Cl$$

Frequently the most difficult part of the preparation of a water-soluble amino acid is the isolation of the product. This arises from the amphoteric nature of these substances. It is usually necessary to obtain an aqueous solution of the amino acid which is free from non-volatile impurities.

In the method described below, the glycine is first isolated in the form of a complex copper salt (somewhat similar, as indicated by the color, to the complex copper-ammonia salts). The free amino acid is then obtained by removal of the copper as cupric sulfide by the action of hydrogen sulfide.

Procedure.—A solution of 25 g. of chloroacetic acid in 25 cc. of water is added to 300 cc. of concentrated ammonium hydroxide and allowed to stand in a loosely stoppered flask under the hood for 24 hours or longer. The mixture is then boiled down in an open beaker to a volume of 200 cc. or until the evolution of ammonia is completed. While the solution is still hot, an excess of cupric carbonate is cautiously added (about 20 g. will be required). After cooling in an ice bath, the precipitate is filtered off by suction and washed with a little 50 per cent alcohol. A small second crop of the copper salt can be obtained by evaporation of the filtrate to a small volume.

The copper salt is suspended in hot water and treated with hydrogen sulfide until the precipitation of the copper is complete. The precipitate is removed by suction filtration and washed thoroughly with hot water. It may be necessary to repeat the hydrogen sulfide treatment to remove the copper completely. The filtrate is evaporated to a volume of 10 cc., boiled with a small amount of norite, again filtered, and is then cooled in an ice bath. After the glycine has crystallized out, an equal volume of alcohol is added slowly with vigorous stirring. After again cooling, the crystals of glycine are collected, washed with alcohol and dried. Glycine melts with decomposition at 233°. The yield is 5 to 7 g.

Questions

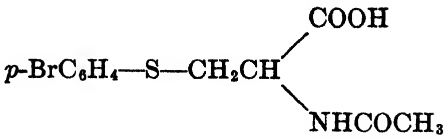
1. Outline, by equations if possible, two other methods for preparing glycine.

2. Hydrogen sulfide is a weak acid and therefore forms a salt with glycine. Explain the fact that evaporation of a solution containing these two substances yields only free glycine. Why cannot free glycine be isolated by evaporation of the original reaction mixture?

3. Write equations for the reactions of glycine with each of the following substances: (*a*) Nitrous acid; (*b*) sodium hydroxide; (*c*) hydrochloric acid; (*d*) benzoyl chloride and aqueous alkali; (*e*) phosphorus pentachloride; (*f*) ethyl alcohol and hydrogen chloride.

Preparation 31. Hippuric Acid

One of the very interesting functions performed by the so-called higher forms of life is what is known as *detoxification.* When certain poisons, chiefly organic ones, are ingested, they are changed within the body to less toxic substances and these substances are excreted. For example, the ingestion of bromobenzene in sublethal doses results in its excretion as *p*-bromophenyl mercapturic acid,



$$p\text{-BrC}_6\text{H}_4\text{—S—CH}_2\text{CH}\begin{cases}\text{COOH}\\ \text{NHCOCH}_3\end{cases}$$

Similarly, benzoic acid is conjugated in the body with the amino acid, glycine, to form the less toxic hippuric acid, the name of which results from the fact that it is an important nitrogenous excretory product in the urine of the horse. In the following paragraphs is given a method for the isolation of hippuric acid from urine. It is interesting to calculate the percentage yield of this *in vivo* reaction.

Procedure.—Just before retiring on the night before the isolation of hippuric acid is to be attempted, a solution of 2 g. of sodium benzoate in a glassful of water is drunk. The next morning, the overnight sample of urine is collected and the isolation of the hippuric acid performed as follows: Twenty-five grams of ammonium sulfate and 1.5 cc. of concentrated sulfuric acid are added for each 100 cc. of urine The solution is well stirred and then placed in an ice bath for half an hour with occasional stirring. The precipitated crystals are filtered off by suction and washed with not more than 10 cc. of *ice water*. They are recrystallized from hot water, norite being used to decolorize the product. Hippuric acid melts at 187°. About 1.5 g. of substance should be obtained.

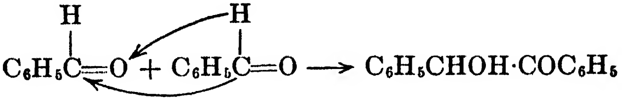
Questions

1. Calculate the theoretical and percentage yields in this biochemical reaction.

2. Write equations for the reactions, if any, of hippuric acid with: (*a*) Sodium carbonate; (*b*) hot aqueous sodium hydroxide; (*c*) methyl alcohol and hydrochloric acid; (*d*) nitrous acid.

Preparation 32. Benzilic Acid

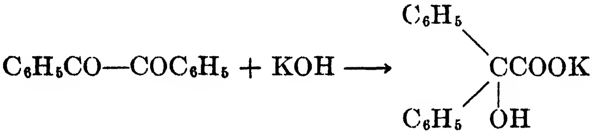
The preparation of benzilic acid described below involves several different reactions. The first of these is the so-called *benzoin condensation.* Many aromatic aldehydes undergo this condensation in the presence of an alkali cyanide, which appears to be a highly specific catalyst for this reaction. In the condensation, one molecule of aldehyde adds to the carbonyl group of another molecule:



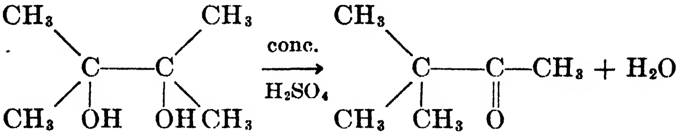
The mode of addition here should be compared with that in the Cannizzaro reaction (page 67).

The second reaction below, leading to the formation of benzil, $C_6H_5CO—COC_6H_5$, is an example of the oxidation of a secondary alcohol to a ketone, in this case by means of nitric acid.

When benzil is heated with aqueous potassium hydroxide, a curious reaction, known as the *benzilic acid rearrangement*, takes place. Without going into the mechanism of the reaction, about which there has been much discussion, the equation may be written as follows:



Rearrangements of this general type, where an aryl or alkyl group has definitely changed its position, are by no means rare in organic chemistry. Another important case is the so-called *pinacone-pinacoline rearrangement*, which in the case of pinacone itself proceeds as follows:



Compare also the intermediate steps in the Hofmann acid amide reaction (page 99), where a rearrangement of an alkyl or aryl group from carbon to nitrogen, rather than from carbon to carbon, occurs.

Procedure. *Benzoin.*—A mixture of 25 g. of benzaldehyde, 4 g. of sodium cyanide (**Highly toxic!**) 50 cc. of alcohol, and 30 cc.

of water is refluxed for an hour. After the solution is cooled, the benzoin is filtered off and washed with a small amount of cold alcohol followed by water. The product need not be purified before use in the next step. Benzoin melts at 133°. The yield should be over 20 g.

Benzil.—Twenty-five grams of benzoin and 65 cc. of concentrated nitric acid are heated on a water bath for an hour, with occasional shaking. At the end of this period no more brown fumes should be evolved. The mixture is poured into 500 cc. of cold water and the crude benzil is filtered off and washed thoroughly with cold water. It may be recrystallized from alcohol though this is unnecessary if it is to be changed into benzilic acid. Pure benzil melts at 95°. The yield is practically quantitative.

Benzilic Acid.—Twenty-five grams of benzil and 50 g. of alcohol are added to a solution of 25 g. of potassium hydroxide in 50 cc. of water. The mixture is refluxed on a steam bath for 10 minutes and is then cooled with occasional stirring in an ice bath. After 1½ hours the potassium benzilate is removed by suction filtration (a hardened paper being used if necessary) and is washed with about 40 cc. of ice-cold alcohol. The salt is dissolved in 400 cc. of water, norite is added, and the mixture is heated to boiling and then filtered. The hot filtrate is acidified with dilute sulfuric acid. Part of the benzilic acid precipitates out as an oil, which soon solidifies, and the rest crystallizes out on cooling. It is filtered off and dried. Further purification can be effected by recrystallization from hot water. Benzilic acid melts at 150°. The yield should be about 18 g.

Questions

1. Balance the equation for the oxidation of benzoin by nitric acid. Balance the equation using dilute alkaline permanganate as the oxidizing reagent.

2. Discuss the difference between the mechanism of the Cannizzaro reaction and that of the benzoin condensation.

3. Suggest two other methods for the preparation of benzilic acid.

4. Indicate by equations the characteristic reactions to be expected of each of the three substances prepared in this experiment. Note that benzoin is a secondary alcohol and a ketone, benzil is a diketone, and benzilic acid is an α-hydroxy acid.

Preparation 33. Benzyl Chloride

The side-chain halogenation of aromatic hydrocarbons is a process of considerable importance as it constitutes a starting point for the introduction of a variety of groups such as hydroxyl, carboxyl, carbonyl, etc., into side-chains. The conditions described below are typical of those generally used in this type of reaction. The important points are the elevated temperature and the absence of a "carrier" catalyst (compare page 62) such as iodine or amalgamated aluminum. Such catalysts have a much greater accelerating effect on nuclear halogenation than on side-chain halogenation. On the other hand, the rate of side-chain halogenation is increased by ultraviolet light much more than is that of nuclear halogenation so that yields of the side-chain halides are increased by irradiation of the reaction mixture.

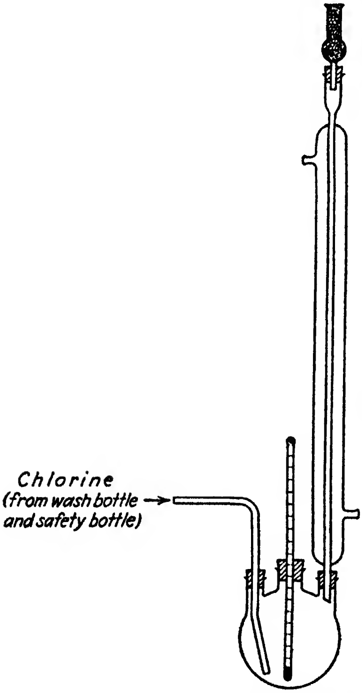


Fig. 24.—Apparatus for benzyl chloride.

Procedure.—Chlorine is a highly toxic gas, and benzyl chloride has a strongly irritant action on the skin and mucous membranes. The entire experiment is therefore to be performed in the hood. **Great care should be exercised in handling cylinders of liquefied chlorine. Read carefully the directions on page 47.**

The reaction is conveniently carried out in a 250-cc. three-neck flask (see Fig. 24). In the center neck is placed a thermometer the bulb of which will extend below the surface of the toluene to be introduced. In one of the side necks is placed an inlet tube extending to the bottom of the flask. The third neck is fitted with a reflux condenser, the top of which carries a calcium chloride tube. Tightly fitting cork stoppers must be used throughout.

Fifty grams of toluene (dried over calcium chloride) and a few pieces of porous plate are placed in the flask. The toluene is gently boiled and a stream of dry chlorine (see page 47) is passed in until the thermometer registers 158°. If the toluene is vigorously boiled or if the chlorine is passed in too rapidly, a considerable amount of toluene may be carried out of the condenser. The reaction time will be shortened very materially by exposing the mixture to a small mercury-vapor lamp. If such a lamp is not available, a 200-watt light bulb supported a few inches from the flask will make a fairly satisfactory substitute.

The reaction mixture is transferred to a Claisen flask and distilled under atmospheric pressure until a temperature of 135 to 140° is reached. The residue is distilled under reduced pressure (see page 16), the benzyl chloride being collected over a range of 5 to 8°, most of which is to be taken above the true boiling point of the substance. Benzyl chloride boils at 64°/12 mm.

A product of lower purity is yielded by distillation under atmospheric pressure. The material boiling between 165 and 185° is collected and redistilled. The final product is collected between 178 and 182°. The boiling point of benzyl chloride under atmospheric pressure is 179°. The yield should be 45 to 50 g. of nearly colorless material.

Questions

1. A mixture of toluene (B.P. 111°) and benzyl chloride which boils at 158° contains a considerable amount of toluene. Explain why this temperature rather than a higher one is recommended in the procedure above.

2. Calculate the volume of chlorine at 25°/760 mm. needed to react with 50 g. of toluene to form benzyl chloride, assuming that chlorine obeys the perfect gas laws.

3. What are the more important side products in the above reaction?

4. Write equations for the reactions of each of the following reagents with benzyl chloride: (*a*) Aqueous alkali; (*b*) potassium permanganate; (*c*) sodium cyanide; (*d*) ammonia; (*e*) magnesium; (*f*) chlorine; (*g*) sodium acetate.

Preparation 34. Anthranilic Acid

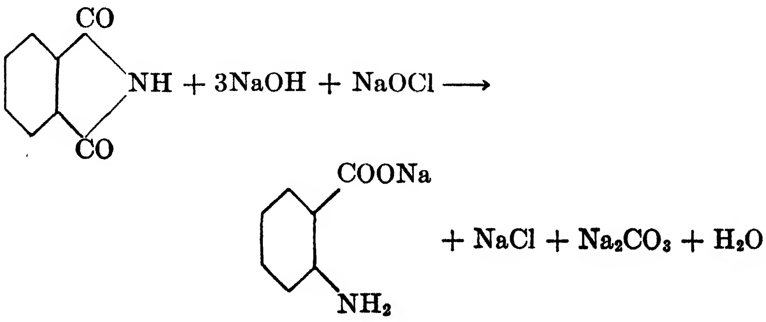
This preparation is adapted from the most important commercial application of the Hofmann acid amide reaction. The reaction accomplishes the degradation of an amide into an amine with one less carbon atom in its molecule. The reaction is of preparative importance in the formation of primary aliphatic amines. Perhaps the most important scientific application of the Hofmann reaction is to the elucidation of the structure of organic substances, since it constitutes a method for the orderly degradation of a substance containing an acid group or one convertible into an acid group.

There has been a great deal of discussion concerning the mechanism of the Hofmann reaction. There seems to be little doubt that the acid amide is first halogenated on the nitrogen atom. This halogenated compound is then changed under the influence of alkali with loss of hydrogen halide to an isocyanate, which in turn is hydrolyzed to an amine and carbon dioxide (carbonate):

$$\mathrm{RCONH_2} \xrightarrow{\mathrm{X_2}} \mathrm{RCONHX} \xrightarrow{\mathrm{NaOH}} \mathrm{RNCO} \xrightarrow{\mathrm{NaOH}} \mathrm{RNH_2}$$

Evidently a rearrangement occurs in the formation of the isocyanate, since the R group originally joined to carbon is found joined to nitrogen (see the remarks on rearrangements on page 96).

In the reaction described below, the degradation of phthalimide to anthranilic acid,



the first step is probably the partial hydrolysis of the imide to a half-amide.

Procedure.—Twenty-five grams of phthalimide is suspended in a cold solution of 50 g. of sodium hydroxide in 100 cc. of water. The solution is then treated with a solution of the calculated amount of sodium hypochlorite. This latter solution is prepared by dissolving 13.6 g. of sodium hydroxide in 50 cc. of water and passing chlorine (**Caution!** Read carefully the directions on page 47.) into the well-cooled solution until the gain in weight is 12.0 g. On the addition of the hypochlorite to the phthalimide, the temperature rises to about 50°. The mixture is then heated to 80° for 30 minutes. After cooling, the excess alkali is *almost* neutralized with hydrochloric acid, an excess of this reagent being carefully avoided, and the anthranilic acid is precipitated by making the solution acid with acetic acid, a *small* excess of this reagent being added. After thorough cooling in an ice bath, the product is removed by suction filtration and recrystallized from the least possible quantity of water, norite being used. The filtered solution should be cooled in an ice bath to insure complete precipitation of the anthranilic acid. A second crop may be obtained by evaporating the original mother liquor to half its volume. Anthranilic acid melts at 145°. The yield should be about 15 g.

Questions

1. In the isolation of the anthranilic acid, why is care taken not to acidify the solution with hydrochloric acid, but to use acetic acid for this purpose?

2. One of the inorganic side products of the reaction is ammonium acetate. What is the source of this substance?

3. What inorganic products of the reaction indicate that the Hofmann reaction is essentially an oxidation of the original amide?

4. How could anthranilic acid be prepared from a solid sample of its hydrochloride?

5. Write equations for another method of preparing anthranilic acid and comment on the relative practicability of the two methods.

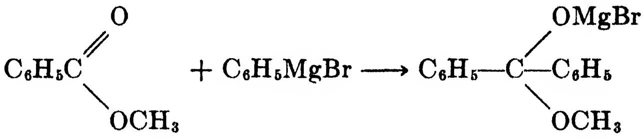
6. What is the commercial source of phthalimide? Give equations for one of the principal commercial uses of anthranilic acid.

7. Write equations for the reactions of anthranilic acid with: (*a*) Sodium hydroxide; (*b*) benzoyl chloride; (*c*) nitrous and hydrochloric acids; (*d*) acetic anhydride; (*e*) phosphorus pentachloride; (*f*) ethyl alcohol and hydrogen chloride.

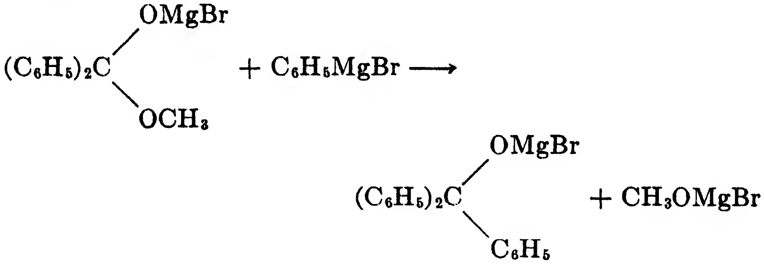
Preparation 35. Triphenylcarbinol

Some of the most important general synthetic methods in organic chemistry involve the reaction of Grignard compounds, RMgX, with a wide variety of reagents. A very important application of the Grignard method is in the preparation of alcohols by the reaction of Grignard compounds with aldehydes, ketones or esters.

In the reaction between methyl benzoate and phenyl magnesium bromide, the first step is addition of the Grignard compound to the ester group:



The product of this addition reacts with another molecule of the Grignard reagent as follows:



The resulting compounds are hydrolyzed to give the corresponding alcohols.

Procedure.—For success in this preparation, the reagents must be thoroughly dried. The magnesium powder should be dried at 110 to 120° for a half hour; the bromobenzene is to be redistilled, if impure, and then dried over calcium chloride. The ether used as solvent is purified and dried over sodium as described on page 43.

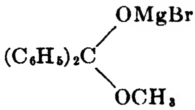
Four and eight-tenths grams of magnesium powder, 100 cc. of ether, and a small crystal of iodine are placed in a flask attached to a reflux condenser by means of a three-way tube carrying a dropping funnel. Access of moisture into the apparatus is prevented by a calcium chloride tube attached to the upper end of the condenser. Thirty-nine grams of bromobenzene is *slowly* added through the dropping funnel. If the reaction does not start after a little of the halide has been added, the addition is interrupted and the flask warmed in a water bath until the reaction starts. It is not necessary to apply further heat during the addition of the bromide. After the addition of the bromobenzene is complete, the mixture is heated on a water bath for an hour. The mixture is cooled, and 14 g. of methyl benzoate is slowly added. The reaction with the ester is completed by an hour's digestion on the water bath. Several pieces of cracked ice are then added, followed, after any reaction has subsided, by sufficient dilute sulfuric acid to make the mixture acid. The bromobenzene, methyl benzoate and diphenyl are removed by steam distillation, and the remaining triphenylcarbinol is filtered off and recrystallized from alcohol. It is advisable to evaporate the mother liquor from the recrystallization to obtain a second crop of crystals which are then recrystallized from a small volume of alcohol before being added to the first crop. Triphenylcarbinol melts at 163°. The yield should be 8 to 9 g. of colorless material.

Questions

1. How can one tell when the reaction leading to the formation of phenyl magnesium bromide has started? Explain all the phenomena observed at that time. Why is it necessary to insure that the reaction has started before adding all the bromobenzene?

2. What is the source of the diphenyl mentioned in the last paragraph of the procedure?

3. What would be the product of the hydrolysis of the intermediate compound



$$(C_6H_5)_2C\begin{matrix} \diagup OMgBr \\ \diagdown OCH_3 \end{matrix}$$

Give equations for a good method of preparing this substance.

4. Write equations for the reactions of phenyl magnesium bromide with each of the following reagents: (*a*) Water; (*b*) ethyl alcohol; (*c*) formaldehyde; (*d*) acetaldehyde; (*e*) acetone; (*f*) benzoyl chloride.

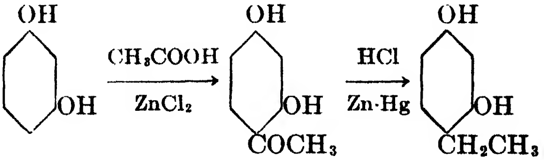
5. Indicate by equations how triphenyl carbinol reacts with: (*a*) Phosphorus pentachloride; (*b*) metallic sodium; (*c*) acetyl chloride

Preparation 36. Ethylresorcinol

The preparation of ethylresorcinol illustrates two important reactions. The first step in the synthesis, which yields resacetophenone, is an example of the *Nencki condensation,* a method for preparing phenolic ketones. The reaction is fundamentally similar to the Friedel-Crafts reaction using acid chlorides (compare with the preparation of *p*-bromoacetophenone on page 111), but is more convenient than the latter process in that it is not necessary to "block" the phenolic group. In the Friedel-Crafts method, phenolic groups must be "blocked" by being converted to ether groups, and the product of the Friedel-Crafts reaction must then be dealkylated. In the Nencki condensation, a phenol is heated with a fatty acid in the presence of anhydrous zinc chloride.

The second step in the preparation of ethylresorcinol illustrates the so-called *Clemmensen reduction,* a method widely used for the reduction of carbonyl groups to methylene groups. Other methods of reduction, including catalytic reduction, usually only lead to the formation of an alcohol or pinacol. It is remarkable that in many cases where the reduction of a ketone with zinc and hydrochloric acid yields an alcohol, reduction by the Clemmensen method using *amalgamated* zinc and hydrochloric acid leads to practically quantitative yields of the substance having a methylene group in place of the carbonyl group. Such facts throw doubt on the validity of the concept of "nascent hydrogen" (see page 86) in the explanation of reductions with reagents which yield hydrogen gas.

The synthesis of ethylresorcinol is represented by the equations:



The corresponding case where caproic acid replaces the acetic acid yields the well-known internal antiseptic, hexylresorcinol.

Procedure. *Resacetophenone.*—Thirty grams of anhydrous zinc chloride is dissolved in 30 g. of warm glacial acetic acid contained in a 250-cc. flask. Twenty grams of resorcinol is added and the mixture is heated *gradually* under an air reflux condenser until the temperature of the mixture reaches about 140°, when a vigorous reaction sets in. The flame is immediately removed and the reaction allowed to proceed. If the heating has been too rapid or the temperature during the reaction is allowed to rise too high, considerable resinification takes place. The temperature should not go above 150°. After the reaction is finished, the mixture is allowed to cool somewhat and is then poured into 500 cc. of cold water. The solid product is filtered off and washed with cold water. It can be used in the next step without further purification. Resacetophenone melts at 142°. The yield should be about 20 g.

Ethylresorcinol.—Amalgamated zinc is prepared by allowing 80 g. of granulated zinc to stand completely covered by a 5 per cent mercuric chloride solution for 2 or 3 hours. The excess solution is then decanted and the zinc washed once with water.

The amalgamated zinc is heated, under a reflux condenser, with the resacetophenone prepared as described above and 300 cc. of dilute hydrochloric acid (1 volume of concentrated acid and 2 volumes of water). When vigorous reaction starts, the flame is removed until it subsides; the mixture is then refluxed for 3 hours, during which time occasional additions of small amounts of concentrated hydrochloric acid are made through the condenser. The oily reaction product and the aqueous layer are decanted from the unchanged zinc, the hot aqueous layer is *saturated* with sodium chloride, decanted from any excess of the salt and chilled in an ice-salt bath. The precipitated ethylresorcinol is filtered off, *dried*, and recrystallized from toluene. Ethylresorcinol melts at 97°. The yield should be about 12 g.

Questions

1. Write the equations involved in the preparation of resacetophenone from resorcinol by means of the Friedel-Crafts reaction.

2. How many products could theoretically result from the introduction of one acetyl group into resorcinol? Give their structures.

3. Contrast the reactions of acetic acid and acetyl chloride with resorcinol.

4. How could ethylresorcinol be prepared from resorcinol by a method not involving a reduction?

5. Write equations for the reactions of resacetophenone with: (*a*) Hydroxylamine; (*b*) acetic anhydride; (*c*) sodium hydroxide and iodine; (*d*) phenylhydrazine.

6. Write equations for the reactions of ethylresorcinol with: (*a*) Acetic anhydride; (*b*) bromine water; (*c*) dimethyl sulfate and sodium hydroxide; (*d*) distillation with zinc dust.

Preparation 37. Sodium *p*-Toluenesulfonate and *p*-Toluenesulfonamide

The sulfonation of aromatic hydrocarbons is a very important reaction. The sulfonic acid group may be replaced by other groups such as hydroxyl, cyano and sulfonamido. A sulfonic acid group is also frequently introduced into a molecule, particularly of a dye, to confer on the substance the desirable property of water solubility.

In sulfonations where the product is very soluble in water difficulty is encountered in isolating the substance. This follows from the fact that usually a large excess of sulfuric acid is used in the reaction. One method for the isolation of the sulfonic acid depends on the fact that the barium salts of sulfonic acids are usually quite soluble in water. The sulfonation mixture is diluted and treated with excess barium carbonate and filtered. The filtrate is a solution of the barium sulfonate, from which the free sulfonic acid may be obtained by the addition of just the amount of sulfuric acid needed to completely precipitate the barium.

An ingenious method[1] to obtain the free sulfonic acid is to perform the reaction in the presence of *excess* of the organic reagent and to remove the water as it is formed in the reaction. In this way, the sulfuric acid may be completely used up and the isolation of the product from the excess of organic reagent is comparatively easy.

In the method described below, the sodium salt of the sulfonic acid, which is the substance usually desired rather than the free acid, is obtained from the reaction mixture by utilization of the fact that it is only slightly soluble in cold saturated sodium chloride solution. The sodium sulfonate is said to be *salted out* by the sodium chloride.

In the second part of the preparation, the crude sodium toluenesulfonate is transformed to the sulfonamide by a series

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[1] Compare L. GATTERMAN and H. WIELAND, "Laboratory Methods of Organic Chemistry," p. 183, The Macmillan Company, 1932.

of reactions which offer one of the most convenient methods for the preparation of amides, whether of sulfonic or carboxylic acids.

Procedure.—Fifty grams of toluene is shaken thoroughly with 10 cc. of concentrated sulfuric acid for several minutes. The temperature of the mixture is kept from rising above 25 to 30° by holding the small separatory funnel, in which the operation is performed, under running cold water if necessary. The acid layer is then removed. Thirty grams of the toluene treated in this way (care must be taken that no water from the wet separatory funnel gets into the toluene), 30 g. of fresh concentrated sulfuric acid, and a few pieces of porous plate are placed in a flask to which a reflux condenser is attached by means of a cork. The mixture is heated in an oil bath to 110 to 120°, and is very frequently shaken. (A mechanical stirrer is to be recommended if it is available.) It is to be noted that the reaction is heterogeneous; the toluene and acid are immiscible, or nearly so, so that most of the reaction must take place at the phase boundary. It is therefore desirable to insure that the interface has as large an area as possible, and that water and sulfonic acid are not allowed to accumulate in the neighborhood of the boundary.

After the toluene layer has disappeared, the mixture is cooled and poured slowly with stirring into 150 cc. of cold water. The resulting solution is made just alkaline with concentrated sodium hydroxide and then just acid with hydrochloric acid. The total volume is made up to about 300 cc. with water and the solution is then *saturated* at the boiling temperature with sodium chloride, boiled for a few minutes with norite, and filtered hot through a fluted filter paper. The filtrate is cooled thoroughly in an ice bath and the sodium toluenesulfonate which separates is filtered, washed with a small amount of *cold saturated* sodium chloride solution, and thoroughly dried. If a chloride-free preparation is desired, this crude product may be recrystallized from 95 per cent alcohol. About 2 l. of alcohol is required in the recrystallization, and 30 to 35 g. of recrystallized product should be obtained. If the sulfonamide is to be prepared, it is unnecessary to recrystallize the sodium toluenesulfonate.

p-Toluenesulfonyl Chloride.—**(Hood!)** The well-dried crude sodium toluenesulfonate prepared as described above is finely powdered and mixed thoroughly in a flask fitted with a reflux condenser with an equal weight of phosphorus pentachloride. (*This reagent must be handled with care.*) The mixture is heated in an oil bath to 130° for 3 hours and, after being cooled somewhat, is added to several volumes of cold water. The lumps of precipitated sulfonyl chloride are broken up and after they have stood under cold water for about 1 hour the sulfonyl chloride is filtered off by suction.

p-Toluenesulfonamide.—The crude sulfonyl chloride is ground to a powder and then added slowly with continual stirring and cooling to twice its weight of concentrated ammonium hydroxide. The mixture is finally heated to boiling and then well cooled. The sulfonamide which precipitates is filtered off and recrystallized from hot water, norite being used. Pure *p*-toluenesulfonamide melts at 138°. The yield should be about 20 g.

Questions

1. Explain the fact that the precipitate obtained on cooling a hot solution saturated with both sodium *p*-toluenesulfonate and sodium chloride is mainly the former salt.

2. How could you determine quantitatively the amount of sodium sulfate and sodium chloride present in a solution of these two salts and sodium *p*-toluenesulfonate?

3. Give one technical application each of *o*- and *p*-toluenesulfonamides. Write equations for all reactions involved in each case.

4. What is the purpose of the preliminary treatment of the toluene with concentrated sulfuric acid?

5. Write equations for the reactions: (*A*) Of *p*-toluenesulfonic acid with: (*a*) sodium carbonate; (*b*) sodium acetate; (*c*) ethyl alcohol; (*d*) superheated steam; (*B*) Of sodium *p*-toluenesulfonate on fusion with: (*a*) sodium hydroxide; (*b*) sodium cyanide; (*c*) phosphorus pentachloride.

6. Indicate by means of equations how each of the following reagents affects *p*-toluenesulfonyl chloride: (*a*) Methylamine; (*b*) hot water; (*c*) hot aqueous alkali; (*d*) ethyl alcohol; (*e*) dimethylamine; (*f*) trimethylamine.

7. Write an equation for the reaction of *p*-toluenesulfonamide with benzyl chloride and sodium hydroxide (see page 200).

Preparation 38. Phenylisothiocyanate and Triphenylguanidine

Most primary amines react with carbon disulfide to form substituted thioureas. The reaction proceeds with evolution of hydrogen sulfide:

$$2RNH_2 + CS_2 \longrightarrow RNH{\cdot}CS{\cdot}NHR + H_2S$$

The thiourea may be partially converted into a mustard oil (isothiocyanate) by heating with concentrated hydrochloric acid:

$$\text{RNH·CS·NHR} \xrightarrow[\text{HCl}]{\text{conc.}} \text{RNCS} + \text{RNH}_2\text{·HCl}$$

A side reaction here leads to the formation of a symmetrically trisubstituted derivative of guanidine:

$$\text{RNHCSNHR} + \text{RNH}_2 \longrightarrow (\text{RNH})_2\text{C}{=}\text{NR} + \text{H}_2\text{S}$$

Procedure. *Diphenylthiourea.*—(**Caution!** *Carbon disulfide is highly inflammable!*) A mixture of 40 g. of aniline, 50 g. of carbon disulfide, 65 cc. of alcohol, and 10 g. of finely powdered potassium hydroxide is heated on a steam bath under an efficient reflux condenser for 3 hours. (**Hood!**) The mixture is allowed to cool, the condenser is arranged for distillation, and the alcohol and excess carbon disulfide are removed. (**Caution!** See page 41.) The crude product is filtered off by suction and washed with water, dilute hydrochloric acid, and finally with water again. About 25 g. of diphenylthiourea should be obtained.

Phenylisothiocyanate.—The crude diphenylthiourea is placed in a 250-cc. distilling flask and 100 cc. of concentrated hydrochloric acid for each 25 g. of thiourea is added. The flask is placed in a boiling water bath for 1 hour (**Hood!**) and the mixture is then distilled until the oily phenylisothiocyanate has all distilled over. During the latter part of the distillation, crystals of triphenylguanidine hydrochloride may appear in the distilling flask. The distillate is then diluted with an equal volume of water and the mustard oil is extracted with ether. The extract is washed with dilute sodium carbonate and dried over calcium chloride. After removal of the ether (see page 41) the residual oil is purified by distillation. Phenylisothiocyanate boils at 218°. The yield is usually about 10 g.

Triphenylguanidine.—The residue in the flask contains triphenylguanidine hydrochloride. It is diluted with 100 cc. of water, heated to boiling with norite and filtered. The solution is cooled in an ice bath, after which the hydrochloride is filtered off by suction. It is then dissolved in the least possible quantity of hot water and the solution is made alkaline with sodium hydroxide. After cooling, the free triphenylguanidine is filtered off and purified by recrystallization from alcohol. Triphenylguanidine melts at 145°. The yield should be 2 to 3 g.

Question

Write equations for the reactions of phenylisothiocyanate with each of the following substances: (*a*) Ethyl alcohol; (*b*) methylamine; (*c*) dimethylamine.

Preparation 39. *p*-Nitrobenzoyl Chloride

For a discussion of the preparation of acid chlorides see page 76. In the procedure described below, thionyl chloride is used. The reaction with this reagent proceeds as follows:

$$RCOOH + SOCl_2 \longrightarrow RCOCl + SO_2 + HCl$$

One advantage of this reagent is that the inorganic products are gaseous.

Procedure.—(*Acid chlorides react with water. Access of atmospheric moisture must be prevented throughout the preparation.*) Fifty grams of thoroughly dried and powdered *p*-nitrobenzoic acid and 20 per cent more than the theoretically required amount of thionyl chloride are placed in a Claisen flask the side-arm and side neck of which are closed. The flask is attached to a reflux condenser and the reaction mixture gradually heated to gentle boiling and refluxed for an hour. It should then be a clear yellow liquid.

The excess thionyl chloride is removed by distillation from an oil bath under atmospheric pressure. When distillation with the oil bath heated to 200° has ceased, the nitrobenzoyl chloride is distilled under reduced pressure, the apparatus described on page 17 being used. Care must be taken to prevent the side-arm of the Claisen flask from becoming clogged with solid material. The *p*-nitrobenzoyl chloride boils at 155°/20 mm. The distillate is removed from the receiver by heating it just to melting, and it is poured carefully into a dry, weighed, wide-mouthed, glass-stoppered bottle. The product as obtained after one distillation is usually pure enough for ordinary purposes. If necessary, it may be redistilled or purified by recrystallization from carbon tetrachloride. *p*-Nitrobenzoyl chloride melts at 72°. The yield of unrecrystallized product should be about 50 g.

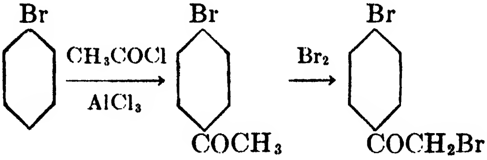
Question

Write equations for the reactions of *p*-nitrobenzoyl chloride with each of the following reagents: (*a*) Water; (*b*) ethyl alcohol; (*c*) ammonia; (*d*) dimethylamine; (*e*) tin and hydrochloric acid.

Preparation 40. *p*-Bromophenacyl Bromide

p-Bromophenacyl bromide is a convenient reagent for the identification of many acids, since the esters that it readily yields on treatment with salts of acids are usually crystalline solids. The ease of this reaction is characteristic for halides in which the halogen is on a carbon adjacent to a carbonyl group. The general equation for these reactions is given on page 184.

The first step in the preparation is the formation of the ketone, *p*-bromoacetophenone, by means of the Friedel-Crafts reaction. The ketone is then brominated in the side-chain.



The presence of the carbonyl group makes it unnecessary to use the special conditions generally employed in "side-chain halogenation" (page 98). The methyl group is so readily brominated that the side reaction of nuclear halogenation is negligible.

Procedure.—(**Carbon disulfide is extremely inflammable!** *For precautions to be used in its distillation see page* 41.) The bromobenzene and carbon disulfide used in this preparation must be dried overnight with calcium chloride. Seventy-five grams of bromobenzene, 100 g. of *anhydrous* aluminum chloride, and 200 cc. of carbon disulfide are placed in a 500-cc. round-bottomed flask. The flask is attached to a reflux condenser by means of a three-way tube carrying a dropping funnel (see Fig. 21, page 63). A tube leading to an inverted funnel supported over water is attached to the upper end of the condenser.

(**Caution!** *Water must not be allowed to suck back into the apparatus.*) While the temperature is kept at 15 to 20°, 43 g. of acetyl chloride is added in small portions from the dropping funnel. After the evolution of hydrogen chloride has slackened, the mixture is warmed to 40° until the evolution of gas ceases. The apparatus is then arranged for distillation and the carbon disulfide removed.

After the carbon disulfide has been removed, the residue is cooled slightly, but while still warm it is poured onto 500 g. of cracked ice. Twenty cubic centimeters of 10 per cent hydrochloric acid is added and the mixture stirred well to decompose the addition product of aluminum chloride and bromoacetophenone. After the ice has melted, the mixture is extracted twice with ether, using 200-cc. and 100-cc. portions. The combined ether extracts are then washed twice with water and once with saturated sodium bicarbonate, any precipitate being discarded with the washings. After drying the extract with calcium chloride, the ether is removed by distillation, using the precautions referred to above. The *p*-bromoacetophenone is then distilled *in vacuo* (see page 16). This substance boils at 117°/7 mm. and 129°/15 mm. It melts at 50°. It is permissible to collect the material over a fairly wide boiling range, as it will be further purified during the next stage of the preparation. The yield should be about 60 g.

The *p*-bromoacetophenone is dissolved in glacial acetic acid, 100 cc. of the solvent being used for 50 g. of the ketone. The calculated quantity of bromine, *carefully weighed*, is added slowly from a dropping funnel. The mixture should be shaken frequently, the bromophenacyl bromide separating as the reaction proceeds. The mixture is cooled and the product filtered off by suction and washed, first with a small amount of cold glacial acetic acid and then thoroughly with water. If necessary, it is purified by recrystallization from alcohol. M.P. 109°. Yield 60 to 70 g.

Questions

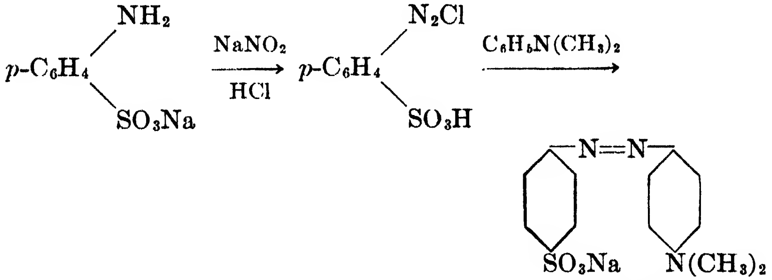
1. In Friedel-Crafts reactions with substances such as phenol ethers, benzene is sometimes used as solvent. Why could not benzene be used in the present case?
2. Write equations for the principal side reactions in this preparation.

3. It is essential that all the reactants in this preparation be dry. Why is it unnecessary to prevent the entrance of atmospheric moisture by the use of a calcium chloride tube?

4. Write equations for the reactions of *p*-bromophenacyl bromide with each of the following substances; (*a*) Sodium cyanide; (*b*) sodium acetate; (*c*) ethyl magnesium bromide; (*d*) reducing agents; (*e*) potassium permanganate; (*f*) aqueous sodium hydroxide; (*g*) sodium ethoxide.

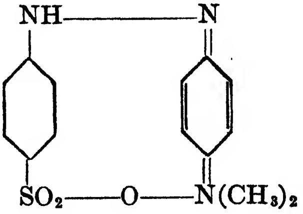
Preparation 41. Methyl Orange

This reaction is typical of those used in the chemical industry for the production of azo dyes, which go to make up a large proportion of the total production of synthetic dyestuffs. In this particular case, sulfanilic acid is diazotized and coupled with the tertiary amine, dimethylaniline, to produce methyl orange, which is not only a dye but which is also used as an indicator for acid-base titrations. The equations follow:



Methyl Orange

The yellow or alkaline form of methyl orange is the sodium salt, the formula being shown above. Addition of mineral acid converts it to the red or acid form, probably having the following structure:



When the preparation has been completed, a particle of the substance should be tested for its indicator properties by dissolving it in water, making the solution slightly alkaline, and then acidifying.

Procedure.—Twenty grams of sulfanilic acid and 5.2 g. of anhydrous sodium carbonate are dissolved in 100 cc. of boiling water and filtered, if necessary. After cooling, 7.5 g. of sodium nitrite is dissolved in the solution and it is poured, with constant stirring, into a cold solution of 20 cc. of concentrated hydrochloric acid in 100 cc. of water. After standing for 3 minutes, the solution is tested for completion of the diazotization (see page 89). If a precipitate separates at this point, it can be ignored.

The diazobenzenesulfonate prepared as described above is coupled with dimethylaniline by adding to it a solution of 11.6 g. of dimethylaniline dissolved in 25 cc. of water to which has been added 9 cc. of concentrated hydrochloric acid. The red or acid form of methyl orange begins to separate shortly. After allowing the mixture to stand for 10 minutes, it is made alkaline by the addition of enough 20 per cent sodium hydroxide solution to change the color from red to orange or yellow. It is then heated to boiling, allowed to cool, and filtered off by suction; the precipitate is washed with cold water. It is recrystallized from hot water, a little norite being used. Methyl orange, being a salt, has no well-defined melting point. The yield should be about 25 g.

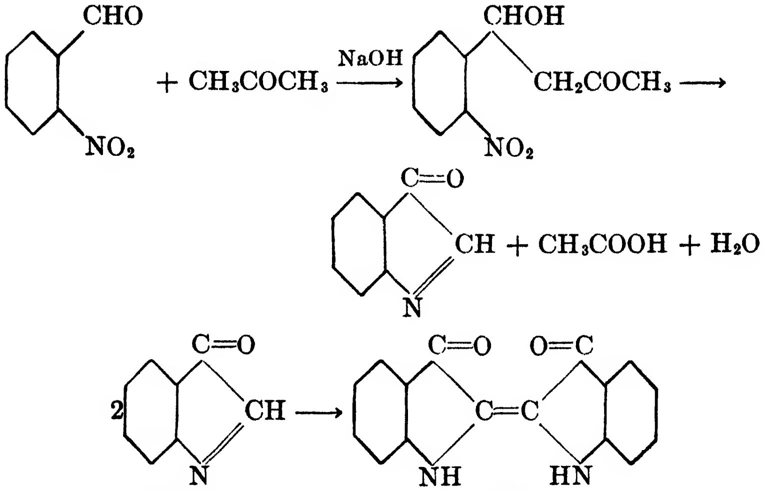
Questions

1. In connection with the precautions to be observed in the diazotization of an amine discussed on page 89, it will be noticed that the first precaution mentioned there has not been observed strictly, while the other two have. Suggest an explanation of this fact.
2. What would be the products of strong reduction of sulfanilic acid?

Preparation 42. Indigo

Indigo was one of the first and most important of the naturally occurring pigments to be synthesized on a commercial scale. At one time produced from the indigo plant in the amount of 1,500,000 pounds annually in India alone, indigo is now synthesized to the extent of about 90 per cent of the total used.

The method to be used here was the first one to be employed commercially, although it has now been superseded by methods less suitable for laboratory adaptation. Baeyer found in 1882 that *o*-nitrobenzaldehyde condenses with acetone in alkaline solution to produce a compound which decomposes spontaneously to form indigo. This series of reactions may be represented as follows:



Indolone **Indigo**

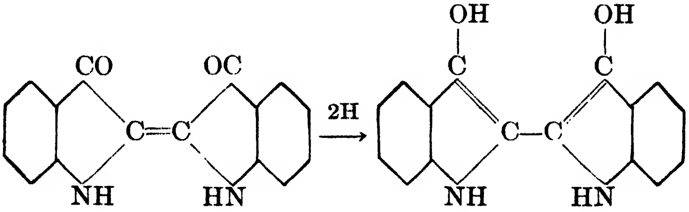
The first step is an aldol condensation, the second a spontaneous decomposition and intramolecular oxidation and reduction, and the final step a polymerization.

In the present experiment the *o*-nitrobenzaldehyde is produced by the nitration of benzaldehyde, this reaction giving approximately 20 per cent of the ortho and 80 per cent of the meta derivative. The latter compound gives a brown colored substance when treated with acetone and alkali but, of course, gives no indigo. It does not interfere, however, with the indigo-producing reaction from the small amount of ortho derivative available.

Procedure.—Twelve grams of finely powdered potassium nitrate is dissolved in 50 cc. of cold concentrated sulfuric acid contained in a 250-cc. Erlenmeyer flask. Ten grams of benzaldehyde is then added, drop by drop, while the mixture is shaken and kept cold in an ice bath. The addition of the aldehyde should require about 10 minutes. The mixture is then slowly poured onto 300 g. of ice with vigorous stirring. The crystalline nitrobenzaldehydes are filtered off on a Büchner funnel and thoroughly washed with water.

While still moist, the nitrobenzaldehydes are dissolved in 50 cc. of acetone and 50 cc. of 5 per cent sodium hydroxide solution is added quickly with stirring, followed by 50 cc. more of water. The indigo will now begin to appear as violet iridescent flakes on the surface of the brown or black liquid. After stirring occasionally for 30 minutes and diluting with another 200 cc. of ice water, the solids are filtered off on a Büchner funnel and washed with small portions of boiling acetone (**Caution!** Inflammable!) until the washings are colorless. This washing removes the *m*-nitrobenzaldehyde and its condensation products. The yield of pure indigo is about 1 g. Dissolve a small flake of the indigo in chloroform and note the deep blue color produced.

Indigo is a so-called *vat dye.* It cannot be applied directly to the material to be dyed because of its insolubility. It must first be changed into a soluble form, the "vat," which is readily changed back to the dye after impregnation of the fiber. The vat in this experiment is prepared by reducing indigo to "indigo white" with ferrous sulfate. This reduction is similar to the reduction of benzoquinone to hydroquinone, and is represented by the following equation:



Indigo white is essentially a dihydric phenol and is therefore soluble in alkali. It is readily oxidized back to indigo by atmospheric oxygen.

Experiment on the Use of Indigo as a Vat Dye.—Half a gram of indigo is refluxed for 15 minutes with a solution of 3 g. of ferrous sulfate in 50 cc. of water which has been made strongly ammoniacal. The mixture is filtered while hot and a small piece of toweling is soaked in the filtrate. After about a minute, the cloth is removed, pressed lightly between filter papers, and hung over a glass rod. After 15 minutes the precipitation of the dye is complete. The cloth can then be thoroughly rinsed with water and dried. The dyed cloth is to be turned in to the instructor with the remainder of the indigo.

Question

Balance the equations for the reduction of indigo with ferrous sulfate and the oxidation of indigo white with atmospheric oxygen.

PART II

THE IDENTIFICATION OF ORGANIC COMPOUNDS

CHAPTER IV

INTRODUCTION

It is frequently necessary in the chemical laboratory to identify a small quantity of some unknown organic compound. This is particularly true in an industrial or medical research laboratory. As the methods of procedure and the techniques employed are so different from those involved in the routine preparation of organic compounds, no course in organic chemistry laboratory is complete without the inclusion of this phase of the subject. In view of the fact, however, that at the present time there are several hundred thousand different organic compounds known, it is obvious that a scheme for their qualitative identification cannot be presented in an elementary course. All that is intended in this section is to acquaint the student with certain fundamental principles which are generally used for the identification of organic compounds and to aid in the development of the technique of handling small quantities of materials.

To this end, the exposition of a method of working, a list of between three and four hundred of the most common organic chemicals has been selected. A system for the identification of these substances has then been devised and a key constructed. Although this key involves a few new features, in the main it makes use of well known qualitative tests. If a more complete work is desired, there are several such available, the most comprehensive of which is "Identification of Pure Organic Compounds," by S. P. Mulliken.

Before undertaking the identification of a substance, one should have accurate knowledge as to its state of purity. Qualitative and particularly quantitative determinations of the elements in a compound have little significance unless the material is pure. A section below is devoted to a discussion of the most common methods for the purification of organic compounds.

Assuming that a pure substance is in hand, the first step in its identification is a qualitative determination of the elements present. Except in special cases, these tests are limited to those for carbon, nitrogen, sulfur, and the three halogens, chlorine, bromine, and iodine. Having ascertained what elements are present, a quantitative determination is always very helpful but generally not essential. It is not necessary in the key to be used in this work.

For the tentative identification of the substance, use is made of its most easily determinable physical and chemical properties. The physical properties which are most important are physical state, color, melting point, boiling point, density or specific gravity, and the solubility in various organic and inorganic solvents. The chemical properties which are most important are the reactions with acids and bases, although the behavior towards many other reagents is frequently used, depending upon the type of substance under examination.

The tentative identification having been made on the basis of the properties mentioned above, further steps must be taken before one is reasonably certain that a mistake has not been made. It seems self-evident that, because of the large number of organic compounds known, and the limited number and range of values of their properties, there may frequently be several different substances with approximately the same properties. For this reason further confirmation is desirable. There are two different methods which may be used to affirm the original identification.

The first of these, but one which is frequently inapplicable owing to unavailability of material, is the determination of the mixed melting point with an authentic sample of the substance the unknown is thought to be. The actual procedure to be followed is described on page 35.

The second method, and one of much greater applicability, is the preparation of a derivative. Most compounds permit of a transformation by some chemical means such as acylation, oxidation, reduction, or other reactions, into new substances. If a derivative prepared in some such manner has the melting point which its supposed formula would require, the chances are greatly increased that the original substance has been correctly identified. If more confirmation is still desired, other derivatives may be prepared, the probability of error decreasing as the number of derivatives increases. In general, the preparation of one derivative is deemed sufficient.

THE PURIFICATION OF UNKNOWN SUBSTANCES

Liquids.—By far the greater number of the liquid unknowns can be purified by distillation, for which purpose a 25- or 50-cc. distilling flask should be used. The exact procedure to be followed has already been described on page 32. By distilling in this fashion, it is not only possible to purify the sample, but also to determine the boiling point at the same time. This latter property is of prime importance in the later identification of the substance. If the unknown is reasonably pure, the major portion of it will distil over within a fairly narrow range, say of one or two degrees. It is advisable to heat to boiling a small sample of the unknown in a test tube to be certain that it may be distilled without decomposition, and then to run a preliminary distillation to gain an idea of the boiling range of the main portion. In this first distillation the high boiling residue can be discarded. The distillate is then returned to the flask and distillation carried on until a temperature a degree or two below the true boiling point is reached. Heating is then discontinued while the condenser is cleaned and dried. The compound can now be distilled and that portion boiling at a fairly constant temperature collected and regarded as reasonably pure.

In case the substance will not distill undecomposed at atmospheric pressure, it is advisable to attempt a vacuum distillation. A great many compounds can be distilled at a pressure of 10 to 20 mm. of mercury which will decompose when distilled at ordinary pressures. The method of procedure is the same as that described on page 17, care being taken that the small amount of material available is not wasted by contact with pieces of apparatus which are larger than necessary. When working with small quantities, a side-arm test tube makes an excellent receiver.

It so happens that some compounds will not distill undecomposed even under reduced pressure. In these cases, either one proceeds with the identification without further purification, or recourse is had to a freezing-out method. This consists in partially freezing the substance in an ice-salt bath and filtering off the solid material by suction, using very cold apparatus and working as rapidly as possible. The solid material so obtained is purer than the original or the mother liquor, and can be repurified to constant melting point in a similar manner if so desired.

Solids.—Aside from the relatively few solids with a sufficiently low boiling point to allow for their purification by distillation, this class of compounds must be purified by some manner of recrystallization. The various methods which may be used have been discussed in Chap. II.

There is one very important point in connection with the purification of unknown substances which must be constantly borne in mind. There is always a chance that the substance may be decomposed or changed into another substance during the attempted purification. This is particularly true in the recrystallization of solids. To cite a specific example, it would appear superficially that phthalic anhydride recrystallizes very nicely from water. But this is not the case, since the product of this recrystallization is phthalic acid. Such mistakes can usually be avoided by comparing the melting points of the original substance and the product of recrystallization. If a reaction has taken place there will usually be a large difference, 40° or more, in the melting points, while a simple purification by one recrystallization will rarely cause such a large change in the melting point of a substance. It is also frequently helpful to determine the melting point of a mixture of the original substance and the product of recrystallization. If no reaction has taken place, the melting point of the mixture will be intermediate between the other two.

In the recrystallization of small amounts of material, extra care must be taken that loss of material owing to contact with the apparatus is kept at a minimum. This necessitates the use of apparatus which is as small as possible, 25-cc. beakers and test tubes being very useful for this purpose. A filter paper may also be cut down to as small a size as possible, thus avoiding the loss of as much liquid as it takes to wet the paper so discarded. An ice or ice-salt bath will be found useful to increase the yield of crystals, and finally, in the separation of the crystals from the mother liquor, filtration should be done either on a small Hirsch funnel or on a filter plate.

It frequently happens that crystals fail to put in their appearance when they should, or an oil is obtained in their place. Such solutions should not be thrown away, as there are several practices which can be resorted to in order to force results. The easiest of these is to cool the solution thoroughly in an ice-salt bath, and to scratch the inside of the container with a sharp glass rod. If this procedure does not produce results after 15 minutes, another expedient is to remove the glass rod with its adhering material and carefully dry it at a safe distance above a free flame. This evaporation of the solvent will frequently leave crystals which will act as "seeds" when the rod is replaced in the solution.

Another method which can be used in the cases of ether- or benzene-soluble substances, particularly those which tend to "oil out," is to dry the ether or benzene solution of the substance with anhydrous sodium sulfate, and after decanting from the drying agent, to remove the solvent *in vacuo* at room temperature.

In general, a substance becomes easier to handle as the purity increases. In any case, do not throw away a product which fails to crystallize properly without first consulting the instructor. These remarks should also be kept in mind in connection with the preparation of derivatives.

Separation of Mixtures.—In the identification of an unknown mixture it is obviously first essential to separate the mixture and purify each of the components. It may be stated at the start that fractional distillation or fractional recrystallization should be employed only as last resorts in the separation, since they are in many cases replaceable by more effective and less tedious methods. However, if there appears to be a very volatile substance present, it may be removable by distillation on a water bath.

If a mixture contains a basic substance, such as an amine, use may be made of the property of forming salts with hydrochloric or sulfuric acid. Such salts are usually *soluble in water* and *insoluble in ether.* Similarly, acidic substances form salts with sodium or potassium hydroxides which in general are *soluble in water* and *insoluble in ether.* The problem of the separation of a water-insoluble phenol from a water-insoluble amine will illustrate the application of these facts. The mixture could be treated with dilute sulfuric acid, the amine in the form of a salt passing into the aqueous phase. The phenol could then be removed by ether extraction or filtration, if it is sufficiently insoluble. The amine could be reprecipitated from the aqueous solution by making the solution alkaline (usually with ammonia). Or the phenol could first have been removed by treatment with dilute alkali, the amine being extracted with ether.

Phenols (except nitrophenols with one or more nitro groups ortho or para to the hydroxyl group) may be separated from carboxylic or sulfonic acids by utilization of the fact that phenols are weaker acids than carbon dioxide while organic acids are stronger. Thus sodium carbonate will form sodium salts with carboxylic or sulfonic acids but will give no reaction with phenols. Similarly, phenols are displaced from their salts by carbon dioxide while other acids are not.

One of the commonest means of separation involves the use of some solvent that will dissolve one component but not the others. Water and ether are the two solvents most apt to be useful in this connection. If they are found to be ineffective in any case, the other solvents listed on page 27 should be tried.

It is obvious that preliminary tests on small samples should always be carefully performed before the main body of the mixture is risked in a procedure which may prove to be ineffective. It is also advisable to save all solutions, filtrates, and precipitates obtained in the process of separation until one can be sure they contain nothing of importance.

It is always advisable to perform elementary tests on the original mixture, and on the various fractions obtained from it. In this way it is frequently possible to judge the efficacy of the separation method employed. In all cases in which the mixture contains nitrogen the possible presence of a basic substance should be kept in mind. The determination of the convenient physical properties, such as melting points, boiling points, and specific gravities, may also be of considerable help in deciding whether a satisfactory separation is being accomplished.

The student should in every case satisfy himself that the various components isolated account for the major part of the original mixture, so that no further components may be entirely missed.

The above suggestions are not intended to serve as a complete discussion of the available methods of separation. Indeed, one of the chief values in the assignment of mixed unknowns is that the student is called upon to devise his own methods of separation rather than to follow some standard procedure.

CLASSIFICATION OF COMPOUNDS AND OUTLINE OF PROCEDURE

The organic compounds included in this qualitative analytical scheme are classified primarily according to the elements other than carbon, hydrogen, and oxygen which they contain. Each order corresponding to a particular elementary composition is further subdivided into groups containing the solid and the liquid species. These groups in Order I, which contains the greatest number of compounds, are divided according to water solubilities. This classification is outlined in the table on page 150.

Within each group the substances are further characterized by their behavior in certain prescribed "Special Tests" (page 137) and finally according to melting points or boiling points. In the rather frequent border-line cases which occur, the substances are listed in more than one place. It is always advisable for the student to perform any special tests, in addition to those specified in the key, which may help to make the identification more certain before a derivative preparation is attempted.

An actual illustration will make the use of the table of compounds more clear. Let us suppose that we have for identification an unknown solid substance. After purification by recrystallization, it is found to melt at 41° and to give negative tests for nitrogen, sulfur and halogen. It must therefore belong in Order I, Group A or B. Obviously we next need to investigate its solubility in water (Test 2, page 138); we find it to be insoluble, so that we may confine further attention to compounds in Group B.

Under Order I, Group B, we are first directed to try Test 9. In the present case we find it to be negative, so we turn to the second subdivision of this group and apply Test 15*a* as directed. We find that Test 15*a* is positive and that a purple color is obtained in the test. The only compounds, among the substances listed here as giving a positive reaction in Test 15*a*, that have melting points close to 41° are phenol and phenyl salicylate. The solubility in warm water is investigated as suggested, and the substance is found to be insoluble. The compound is thus judged to be phenyl salicylate. To confirm our results we prepare a derivative. Phenyl salicylate is an ester and is therefore considered as an acid derivative. We find on reference to the proper section in Chap. VII that several derivatives could be prepared. The substance could be saponified to give salicylic acid. Or the products of saponification could be treated to give satisfactory derivatives. The salicylic acid could be transformed to the *p*-nitrobenzyl ester, the acetate (aspirin), or the 5-nitro-derivative. The phenol could be brominated to give tribromophenol. Of these possibilities, all except the last should serve equally well to distinguish the unknown from any substances with which it might reasonably have been confused (in this case, phenol or possibly *p*-cresol), and obviously the first one offers the simplest procedure. We therefore saponify the unknown as directed on page 192, and the isolation of a product (salicylic acid), melting, after recrystallization, at 157° to 158°, gives ample confirmation to all our previous conclusions.

A similar systematic procedure should be followed in all cases. Experience has shown that mistakes are much more likely to be made if a systematic procedure is sacrificed in an attempt to save time. Usually a hit-or-miss method, relying very largely on "hunches," will result in a great waste of time because a larger number of specific tests will have to be run to disprove the various hunches.

Remarks concerning the choice and preparation of a derivative will be found on page 164.

METHOD OF RECORDING RESULTS

After the unknown has been identified and the derivative prepared and thoroughly dried, it should be turned in to the office in a small specimen tube, labeled with the number of the unknown, the name and desk number of the student, and the name and melting point of the derivative. A 3 by 5-inch card should accompany the derivative with the *name of the unknown in the upper left-hand corner* and the student's name in the upper right corner. This card should contain:

1. The observed and the known melting or boiling points of the unknown.
2. The tests performed, in the order of performance, with results and, where possible, equations.
3. The name of the derivative and the equations for its preparation.
4. The observed and known melting points of the derivative.

In addition, the student should keep his own record in his laboratory notebook, giving the following information in the order indicated:

1. Number of the unknown.
2. Name of the unknown.
3. A list of the observed and known values of all the physical properties which were determined, including all data and calculations for the determination of the neutralization equivalent, saponification equivalent, or specific gravity, if any of these properties were determined.
4. Results of all tests run, with equations wherever possible.
5. A brief summary with equations of *all* derivatives that might be prepared and reasons for the choice of the derivative actually prepared.
6. Equations for the preparation of the derivative and reasons for all important manipulative steps in the preparation.
7. A comparison of the observed values of the properties of the derivative with the true values.

In the case of unknown *mixtures*, a card containing the material outlined above for each constituent should accompany each derivative. In addition a description of the method of separation used, including equations for any reactions involved and the name and formula of each constituent, should be recorded on a separate card and turned in at the same time. All pertinent information concerning the method of separation should also be recorded in the student's laboratory notebook before the detailed points listed above.

In any case where a derivative cannot be prepared a report card should nevertheless be turned in at the completion of the analysis, and the appropriate information recorded in the student's notebook.

CHAPTER V

ANALYTICAL METHODS

A rather large number of qualitative tests, together with a few quantitative determinations, are used in the identification of organic substances. The present chapter will include descriptions of those tests and determinations which are utilized in the identification of the substances listed in Chap. VI.

QUANTITATIVE PROCEDURES

Two of the most frequently used quantitative procedures, the determination of melting and boiling points, have been described in detail in Chap. II. In the determination of the structure of a new organic substance, it is usually necessary to perform a quantitative elementary analysis. However, in the identification of a compound which has been previously described in the literature, it is very seldom necessary to resort to such analyses, so that descriptions of them have not been included. Brief discussions of the theory of these analyses may be found in most textbooks of organic chemistry, and detailed directions in many laboratory manuals.

Determination of Specific Gravity.—The density of a substance is defined as the weight in grams of 1 cc. The density varies with the temperature, so that in accurate work it is necessary to specify the temperature at which the density was determined. The specific gravity of liquids is defined as the ratio of the weight of 1 cc. of a substance at a specified temperature to the weight of the same volume of water at the same or a different temperature. The specific gravity is also a function of the temperature. Since, by definition, 1 g. of water at 4° occupies 1 cc., it follows that the density is numerically equal to the *specific gravity referred to water at* 4°. The symbol frequently used for these two quantities is:

$$d^{t_1}_{t_2}\ (i.e.,\ d^{24}_{4})$$

where t_1 is the temperature of the sample of substance measured and t_2 is that of the water to which the measurement is referred. Thus in any case where $t_2 = 4°$, the quantity given is a *density;* otherwise it is a specific gravity. For the present purposes it will be unnecessary to make the determinations at carefully controlled temperatures.

The specific gravity is determined with sufficient accuracy in the following manner: A tightly corked specimen bottle is weighed to the nearest centigram on an analytical balance. Five cubic centimeters of substance, measured with a clean, dry pipette, is introduced and the tube weighed again. The determination should have an accuracy of about 1 per cent. It may be advisable to check the pipette used by weighing 5 cc. of water.

Determination of Neutralization Equivalent.—The neutralization equivalent, or equivalent weight, of an acid or of a substance which readily yields an acid, is determined by titrating a weighed sample with a standardized solution of alkali. The neutralization equivalent is equal to the number of grams of acid required to neutralize 1 l. of normal alkali.

A sample of acid (0.2 to 0.5 g.) is weighed on an analytical balance to the nearest milligram and is dissolved in 50 cc. of freshly boiled water (or in pure alcohol, if it is insoluble in water) contained in a 250-cc. Erlenmeyer flask. The solution is titrated with 0.2N sodium hydroxide, phenolphthalein being used as indicator. The sample of acid taken should be large enough to require at least 20 cc. of alkali.

Insoluble acids can frequently be titrated in aqueous suspension, if they are finely divided and if the titration is performed slowly enough. If alcohol is used as solvent, it is advisable to titrate 50 cc. of the alcohol alone and to subtract the volume of alkali used from the volume required in the titration of the acid, since the alcohol may contain small amounts of organic or inorganic acids.

Determination of Saponification Equivalent.—The saponification equivalent of an ester or similar substance is defined as the number of grams of the substance saponified by 1 l. of normal alkali. This quantity is thus equal to the equivalent weight.

A sample of substance (0.2 to 0.5 g.) is weighed on an analytical balance to the nearest milligram. Great care to avoid loss by vaporization must be exercised in the accurate weighing of volatile materials. The sample is boiled in a Pyrex test tube under a reflux condenser for 30 minutes with 10 cc. (accurately measured) of 0.5N alcoholic potassium hydroxide. The potash solution need not be previously standardized. The mixture is transferred quantitatively to an Erlenmeyer flask, and the excess alkali is titrated with 0.2N (standardized) acid, phenolphthalein being used as indicator.

The alcoholic potash is standardized, and any necessary "blank" corrections are included, by titration of a 10-cc. sample of the potash which is measured from the same pipette as used above, and which is subjected to the same refluxing treatment.

"Saponification numbers" in place of saponification equivalents are frequently used in recording the results of a quantitative saponification. The saponification number of a substance is defined as the number of milligrams of *potassium hydroxide* required to completely saponify 1 g. of the substance.

Problems

1. List the types of substances which would behave in the same manner (1) as acids in the determination of the neutralization equivalent; (2) as esters in the determination of the saponification equivalent.

2. In the titration of a certain organic acid, 0.263 g. of the acid required 20.1 cc. of 0.211N sodium hydroxide. Calculate the neutralization equivalent. If the acid is monobasic what is its structure?

3. The following data were obtained in the determination of the saponification equivalent of a certain ester: 0.256 g. of substance was refluxed with 10.0 cc. of alcoholic potash. The excess potash required 7.1 cc. of 0.198N sulfuric acid. In the blank run, 10.00 cc. of the potash required 24.6 cc. of the same acid. Elementary tests for elements other than C, H and O were negative. Calculate the saponification equivalent, and give a possible structure for the substance.

4. Calculate the neutralization equivalents of each of the following substances: Phthalic acid, butyryl chloride, succinic anhydride. How many cubic centimeters of 0.200N barium hydroxide would be required in the titration of 0.500 g. of each substance?

5. Calculate the saponification equivalent and saponification number of each of the following substances: Potassium ethyl phthalate; ethyl acid succinate; ethyl acetoacetate. In the last case, is the amount of alkali needed dependent on the type of hydrolysis?

6. Change the following specific gravities to densities at the indicated temperatures: 1.0848^{18}_{0}; 1.1129^{15}_{15}; 1.0397^{35}_{35}. How many grams of water occupy 15 cc. at 65°? Necessary data can be found in a chemical handbook.

7. Deduce general formulae for the following: (*a*) The number of carboxyl groups in an acid in terms of the neutralization equivalent and the molecular weight; (*b*) the number of ester groups in an ester in terms of the saponification equivalent and the molecular weight; (*c*) the calculation of the saponification *number* when only the saponification *equivalent* is given.

ELEMENTARY TESTS

Organic compounds may be very conveniently separated into several orders, according to the elements they contain. Since this information is readily obtained by a few simple qualitative tests, the first step in the identification of a pure organic substance is always a qualitative elementary analysis. The importance of this analysis cannot be too strongly emphasized, since all the subsequent tests performed in an attempt to identify a substance may be of no value if the elementary tests have not been correctly performed. It is advisable for the student to perform the tests described below on known substances before attempting unknowns, since some practice is usually necessary, particularly in the performance of the sodium fusion. *Distilled water is to be used throughout in these tests.* All apparatus used should be rinsed with distilled water after being cleaned.

In the qualitative analysis of inorganic substances, a rather involved series of elementary tests is necessary because of the wide variety of elements which may be present. This is not the case with organic substances, since the vast majority contain no elements other than carbon, hydrogen, oxygen, halogen, nitrogen, and sulfur. On the other hand, tests for elements and ions are usually sufficient to identify an inorganic substance, while the identification of organic substances involves not only such tests but also determinations of physical properties and tests for *groups*, and in many cases tests of a highly specific nature.

There are no simple tests for the presence of hydrogen and oxygen in organic compounds, so that these elements are not included in the classification of substances for purposes of qualitative identification.

Test for Carbon.—One-tenth of a gram of the substance is heated in a small porcelain crucible. If the substance inflames and burns away, or chars, giving a black mass which disappears on strong ignition, it is in all probability organic. The presence or absence of an inorganic residue after ignition should be noted.

If charring does not occur, 0.1 g. of the substance is mixed with 3 g. of powdered cupric oxide and the mixture heated to redness in a glass tube sealed at one end, the resultant gases being led into limewater. Since all organic compounds give carbon dioxide under these conditions, a precipitate of calcium carbonate indicates carbon.

Fusion with Sodium.—A cube of clean sodium of edge about 4 mm. is heated in a 12- by 100-mm. soft-glass test tube until it melts and begins to vaporize. Five-hundredths of a gram of substance is added (**Caution!**) so that it falls directly upon the sodium without hitting the wall of the tube. After the first violent reaction has subsided, the tube is heated to dull redness for a few moments and is then allowed to cool to room temperature. The end of the tube is placed under 20 cc. of water contained in a mortar and broken off with a pestle. (**Caution!** Any sodium left in the tube may cause a slight explosion on reaction with the water, so that *care should be taken to protect the eyes.*) After the reaction has ceased, any solid material is ground up and the mixture is filtered. The filtrate, which should be colorless, is used in the tests described below.

Under the conditions of the sodium fusion, the halogen in organic substances becomes sodium halide, the nitrogen becomes sodium cyanide (or occasionally sodium cyanamide or, if sulfur is present, sodium thiocyanate), and the sulfur is changed to sodium sulfide. These inorganic ions are readily detected by the usual tests.

Tests for Nitrogen.—To 5 cc. of the filtrate from the sodium fusion 10 drops of a saturated solution of ferrous sulfate is added and the mixture is heated to boiling. After cooling, the mixture is acidified with dilute sulfuric acid. The dirty greenish precipitate of ferrous and ferric hydroxides dissolves and, if nitrogen is present, a blue or green solution or a blue precipitate remains. This test should not be considered negative until it has stood for at least 15 minutes. In some cases, if sulfur is also present, a red color is observed after the acidification, due to the presence of ferric thiocyanate, $Fe(SCN)_3$.

In case a negative test is obtained by the above procedure, a test for nitrogen in the form of sodium cyanamide should be performed. Three cubic centimeters of the original filtrate is made just acid with dilute nitric acid and the solution is boiled down to one-half volume. It is then made alkaline with ammonium hydroxide and a few drops of silver nitrate solution is added. A yellow precipitate of silver cyanamide, Ag_2CN_2, insoluble in ammonia but soluble in nitric acid, indicates the presence of nitrogen. It should be stated that a positive cyanamide test is obtained only relatively rarely; if nitrogen is present it nearly always appears as cyanide or thiocyanate.

In the test for nitrogen the following reactions occur:

$$FeSO_4 + 2NaOH \longrightarrow Fe(OH)_2 + Na_2SO_4$$
$$Fe(OH)_2 + 6NaCN \longrightarrow Na_4Fe(CN)_6 + 2NaOH$$

Part of the ferrous hydroxide is oxidized by the air during the boiling:

$$4Fe(OH)_2 + O_2 + 2H_2O \longrightarrow 4Fe(OH)_3$$

On acidification, the excess ferrous and ferric hydroxides are redissolved, and the ferrocyanide reacts with ferric ions to give Prussian blue:

$$2Fe_2(SO_4)_3 + 3Na_4Fe(CN)_6 \longrightarrow Fe_4[Fe(CN)_6]_3 + 6Na_2SO_4$$

The Prussian blue is sometimes produced in the form of a colloidal suspension. If sodium thiocyanate is present, the deep red solution of the corresponding undissociated ferric salt will be observed after acidification:

$$Fe_2(SO_4)_3 + 6NaSCN \longrightarrow 2Fe(SCN)_3 + 3Na_2SO_4$$

Sodium cyanamide will not form ferrocyanide with ferrous hydroxide. The presence of this substance can be detected by its formation, with silver nitrate, of the insoluble silver cyanamide, Ag_2CN_2, which in turn may be distinguished from the silver halides by its solubility in nitric acid. Before testing for sodium cyanamide, it is necessary to remove sulfide ions by boiling the acidified solution.

Tests for Halogens.—Two cubic centimeters of the filtrate from the sodium fusion is acidified with dilute sulfuric acid and boiled for several minutes to expel hydrogen cyanide and hydrogen sulfide. The formation of a precipitate upon the addition of a few drops of aqueous silver nitrate solution indicates the presence of halogen. (A *very slight* precipitate of silver chloride may result from impurities in reagents or contamination of the glassware used.) If the precipitate is white and readily soluble in ammonium hydroxide, it is probably silver chloride. If it is yellowish and difficultly soluble in ammonium hydroxide, it is probably silver bromide or iodide or a mixture of the two. However, it is unsafe to base a final decision as to which halogen is present on these observations.

The halogen is identified as follows: Five cubic centimeters of the original filtrate is acidified with dilute sulfuric acid, and 1 cc. of carbon tetrachloride and 1 drop of chlorine water are added. After thorough shaking, the liquid layers are allowed to separate and the color of the lower layer is observed. If this layer is colored violet, iodine is present; an orange-brown color indicates bromine. (If the chlorine water is not very fresh, no color due to bromine will be observed until after several cubic centimeters of chlorine water has been added.) In case iodine is present, the dropwise addition of chlorine water, with thorough shaking, is continued until the violet color disappears. If a red or brown color remains, or is produced on further addition of chlorine water, bromine is also present.

The partial distinction between chlorine, bromine, and iodine depends on the difference in ease of oxidation of the corresponding ions. The following reactions are involved:

$$2HI + Cl_2 \longrightarrow I_2 + 2HCl \qquad 2HBr + Cl_2 \longrightarrow Br_2 + 2HCl$$

The carbon tetrachloride extracts the halogen from the aqueous phase, making it more readily observable. Further addition of chlorine water oxidizes the iodine to colorless iodate, without affecting the bromine, the characteristic color of which can then be observed:

$$I_2 + 5Cl_2 + 6H_2O \longrightarrow 2HIO_3 + 10HCl$$

Obviously, if halogen is present, and no change is observed after the first addition of chlorine water, the halogen present is chlorine. This test cannot detect chlorine in the presence of bromine or iodine.

The presence of halogen may be confirmed by the Beilstein test: A copper wire is heated in a Bunsen flame until the flame is no longer colored green. The wire is then cooled and dipped into the substance to be tested. When the wire is replaced in the flame, the production of a blue or green color, which may be only a momentary flash, indicates halogen. This test depends on the fact that the copper halides are comparatively volatile and impart a characteristic blue or green color to a Bunsen flame. The film of CuO on a copper wire which has been heated in a flame oxidizes the organic halide with the formation of copper halide, in the course of this test.

Test for Sulfur.—Two cubic centimeters of the filtrate from the sodium fusion is acidified with dilute nitric acid and 2 or 3 drops of lead acetate solution is added. A black or brown precipitate of lead sulfide indicates the presence of sulfur:

$$H_2S + (CH_3COO)_2Pb \longrightarrow PbS + 2CH_3CO\text{[illegible]}$$

The presence of sulfur is confirmed by adding 2 or 3 drops of the original filtrate to 5 cc. of a freshly prepared solution of sodium nitroprusside, $Na_2[Fe(CN)_5NO]$. A violet coloration, sometimes of short duration, is produced if sulfide ions are present.

SPECIAL TESTS

For purposes of qualitative identification, it is by no means sufficient to classify organic compounds according to the elements they contain. The special tests described in the following pages serve as a basis for the further subdivision of the [illegible] classes or orders of organic compounds which are defi[illegible] by elementary composition. It is evident that this extension of the classification could be based on an entirely different set of tests, and indeed such is the case in some schemes of qualitative organic analysis. Included in the special tests are a few tests of rather specific nature which are used to distinguish between substances which are in other respects quite similar.

The special tests are numbered, and are [illegible]ed to by number in the lists of compounds in Chap. VI. There is no need for the student to practice these tests before making actual use of them in analyses. It is sometimes helpful, however, to try a test on a known substance if some doubt arises in connection with its application to an unknown.

In performing the special tests it is essential that the directions be followed in all details. This is particularly true in connection with the amounts of materials used. Some of the tests, for example, the second one, are arbitrarily defined, and their application has no significance unless they are very carefully performed.

1. Test for Inorganic Residue.—About 0.1 g. of substance is strongly ignited in a small crucible. A residue after ignition indicates the presence of a metallic element. The residue is extracted with a little water and the solution tested with litmus. An alkaline reaction generally indicates Na or K. Organic compounds are almost without exception decomposed by strong ignition. If the original substance contained an alkali metal, part of the residue after ignition will usually be an alkali carbonate. [illegible] in this test the substance volatilizes without decomposing, it may be assumed that it contains no metallic element.

2. Solubility in Water.—One-tenth of a gram of substance, weighed to the nearest centigram (if liquid, 2 drops), is treated with 3 cc. of water and the mixture is shaken well. If the substance dissolves completely it is designated as soluble in water. Solid substances must be finely pulverized for this test. If the substance appears to be insoluble, the mixture may be warmed *gently* for a minute and then *cooled thoroughly with shaking.* If there still remains some undissolved material, the substance is "insoluble in water." Any border-line compounds are listed both as soluble and as insoluble.

3. Test for Solubility in Hydrochloric Acid.—One-tenth of a gram of substance (in the case of liquids, 2 drops) is suspended in 3 cc. of water and a 10 per cent solution of hydrochloric acid is added, 1 drop at a time with shaking, until 20 drops have been added. An excess of acid is to be avoided as certain bases form hydrochlorides which are insoluble in an excess of acid. Solution of the substance at any time during or after the addition of the acid is regarded as a positive test. The hydrochloric acid can be added directly to the test tube in which the test for water solubility was performed. This test depends on the fact that the hydrochloride of an amine is generally much more soluble than the free base.

4. Test for Solubility in Sodium Hydroxide.—One-tenth of a gram of substance (in the case of liquids, 2 drops) is suspended in 3 cc. of water, and a 5 per cent solution of sodium hydroxide is added drop by drop until 2 cc. have been added. Solution of the substance at any time during or after the addition of the alkali is a positive test. Many organic compounds, chiefly acids and phenols, form sodium salts which are more soluble than the original substances. In some cases the salts are comparatively insoluble in the presence of an excess of alkali, so that care must be taken not to add too much.

5. Solubility in Concentrated Sulfuric Acid.—To 0.2 g. of substance is added *cautiously* 3 or 4 cc. of concentrated sulfuric acid. If no reaction is evident, the mixture is shaken thoroughly. It is carefully observed whether the material has dissolved or not. If it has dissolved, the solution is poured onto about 10 g. of ice and the presence or absence of two phases (after the ice has melted) is again observed. A substance that is itself soluble in sulfuric acid is classed as insoluble if it reacts with this reagent to form another substance which is insoluble in the concentrated acid.

Most compounds containing oxygen are soluble in concentrated sulfuric acid, although there are a few exceptions to this rule. Furthermore, certain readily sulfonated aromatic hydrocarbons, such as *m*-xylene, are soluble, owing to the formation of a soluble sulfonic acid. Many of the oxygen compounds, notably aliphatic ethers, are stable toward concentrated sulfuric acid and therefore are reprecipitated unchanged on dilution of the acid, provided they are insoluble in water. On the other hand, in cases where sulfonation or other reactions leading to the formation of water-soluble compounds have been effected by the concentrated acid, dilution of the latter will not cause reprecipitation. Phenols and their ethers and some aromatic hydrocarbons behave in this way.

6. von Baeyer's Test.—*a.* One-tenth of a gram of substance is dissolved or suspended in 5 cc. of 5 per cent sodium carbonate solution and a 2 per cent solution of potassium permanganate is added drop by drop. Decolorization of the permanganate, with the formation of a brown precipitate or a brown or green solution, is a positive reaction.

b. The procedure in (*a*) is followed except that the mixture is heated to gentle boiling after the addition of 5 drops of the permanganate solution.

Alkaline permanganate is a strong oxidizing agent. It will in general attack unsaturated compounds, alcohols, aldehydes, etc. In some cases reaction does not take place unless the mixture is heated. In alkaline solution the permanganate is reduced to manganese dioxide, or in some cases to manganate (green color).

7. Bromine-water Test.—A mixture of 0.1 g. of substance and 10 cc. of bromine water is heated to boiling. The test tube is then stoppered lightly and set aside. A positive reaction is indicated by disappearance of the bromine color within 5 *minutes.* This test is not specific for any particular class of compounds. Many easily oxidized or readily halogenated substances will decolorize the bromine water within the specified time.

8. Test with a Carbon Tetrachloride Solution of Bromine.—One-tenth of a gram of substance is dissolved or suspended in 2 cc. of chloroform, 5 drops of a 5 per cent solution of bromine in carbon tetrachloride is added, and the mixture is well shaken. A "blank" is prepared by adding the same amount of bromine solution to 2 cc. of chloroform. Addition or substitution of bromine is indicated if the test solution is distinctly lighter than the blank after 5 *minutes.*

A very great variety of organic compounds react with bromine. Since the rates of reaction vary between wide limits, it is necessary for the purposes of a qualitative test to arbitrarily define what is to be considered as a positive reaction. Thus fumaric acid, which contains a double bond and will therefore add bromine, is nevertheless classed with substances that do not react with this reagent because the reaction is comparatively slow. Similarly, many aromatic hydrocarbons are substituted by bromine but so slowly in the absence of catalysts that no decolorization of the bromine solution is observable under the specified conditions.

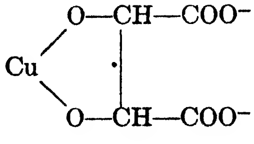
9. Test for Acids.—Two-tenths of a gram of substance is dissolved in water and several drops of a saturated solution of sodium bicarbonate is added. If the substance is insoluble in water, it is dissolved in 2 cc. of alcohol and diluted with an equal volume of water before the addition of the bicarbonate. Evolution of carbon dioxide is the criterion of a positive reaction. *Observations should be carefully made.* In case alcohol is used as the solvent in this test, no attention is to be paid to the formation of a precipitate on the addition of the sodium bicarbonate. This precipitate is crystalline sodium bicarbonate which is relatively insoluble in alcohol.

Several classes of compounds other than acids will cause evolution of carbon dioxide in this test. Any substance that is hydrolyzed under the conditions of the test to give an acid stronger than carbonic acid will react positively, for example, many acid anhydrides, acid chlorides, etc. Most phenols are too weakly acidic to displace carbonic acid from its salts.

10. Fehling's Test. *a.* Five-hundredths of a gram of substance is dissolved or suspended in 5 cc. of water; this is treated with 5 drops each of Fehling's solutions A and B, and the mixture is boiled for 1 minute. Formation of a colored precipitate is a positive reaction.

b. Before the addition of the Fehling's solutions the mixture is boiled for 2 minutes with 1 drop of concentrated hydrochloric acid and then neutralized with dilute sodium hydroxide. The test is then carried out as in (*a*).

Fehling's test is positive for certain easily oxidized substances. Fehling's solution A is an aqueous solution of cupric sulfate; the B solution contains sodium hydroxide and sodium tartrate. When the two solutions are mixed a complex ion containing the copper is formed which prevents the precipitation of cupric hydroxide. The complex ion probably has the following structure:



Fehling's solution is thus essentially an alkaline solution of cupric copper. It is reduced with the formation of insoluble cuprous oxide by easily oxidized substances such as aliphatic aldehydes, many sugars, hydrazines, etc.

Some compounds, such as sucrose, do not reduce Fehling's solution, but are readily hydrolyzed by dilute acid to give products which do. In the case of sucrose, these products are *d*-glucose and *d*-fructose.

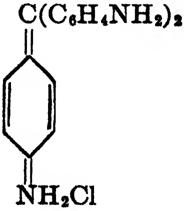
11. Test with Tollen's Reagent.—To 5 cc. of 1 per cent silver nitrate solution is added 1 drop of 10 per cent sodium hydroxide solution and then dilute ammonium hydroxide (1:1) until the precipitate just dissolves. To this solution 0.1 g. of substance is added, and the mixture is shaken and set aside. The formation of a silver mirror on the wall of the test tube (or a precipitate, if the tube is dirty) indicates the presence of an easily oxidizable substance. The test mixture is not to be heated or allowed to stand for a long time since explosive compounds may be formed.

An ammoniacal silver solution is a mild oxidizing agent. It is reduced, with the formation of a silver mirror, by aldehydes, by sugars containing a free aldehyde or ketone group, and by certain other individual substances. Simple ketones are not affected by the reagent.

Silver oxide in the presence of ammonia and organic matter may yield the highly explosive silver fulminate, AgO·N:C, so that the test mixture should not be heated or allowed to stand longer than necessary.

12. Schiff's Test for Aldehydes.—Two drops of substance is added to 5 cc. of Schiff's reagent. If the substance is insoluble, the mixture is well shaken. Aldehydes cause the formation of a red to violet color.

Schiff's reagent is composed of a solution of the violet dye fuchsin which has been decolorized by addition of sulfurous acid. The probable structure of fuchsin is similar to that of para fuchsin:



In fuchsin one of the three rings contains a methyl group in the position meta to the methane carbon atom of para fuchsin. Fuchsin forms a colorless addition compound with sulfurous acid, which reacts with free aldehydes to form dyes of complicated structure.

It is important to bear in mind that prolonged shaking of Schiff's reagent in the presence of atmospheric oxygen, even in the absence of aldehydes, will give a faint coloration as a result of the loss of sulfurous acid from the solution.

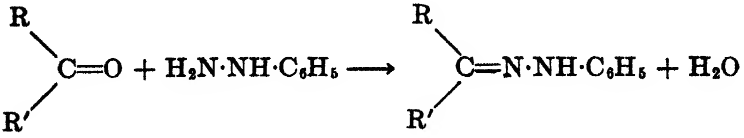
13. Test for Hydroxyl and Amine Groups.—To 0.3 g. of substance in a *dry* test tube is added 0.3 cc. of acetyl chloride. (**Caution! Hood!** Some substances react with acetyl chloride with almost explosive violence. Protect the eyes!) If two layers form, the mixture is shaken well. A very definite rise in the temperature of the contents of the tube within a minute or two indicates the presence of a compound containing hydroxyl or amine groups. It should be borne in mind that any substance containing an appreciable amount of water will appear to react positively in this test.

Compounds containing phenolic or alcoholic hydroxyl groups or amine groups react exothermically with acetyl chloride:

$$ROH + CH_3COCl \longrightarrow CH_3COOR + HCl$$

With a large number of such substances the reaction is rapid enough so that a rise of temperature can be readily observed. It is necessary to be cautious in performing this test because the reaction in some cases is vigorous enough to cause violent, sometimes almost explosive, ebullition.

14. Test for Carbonyl Groups.—Half a cubic centimeter of phenylhydrazine is mixed with an equal amount of the substance to be tested. A noticeable rise in the temperature of the mixture is to be considered as a positive test. Phenylhydrazine reacts with compounds containing the carbonyl group to form phenylhydrazones:



$$\begin{matrix}R\\ & \diagdown\\ & & C{=}O\\ & \diagup\\ R'\end{matrix} + H_2N{\cdot}NH{\cdot}C_6H_5 \longrightarrow \begin{matrix}R\\ & \diagdown\\ & & C{=}N{\cdot}NH{\cdot}C_6H_5\\ & \diagup\\ R'\end{matrix} + H_2O$$

In many cases the reaction proceeds rapidly enough so that a noticeable rise in temperature results.

15. Ferric Chloride Test.—*a.* One-tenth of a gram of substance is dissolved in water (or in alcohol if it is insoluble in water) and 3 drops of a 2½ per cent solution of ferric chloride is added. Distinct coloration, not mere intensification of the yellow ferric chloride color, is to be regarded as a positive test.

b. Some substances give a more intense coloration if 1 cc. of 5 per cent sodium carbonate solution is added before the ferric chloride.

Most phenols and many other compounds containing hydroxyl groups give more or less intense colorations with ferric chloride.

16. Iodoform Test.—To a solution of 0.2 g. of substance in 3 cc. of water is added 6 drops of 10 per cent sodium hydroxide solution and then, drop by drop with continuous shaking, a solution of iodine in potassium iodide is added until a faint yellow color persists. One cubic centimeter more of 10 per cent sodium hydroxide is then added. If no precipitate is formed within 2 minutes, the mixture is heated to 60° for 1 minute, more iodine being added if necessary, and is then allowed to stand for 2 minutes longer. The formation of a yellow precipitate of iodoform (M.P. 119°, characteristic odor) is a positive test.

Any substance having the formula $CH_3{\cdot}COR$ or $CH_3{\cdot}CHOHR$, where R is hydrogen or a carbon with any substitution whatsoever, will yield iodoform under the conditions of this test. If the $CH_3{\cdot}CHOH—$ group is present, the first step is oxidation to $CH_3{\cdot}CO—$:

$$CH_3{\cdot}CHOHR + NaOI \longrightarrow CH_3{\cdot}COR + NaI + H_2O$$

The methyl group of the $CH_3{\cdot}CO—$ is then completely iodinated:

$$CH_3{\cdot}COR + 3NaOI \longrightarrow CI_3{\cdot}COR + 3NaOH$$

Finally, the compound is hydrolyzed by the alkali to give iodoform:

$$CI_3{\cdot}COR + NaOH \longrightarrow CHI_3 + R{\cdot}COONa$$

The R group may also be more or less iodinated or oxidized in the test.

17. Carbylamine Test.—Five-hundredths of a gram of substance is treated with 5 cc. of 10 per cent sodium hydroxide and several drops of chloroform, and the mixture is warmed with *vigorous* shaking (**Hood!**). A positive reaction is indicated by the characteristic stench of the carbylamines.

In this test primary amines are converted to isocyanides (carbylamines):

$$RNH_2 + CHCl_3 + 3NaOH \longrightarrow R{\cdot}N{:}C + 3NaCl + 3H_2O$$

Some amines react slowly. In these cases some care has to be exercised to obtain the proper result.

Certain compounds which yield chloroform on alkaline hydrolysis, such as chloral and trichloroacetic acid, also give carbylamines with primary amines. Traces of carbylamines are formed with a few other halides, as for example, carbon tetrachloride.

18. Test for the —CONH₂ Group.—Two-tenths of a gram of substance is heated to boiling with 5 cc. of 10 per cent sodium hydroxide. The vapors are tested with moistened red litmus paper. Care must be taken to prevent spattering of the solution on the test paper. In some cases the odor of ammonia is apparent. Amides are hydrolyzed by hot alkali:

$$RCONH_2 + NaOH \longrightarrow RCOONa + NH_3$$

Substituted amides that yield on hydrolysis aliphatic amines of low molecular weight will also react positively in this test, since such amines are volatile and are strong enough bases to change the color of litmus paper.

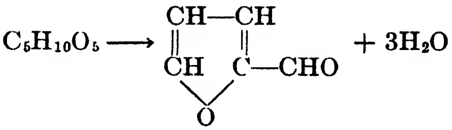
19. Action of Alkali on Amine Salts.—One-half gram of the salt is dissolved in 5 cc. of water with heating if necessary, 2 cc. of 10 per cent sodium hydroxide is added, and the mixture is cooled. The strong inorganic base displaces the weaker organic base from its salt.

$$RNH_2{\cdot}HCl + NaOH \longrightarrow RNH_2 + NaCl + H_2O$$

If the base is insoluble, it is to be noted whether it is liquid or solid. If it is soluble in the sodium hydroxide, the solution is heated to boiling and the vapors are tested with moistened litmus paper to determine whether the base is volatile with steam.

20. Color Test for Pentoses.—Ten milligrams (*not more*) of substance is added to 3 cc. of the orcinol reagent, and the mixture is quickly heated to boiling. The color changes from a light green to red and finally to violet, a violet precipitate being obtained. Hexoses may produce a yellow to deep orange color, but this is not to be regarded as a positive test.

The orcinol reagent is a solution of orcinol (3,5-dihydroxytoluene) in 20 per cent hydrochloric acid. When pentoses are heated with mineral acids they lose three molecules of water to form furfural:



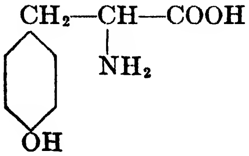
The furfural formed condenses with orcinol to form a dye which gives the coloration in this test. Similar color reactions are obtained with other polyhydric phenols such as resorcinol or phloroglucinol (symmetrical trihydroxybenzene).

21. Seliwanoff's Reaction for Ketoses.—One crystal of the substance to be tested is boiled with 5 cc. of a 1 per cent solution of resorcinol in 20 per cent hydrochloric acid. The production of a deep red solution indicates a keto-sugar, either mono- or polysaccharide. The concentrated acid decomposes the keto-sugar with the formation of hydroxymethylfurfural, which condenses with the resorcinol to produce a red dye. Compare with Test 20.

22. Biuret Test.—One-tenth of a gram of substance is dissolved or suspended in 5 cc. of 10 per cent sodium hydroxide and 1 drop of 1 per cent cupric sulfate is added. A pink to purple solution or precipitate is considered a positive reaction.

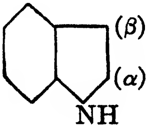
This test is given by any compound having at least two amide groups, one of which must be unsubstituted, and each of which must be attached to a different carbon atom. This includes all proteins and many other substances. The color is due to a complex organic derivative of copper, and in general varies from pink to purple as the organic molecule becomes larger.

23. Millon's Test.—To 5 cc. of Millon's reagent is added 0.05 g. of the substance to be tested. The tube containing the mixture is placed in a beaker of cold water and the water is heated to boiling. The formation of a pink to red solution or precipitate is a positive reaction. This test is not given in the presence of appreciable amounts of chlorides. Millon's reagent, made by dissolving mercury in concentrated nitric acid and then diluting, contains a mixture of mercurous and mercuric nitrite and nitrate. It gives a positive reaction with any monohydric phenol containing a free ortho position. The actual nature of the colored material produced is not well understood. As practically all proteins contain the amino acid tyrosine

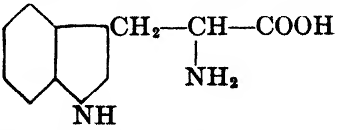


they give a positive reaction to this test.

24. Hopkins-Cole Reaction.—To 3 cc. of a dilute solution of the substance to be tested is added an equal volume of Hopkins-Cole reagent and the mixture is shaken. The tube is inclined at an angle of 45° and 5 cc. of concentrated sulfuric acid is poured carefully down the side of the tube in such a way that it forms a layer under the test solution. A violet or pink color at the zone of contact of the two layers indicates the presence of the indole ring,



Hopkins-Cole reagent is a solution of glyoxalic acid, CHOCOOH. Under the conditions of the test, indoles with a free alpha position will condense with an aldehyde with the formation of a colored product. Most proteins give a positive reaction due to the presence in the molecule of the amino acid tryptophane,



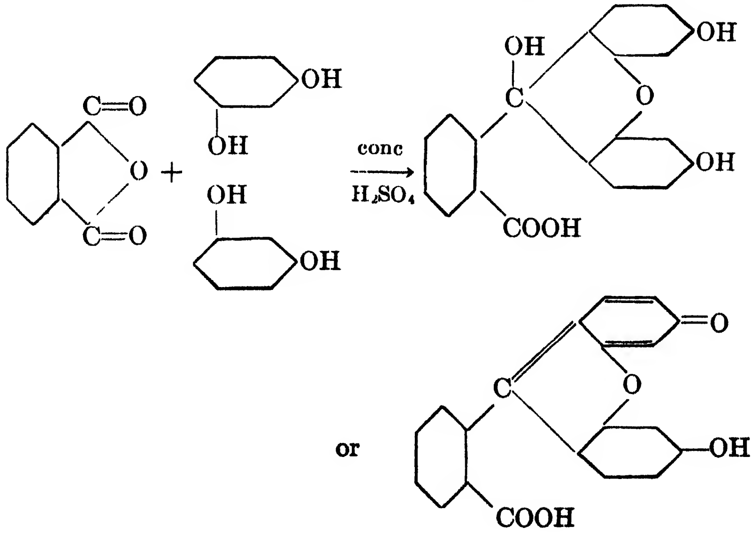
25. Test for Formic Esters.—Half a cubic centimeter of the ester and 3 cc. of 10 per cent sodium hydroxide are heated to 100° for 10 minutes. The solution is cooled, made just acid with dilute hydrochloric acid, and, after treatment with 3 cc. of a 5 per cent mercuric chloride solution, is heated to boiling. The formation of a precipitate of mercurous chloride indicates the original presence of an ester of formic acid or certain other easily oxidized substances. In the case of a formate, the treatment with alkali saponifies the ester, and the resulting formic acid is oxidized by the mercuric chloride:

$$HCOOH + 2HgCl_2 \longrightarrow Hg_2Cl_2 + CO_2 + 2HCl$$

26. Color Reaction for Tartaric Acid.—One-tenth of a gram of substance dissolved in 5 cc. of water is treated with a crystal of ferrous ammonium sulfate, a few drops of 3 per cent hydrogen peroxide solution, and 1 cc. of 10 per cent sodium hydroxide. Tartaric acid gives a very deep violet color. Citric, malic, oxalic, and succinic acids do not give the reaction. The color is due to a complex derivative of iron.

27. Fluorescein Test.—A mixture of 0.05 g. of powdered phthalic anhydride (or phthalic acid), 0.05 g. of resorcinol, and 1 drop of concentrated sulfuric acid is heated in an oil bath to 150° for 5 minutes. The mixture is then cooled, 2 cc. of 10 per cent sodium hydroxide is added, and the solution is poured into 250 cc. of cold water. An intense yellow-green fluorescence is produced.

The product of this test is the phthalein dye fluorescein:



The "quinoid" formula (the lower one) is probably correct because the substance is colored. Certain other dibasic acids, such as malic and maleic, will function in place of the phthalic anhydride to produce "phthalein" dyes which show the same fluorescence.

28. Color Reaction for Benzidine.—Five cubic centimeters of a saturated aqueous solution of benzidine is treated with 5 cc. of a solution of 1 drop of bromine water in 20 cc. of water. An intense bluish green color is produced, due to a dye formed by oxidation of the benzidine.

29. Murexide Formation.—A mixture of 0.05 g. of uric acid and 0.5 cc. of concentrated nitric acid is evaporated to dryness. Addition of ammonia to the residue produces a reddish purple compound, murexide. The nitric acid oxidizes the uric acid to substances that react with ammonia to form murexide. Murexide is the ammonium salt of a complicated heterocyclic acid.

30. Color Test for Thiourea.—One-tenth of a gram of thiourea is heated to fusion. After being cooled, the residue is extracted with 10 cc. of water and the aqueous solution is treated with 1 drop of ferric chloride solution. Formation of the blood-red ferric thiocyanate is a positive test for thiourea. At an elevated temperature equilibrium is established between thiourea and ammonium thiocyanate:

$$NH_2CSNH_2 \rightleftarrows NH_4\cdot SCN$$

This equilibrium is analogous to that existing between urea and ammonium cyanate:

$$NH_2CONH_2 \rightleftarrows NH_4\cdot OCN$$

CHAPTER VI

CLASSIFIED LIST OF COMPOUNDS

ORDINAL AND GROUP CLASSIFICATION

Order I. Compounds containing no nitrogen, sulfur, or halogen.	
Solid and water soluble	Group A
Solid and water insoluble	Group B
Liquid and water soluble	Group C
Liquid and water insoluble	Group D
Order II. Compounds containing halogen, but no nitrogen or sulfur.	
Solid	Group A
Liquid	Group B
Order III. Compounds containing nitrogen, but no halogen or sulfur.	
Solid	Group A
Liquid	Group B
Order IV. Compounds containing sulfur, but no halogen or nitrogen.	
Solid	Group A
Liquid	Group B
Order V. Compounds containing nitrogen and halogen, but no sulfur.	
Solid	Group A
Liquid	Group B
Order VI. Compounds containing nitrogen and sulfur, but no halogen.	
Solid	Group A
Liquid	Group B
Order VII. Compounds containing halogen and sulfur, but no nitrogen.	
Solid	Group A
Liquid	Group B

ORDER I. GROUP A

Apply Test 9.

I. Test 9 positive. Indicates an acid or acid anhydride.

M.P.
72 Crotonic acid. Tests 6*a* and 7 pos., 8 neg.
99 Phenoxyacetic acid. Tests 6*a* and 8 neg., 7 pos.
100 Citric acid (1 H_2O). Tests 6*a* and 7 neg., 6*b* pos. Solution gives no ppt. with $CaCl_2$.
101 Oxalic acid (2 H_2O). Tests 6*b* and 7 neg. Solution gives ppt. with $CaCl_2$.
[illegible] *dl*-Mandelic acid. Tests 6*a* neg., 6*b* pos.
[illegible] Succinic anhydride. Tests 6*b* and 7 neg.
129 *dl*-Malic acid. Tests 6*a* pos., 7 neg.
130 Maleic acid. Tests 6*a* and 7 pos.
153 Citric acid (anhyd.). Tests 6*a* and 7 neg., 6*b* pos.
170 *d*-Tartaric acid. Tests 6*a* neg., 6*b* and 26 pos.
185 Succinic acid. Tests 6*a* and 6*b* neg.
189 Oxalic acid (anhyd.). Tests 6*b* and 7 neg.
240d Gallic acid. Tests 6*a*, 7, and 15 pos.

II. Test 9 negative. Apply Tests 1, 8, and 10*b* in order until a positive reaction is obtained.

1. Test 1 positive. Indicates a soluble salt of an acid. Dissolve 0.5 g. in 5 cc. of H_2O and acidify with dilute H_2SO_4.

   a. If a solid precipitates, treat 5 g. of the salt with dil. H_2SO_4, cool, filter off, and wash the product. Identify under Group B, I.

   b. If an oil separates, treat 5 to 10 g. of the salt with dil. H_2SO_4, cool, take the oil up in ether, and dry with anhyd. Na_2SO_4. Remove the ether by distillation and identify the acid under Group D, I.

   c. If the acid is soluble, identify it by the preparation of one of the derivatives listed on pages 184–189. *Obviously the acid cannot be one of those listed under Group B, I or D, I.*

2. Test 1 negative. Test 8 positive. Indicates a phenol or quinone.

   M.P.
   41 Phenol. Test 15*a* gives violet color.
   110 Resorcinol. Test 15*a* gives violet color. Test 27 pos.
   116 Benzoquinone. Yellow. Test 15*a* neg.
   134 Pyrogallol. Test 15*b* gives brown to red color.
   170 Quinol (hydroquinone). Test 15*a* gives brown color.

3. Tests 1, 8 and 15*b* negative. Test 10*b* positive. Indicates a sugar.

   M.P.
   104 *d*-Fructose (levulose). Tests 10*a* and 21 pos., 20 neg.
   146 *d*-Glucose. Tests 10*a* pos., 20 and 21 neg.
   164 *l*-Arabinose. Tests 10*a* and 20 pos.
   186 *d*-Sucrose (cane sugar). Tests 10*b* strongly pos., 10*a* slightly pos., 20 neg.
   202 *d*-Lactose. Tests 10*a* and 20 neg.

ORDER I. GROUP B

Apply Test 9.

I. Test 9 positive. Indicates an acid or acid anhydride.

M.P.	
43	Benzoic anhydride.
57	Maleic anhydride.
64	Palmitic acid.
69	Stearic acid.
77	Phenylacetic acid.
99	Phenoxyacetic acid.
102	*o*-Toluic acid.
110	*m*-Toluic acid.
120	Succinic anhydride
122	Benzoic acid.
131	Phthalic anhydride. Tests 27 pos., 6*a* neg.
133	Cinnamic acid. Tests 6*a* pos., 27 neg.
148	Diphenylacetic acid. Tests 6*a* and 15*a* neg.
159	Salicylic acid. Test 6*a* pos. Test 15*a* gives blue to purple color.
177	*p*-Toluic acid.
184	Anisic acid.
191d	Phthalic acid. Test 27 pos.
201	*m*-Hydroxybenzoic acid. Test 27 neg.
213	*p*-Hydroxybenzoic acid.
240d	Gallic acid.
287	Fumaric acid.

II. Test 9 negative. Apply Test 15*a* (using alcohol as solvent).

1. Test 15*a* positive. Indicates a phenolic compound. Colors obtained in this test are as indicated below.

M.P.	
30	*o*-Cresol. B.P. 191. Slight brown to green.
35	*p*-Cresol. B.P. 201. Blue.
41	Phenol. B.P. 182. Purple.
43	Phenyl salicylate. To be distinguished from phenol by its insolubility in warm water. Purple.
81	Vanillin. Odor of vanilla. Purple.
96	α-Naphthol. Purple.
122	β-Naphthol. Greenish.

2. Test 15*a* negative.

M.P.	
27	Diphenyl ether. B.P. 259. Tests 6*a* and 13 neg.
33	Cinnamyl alcohol. B.P. 258. Tests 6*a* and 13 pos.
37	β-Naphthyl ethyl ether. Tests 6*a* and 13 neg.
43	Benzoic anhydride.
48	Benzophenone.
69	Diphenyl.

80	Naphthalene.
92	Triphenylmethane.
95	Acenaphthene.
100	Phenanthrene.
116	Benzoquinone.
133	Benzoin.
148	Cholesterol.
162	Triphenylcarbinol.
179	*d*-Camphor. B.P. 209.
218	Anthracene.

Order I. Group C

Apply Test 9.

I. Test 9 positive. Indicates an acid or acid anhydride. Apply Test 6*b*.

1. Test 6*b* positive.

B.P.	
101	Formic acid. Sharp odor. Tests 6*a* pos., 16 neg.
dec.	Lactic acid. Thick syrup boiling with decomposition. Tests 6*a* neg., 16 pos.

2. Tests 6*a* and 6*b* negative.

B.P.	
118	Acetic acid. Sharp odor. Solidifies in an ice bath.
139	Acetic anhydride. Sharp odor.
141	Propionic acid. Sharp odor.
163	*n*-Butyric acid. Rancid odor.
166	Propionic anhydride. Sharp odor.

II. Test 9 negative. Apply Test 10*a*.

1. Test 10*a* positive. Indicates an aldehyde. These compounds will also be positive in Tests 11, 12, and 14.

B.P.	
21	Acetaldehyde. Test 16 pos.
49	Propionaldehyde. Test 16 neg.
52	Acrolein. Test 16 neg.
76	*n*-Butyraldehyde.
97–98	Formalin (40 per cent aqueous formaldehyde). Test 13 pos.
104	Crotonaldehyde. Test 13 neg.
162	Furfuraldehyde. Test 20 pos.

2. Test 10*a* negative. Apply Test 13.

a. Test 13 positive. Indicates an hydroxy compound.

B.P.	
65	Methyl alcohol. Test 16 neg.
78	Ethyl alcohol. Test 16 pos.
82	Isopropyl alcohol. Test 16 pos. in the cold.
97	Allyl alcohol. Tests 8 pos., 16 neg.
98	*n*-Propyl alcohol. Tests 8 and 16 neg.

107	Isobutyl alcohol. Tests 8 and 16 neg.
118	*n*-Butyl alcohol. Test 16 neg.
130	Isoamyl alcohol. Test 16 neg.
154	Ethyl lactate. Test 16 pos.
189	Propylene glycol.
197	Ethylene glycol.
214d	Trimethylene glycol.
290d	Glycerol.

b. Test 13 negative. The esters in this class can be distinguished by the fact that their saponification equivalents are below 300.

B.P.	
35	Diethyl ether. Sp. G. 0.72. Test 6*a* neg.
54	Ethyl formate. Sp. G. 0.94. Test 6*a* pos.
56	Acetone. Sp. G. 0.79. Test 16 pos.
77	Ethyl acetate. Sp. G. 0.92. Test 16 pos.
80	Butanone. Sp. G. 0.81. Test 16 pos.
81	*n*-Propyl formate. Sp. G. 0.92. Test 16 neg.
99	Ethyl propionate. Sp. G. 0.91. Test 16 pos.
102	*n*-Propyl acetate. Sp. G. 0.90. Test 16 neg.
124	Paraldehyde. Sp. G. 0.99.
126	Diethyl carbonate. Sp. G. 0.98. Saponification equivalent larger than the theoretical.
157	Cyclohexanone. Sp. G. 0.95.
180	Ethyl acetoacetate. Sp. G. 1.02. Saponification equivalent smaller than the theoretical.
186	Diethyl oxalate. Sp. G. 1.08.
259	Glyceryl triacetate. Sp. G. 1.16.

ORDER I. GROUP D

Apply Test 9

I. Test 9 positive. Indicates an acid.

B.P.	
187	*n*-Valeric acid.
202	*n*-Caproic acid.
237	*n*-Caprylic acid. Tests 6*a* and 8 neg.
>300d	Oleic acid. Tests 6*a* and 8 pos.

II. Test 9 negative. Apply Test 15*a*.

1. Test 15*a* positive. Indicates a phenol. These compounds are also positive to Test 8.

B.P.	
161	Cyclohexanol. Tests 8 and 15*a* positive because of phenol as impurity. See under Group D, II, 2, below.
191	*o*-Cresol.
196	Salicylaldehyde. Test 14 pos.
201	*p*-Cresol. M.P. 35. Test 14 neg.
203	*m*-Cresol. Test 14 neg.
223	Methyl salicylate (oil of wintergreen).

2. Test 15*a* negative. Apply Test 12.

a. Test 12 positive. Indicates an aldehyde or aldehyde derivative. These compounds are also positive to Test 14.

B.P.	
102	Acetal. Sp. G. 0.83.
124	Paraldehyde. Sp. G. 0.99.
179	Benzaldehyde. Sp. G. 1.05. Odor of bitter almonds.
247	Anisaldehyde. Sp. G. 1.12.
251	Cinnamaldehyde. Sp. G. 1.05. Odor of cinnamon.

b. Test 12 negative. Determine the saponification equivalent.

(1) Saponification equivalent below 300. Indicates an ester. Use value obtained as confirmation of identification based on boiling point.

B.P.	
72	Vinyl acetate. Test 8 pos.
77	Ethyl acetate. Test 8 neg.
99	Ethyl propionate.
102	*n*-Propyl acetate.
126	*n*-Butyl acetate. Sp. G. 0.90.
126	Diethyl carbonate. Sp. G. 0.98. Saponification equivalent larger than the theoretical.
142	Isoamyl acetate. Odor of bananas. Test 16 neg.
154	Ethyl lactate. Test 16 pos.
180	Ethyl acetoacetate. Saponification equivalent smaller than the theoretical.
186	Diethyl oxalate.
196	Phenyl acetate.
200	Methyl benzoate.
213	Benzyl acetate.
213	Ethyl benzoate.
217	Diethyl succinate.
226	Ethyl phenylacetate.
259	Glyceryl triacetate.
324	Benzyl benzoate.

(2) Saponification equivalent above 300.

B.P.	
30–50	Petroleum ether. Sp. G. 0.62 to 0.65. Test 8 neg.
35	Diethyl ether. Sp. G. 0.72. Test 8 neg.
36	Pentene-2. Sp. G. 0.65. Test 8 pos.
80	Benzene. Sp. G. 0.88. Test 8 neg.
81	Cyclohexane. Sp. G. 0.78. Test 8 neg.
84	Cyclohexene. Sp. G. 0.81. Test 8 pos.
111	Toluene. Sp. G. 0.87.
139	*m*-Xylene. Sp. G. 0.87.
141	Di-*n*-butyl ether. Sp. G. 0.77.
144	*o*-Xylene. Sp. G. 0.89.

156 Anisole. Sp. G. 0.99. Test 14 neg.
157 Cyclohexanone. Sp. G. 0.95. Tests 13 neg., 14 pos.
161 Cyclohexanol. Sp. G. 0.96. Tests 13 pos., 14 neg.
172 Phenetole. Sp. G. 0.96.
176 *p*-Cymene. Sp. G. 0.86.
181 *o*-Cresyl ethyl ether. Tests 5 pos., 14 and 16 neg.
190 *p*-Cresyl ethyl ether. Tests 5 pos., 14 and 16 neg.
191 *m*-Cresyl ethyl ether. Tests 5 pos., 14 and 16 neg.
193 Decahydronaphthalene. Tests 5, 14 and 16 neg.
202 Acetophenone. Tests 13 neg., 5, 14 and 16 pos.
206 Benzyl alcohol. Tests 13 pos., 14 and 16 neg.
215 Resorcinol dimethyl ether. Tests 13 and 16 neg.
258 Cinnamyl alcohol. Test 13 pos.
259 Diphenyl ether. M.P. 28. Test 13 neg.
262 Diphenylmethane. M.P. 27.

ORDER II. GROUP A

M.P.
28 *p*-Bromotoluene. B.P. 184. Test 9 neg.
35 *p*-Iodotoluene. B.P. 211. Test 9 neg.
37 *p*-Chlorophenol. B P. 217. Test 9 neg. Test 15*a* gives purple color.
53 *p*-Dichlorobenzene. B.P. 173. Test 9 neg
57 Trichloroacetic acid. B.P. 195. Water soluble. Test 9 pos. Gives positive reaction when substituted for $CHCl_3$ in Test 17.
59 Phenacyl chloride. B.P. 244. Test 9 neg
61 Chloroacetic acid. B.P. 189. Water soluble. Test 9 pos. Gives negative reaction when substituted for $CHCl_3$ in test 17.
87 *p*-Dibromobenzene. B.P. 219.
119 Iodoform. Test 9 neg.
141 *o*-Chlorobenzoic acid. Test 9 pos.

ORDER II. GROUP B

I. With chlorine as the halogen.

B.P.
36 Isopropyl chloride. Sp. G. 0.86.
52 Acetyl chloride. Reacts *vigorously* with cold water. **(Caution!)** Test 9 pos. **(Caution!)**
61 Chloroform. Sp. G. 1.48. Gives Test 17 with aniline.
77 Carbon tetrachloride. Sp. G. 1.60.
78 *n*-Butyl chloride. Sp. G. 0.89.
80 Propionyl chloride. Reacts *vigorously* with cold water. Test 9 pos. **(Caution!)**
102 *n*-Butyryl chloride. Test 9 pos.

117	Epichlorohydrin. Sp. G. 1.20.
121	Tetrachloroethylene. Sp. G. 1.63.
132	Chlorobenzene. Sp. G. 1.11.
146	*s*-Tetrachloroethane. Sp. G. 1.60.
159	*o*-Chlorotoluene. Sp. G. 1.08.
162	*m*-Chlorotoluene. Sp. G. 1.07.
162	*p*-Chlorotoluene. Sp. G. 1.07.
173	*o*-Chlorophenol. Sp. G. 1.24. Test 15*a* gives purple color.
179	Benzyl chloride.
197	Benzoyl chloride. Strong lachrymator. Test 9 pos.
214	Benzal chloride. Tests 9 and 15*a* neg.
217	*p*-Chlorophenol. Test 15*a* gives purple color. Test 9 neg.
221	Benzotrichloride. Test 15*a* neg.
258	*α*-Chloronaphthalene. Test 9 neg.
277	Phthalyl chloride. Test 9 pos.

II. With bromine as the halogen.

B.P.	
38	Ethyl bromide. Sp. G. 1.45.
102	*n*-Butyl bromide. Sp. G. 1.31.
128	*n*-Amyl bromide. Sp. G. 1.22.
132	Ethylene dibromide. Sp. G. 2.18.
140	Propylene dibromide. Sp. G. 1.93.
150	Bromoform. Sp. G. 2.90. Gives positive reaction with aniline in Test 17.
156	Bromobenzene. Sp. G. 1.49.
182	*o*-Bromotoluene. Sp. G. 1.42.
184	*p*-Bromotoluene. M.P. 28. Sp. G. 1.31.
281	*α*-Bromonaphthalene. Sp. G. 1.49.

III. With iodine as the halogen.

B.P.	
43	Methyl iodide. Sp. G. 2.29.
72	Ethyl iodide. Sp. G. 1.92.
89	Isopropyl iodide. Sp. G. 1.71.
102	*n*-Propyl iodide. Sp. G. 1.74.
127	*n*-Butyl iodide. Sp. G. 1.62.
189	Iodobenzene. Sp. G. 1.84.
211	*o*-Iodotoluene. Sp. G. 1.70.

ORDER III. GROUP A

Apply Test 2.

I. Compounds soluble in water.

M.P.	
63	*m*-Phenylenediamine. B.P. 287. Test 18 neg.
74	Lactamide. Tests 16 and 18 pos.
81	Acetamide. B.P. 222. Tests 16 neg., 18 pos.
104	*o*-Phenylenediamine. B P. 252. Test 18 neg.

133	Urea. Tests 18 pos., 22 neg. Heat a few milligrams strongly in a test tube. Cool. Test 22 now pos.
140	*p*-Phenylenediamine. B.P. 267. Test 18 neg.
233d	Glycine. Tests 9 and 18 neg
243	Succinamide. Test 18 pos.
295d	*dl*-Alanine. Tests 9 and 18 neg.

II. Compounds insoluble in water. Apply Test 3.

1. Compounds soluble in HCl. Indicates an amine.

M.P.	
45	*p*-Toluidine. B.P. 200.
50	*α*-Naphthylamine. B.P. 301. Forms an insoluble hydrochloride with excess HCl.
57	*p*-Anisidine. B.P. 245.
63	*m*-Phenylenediamine. B.P. 287.
71	*o*-Nitroaniline. Orange.
90	4,4′-Di-(dimethylamino)-diphenylmethane.
91	Ethyl *p*-aminobenzoate.
104	*o*-Phenylenediamine. B.P. 252.
112	*β*-Naphthylamine. B.P. 306. Forms an insoluble hydrochloride with excess HCl.
112	*m*-Nitroaniline. Bright yellow.
126	*p*-Aminoazobenzene. Brown. Forms an insoluble hydrochloride with excess HCl.
129	Benzidine. Test 28 pos.
140	*p*-Phenylenediamine. B.P. 267.
145	Anthranilic acid. Amphoteric. Alcoholic solution blue fluorescence.
145	Triphenylguanidine. Not amphoteric. Forms an insoluble hydrochloride with excess HCl.
187	*p*-Aminobenzoic acid. Amphoteric.
208d	*d*-Glutamic acid. Amphoteric.
265d	*dl*-Phenylalanine. Amphoteric. Test 23 neg.
295d	*l*-Tyrosine. Amphoteric. Test 23 pos.

2. Compounds insoluble in HCl. Apply Test 4.

a. Compounds soluble in dilute NaOH.

M.P.	
45	*o*-Nitrophenol.
112	2,4-Dinitrophenol.
113	*p*-Nitrophenol.
122	Picric acid. Test 18 neg.
124	Succinimide. Test 18 pos.
141	*m*-Nitrobenzoic acid.
187	Hippuric acid.
205	3,5-Dinitrobenzoic acid.
238	Phthalimide. Tests 9 neg., 18 pos.
242	*p*-Nitrobenzoic acid. Tests 9 pos., 18 neg.
360d	Uric acid. Tests 22 neg., 29 pos.

b. Compounds insoluble in dilute NaOH.

M.P.	
36	Azoxybenzene. Decomposes below its boiling point at atmospheric pressure.
38	*p*-Tolunitrile. B.P. 217.
44	*o*-Nitrobenzaldehyde.
50	α-Naphthylamine. B.P. 301. See above, under II, 1.
51	*p*-Nitrotoluene. B.P. 238.
54	Diphenylamine B.P. 302.
57	Ethyl *p*-nitrobenzoate.
58	*m*-Nitrobenzaldehyde.
67	Azobenzene. Orange. B.P. 297.
70	2,4-Dinitrotoluene. Yellow.
90	*m*-Dinitrobenzene.
106	*p*-Nitrobenzaldehyde.
112	β-Naphthylamine. B.P. 306. See above, under II, 1.
114	Acetanilide.
126	*p*-Aminoazobenzene. Brown. See above, under II, 1.
130	Benzamide.
135	Phenacetin (*p*-ethoxyacetanilide).
145	Triphenylguanidine. See above, under II, 1.
147	Phenylurea. White.
148	*p*-Nitroaniline. Yellow.
153	*p*-Acetotoluide.
161	Benzanilide.
198d	2,4-Dinitrophenylhydrazine.
214	*p*-Nitroacetanilide.
235	Diphenylurea.
243	Succinamide.
>300	Oxamide.

ORDER III. GROUP B

Apply Test 2.

I. Compounds soluble in water. The amines can be distinguished from the neutral compounds by the alkalinity of their aqueous solutions.

B.P.	
56	Diethylamine.
76	*n*-Butylamine.
82	Acetonitrile.
89	Triethylamine.
97	Propionitrile.
102	Nitromethane.
104	*n*-Amylamine.
106	Piperidine.

115	Pyridine.
161	β-Diethylaminoethanol.
171	Ethanolamine.
184	Benzylamine

II. Compounds insoluble in water. Apply Test 3.

1. Compounds soluble in HCl. Apply Test 17.

a. Test 17 positive. Indicates a primary amine.

B.P.	
184	Aniline.
201	*o*-Toluidine.
203	*m*-Toluidine.
216	2-4-Dimethylaniline.
224	*o*-Anisidine.
229	*o*-Phenetidine.
243	Phenylhydrazine.
254	*p*-Phenetidine.

b. Test 17 negative.

B.P.	
161	Di-*n*-butylamine.
194	Dimethylaniline.
196	Methylaniline.
205	Ethylaniline.
216	Diethylaniline.

2. Compounds insoluble in HCl.

B.P.	
118	*n*-Butyronitrile.
141	*n*-Valeronitrile.
166	Phenylisocyanate.
191	Benzonitrile.
204	*o*-Tolunitrile.
211	Nitrobenzene.
222	*o*-Nitrotoluene.
231	*m*-Nitrotoluene.
234	Benzyl cyanide.
269	α-Naphthylisocyanate

ORDER IV. GROUP A

I. Apply Test 2.

1. Compounds soluble in water. Apply Test 1.

a. Compounds leaving a residue upon ignition. Indicates a salt of a sulfonic acid. Identify the parent acid by means of a derivative.

b. Compounds leaving no residue upon ignition. Indicates a sulfonic acid. These substances are difficult to purify, but when pure have the melting points listed below. Final identification should be based largely on the melting point of a suitable derivative.

M.P.	
46	Benzenesulfonic acid.

102	β-Naphthalenesulfonic acid.
105	*p*-Toluenesulfonic acid.

2. Compounds insoluble in water.

M.P.	
129	Diphenyl sulfone.

ORDER IV. GROUP B

B.P.	
46	Carbon disulfide.
93	Thioacetic acid.
169	Thiophenol.
208	Diethyl sulfate.
293	Diphenyl sulfide.

ORDER V. GROUP A

Apply Test 2.

I. Compounds soluble in water. Aqueous solution gives immediate precipitate of silver halide when treated with dilute HNO_3 and dilute $AgNO_3$. Indicates a soluble hydrohalide of an organic base. Apply Test 19.

1. The base is water soluble and volatile. Identify as the corresponding phenylurea.
2. The base is water soluble and non-volatile. Acidify the alkaline solution with acetic acid. If a precipitate forms, filter and identify under Order III, Group A. If no precipitate forms within 10 minutes, identification of the salt is too difficult for an elementary course.
3. The base is water insoluble and solid. Treat 5 g. with dil. NaOH, filter, wash with water, and recrystallize from a suitable solvent. Identify under Order III, Group A, or Order V, Group A, II, depending on the elementary composition of the free base.
4. The base is water insoluble and liquid. Treat 5 g. with dil. NaOH, extract twice with ether, dry the extracts over anhyd. Na_2SO_4, and purify by distillation after removal of the solvent. Identify under Order III, Group B, or Order V, Group B, depending on the elementary composition of the free base.

II. Compounds insoluble in water. Apply Test 3.

1. Compounds soluble in dilute HCl. Indicates an amine.

M.P.	
31	*o*-Bromoaniline. B.P. 251.
66	*p*-Bromoaniline.
71	*p*-Chloroaniline. B.P. 231.

2. Compounds insoluble in dilute HCl.

M.P.	
32	*o*-Chloronitrobenzene. B.P. 246.
44	*m*-Chloronitrobenzene. B.P. 236.
69	3,5-Dinitrobenzoyl chloride.

71	*p*-Nitrobenzyl chloride.	
72	*p*-Nitrobenzoyl chloride.	
83	*p*-Chloronitrobenzene.	B.P. 242.
88	*o*-Chloroacetanilide.	
119	*s*-Tribromoaniline.	
165	*p*-Bromoacetanilide.	
172	*p*-Chloroacetanilide.	

ORDER V. GROUP B

Apply Test 3.

I. Compounds soluble in dilute HCl. Indicates an amine.

B.P.		
210	*o*-Chloroaniline.	
230	*m*-Chloroaniline.	
251	*o*-Bromoaniline.	M.P. 31.
251	*m*-Bromoaniline.	M.P. 18.

II. Compounds insoluble in dilute HCl.

B.P.		
236	*m*-Chloronitrobenzene.	M.P. 44.
246	*o*-Chloronitrobenzene.	M.P. 32.

ORDER VI. GROUP A

Apply Test 22.

I. Test 22 positive. Tests 23 and 24 positive. May be soluble or insoluble in water. Indicates a protein, such as casein or ovalbumin. More specific identification is too difficult for an elementary course.

II. Test 22 negative. Apply Test 2.

1. Compounds soluble in water.

   a. Addition of dilute HCl and dilute $BaCl_2$ gives no precipitate.

M.P.		
182	Thiourea.	Test 30 pos.

   b. Addition of dilute HCl and dilute $BaCl_2$ gives an immediate precipitate of $BaSO_4$. Indicates a soluble sulfate of an organic base. Apply Test 19, and proceed as in Order V, Group A, I, part 1, 2, 3, or 4, depending on the result of the test.

2. Compounds insoluble in water.

M.P.		
138	*p*-Toluenesulfonamide.	Soluble in cold 10 per cent NaOH but not in dilute HCl.
154	*s*-Diphenylthiourea.	
156	Benzenesulfonamide.	
258d	*l*-Cystine.	
288	Sulfanilic acid.	

ORDER VI. GROUP B

B.P.	
151	Allylisothiocyanate.

218	Phenylisothiocyanate.
239	*o*-Tolylisothiocyanate.
245	*m*-Tolylisothiocyanate.

ORDER VII. GROUP A

It should be borne in mind that sulfonic acids and their salts are frequently contaminated with inorganic chlorides.

M.P.	
14	Benzenesulfonyl chloride. B.P. 247.
69	*p*-Toluenesulfonyl chloride.

CHAPTER VII

PREPARATION OF DERIVATIVES

INTRODUCTION

Usually the most convenient and reliable method for verifying the result of a qualitative identification of an organic substance is to prepare a small amount of a derivative of the substance and to compare its physical properties, particularly the melting point, with the known properties of the substance. In this chapter directions are given for the preparation of derivatives of several of the more important classes of compounds, the directions being stated in general rather than in detailed form wherever possible. Most of the substances included in the classified lists in Chap. VI are treated in the present chapter, though a few of these compounds form derivatives only by methods judged to be too difficult or laborious for an elementary course. In order that the student may obtain a better idea of the wide generality of some of the derivative preparations, a rather large number of compounds not listed in Chap. VI are included. It is thus possible to give to students unknowns which are not in the classified lists, but for which derivatives are given. The student should be able to determine rather definitely what class such an unknown belongs to by means of a systematic application of the tests given in Chap. V, and to identify the substance by formation of a derivative. The physical properties of the original substance should then be compared with those given in a chemical handbook or in reference works such as Beilstein's "Handbuch der organischen Chemie."

In many cases a choice of several different derivatives is offered. In such cases the student should study carefully all the possibilities and choose that one best suited to his particular problem. This choice should be based on several considerations. Obviously, other things being equal, the derivative which appears to be the easiest to prepare should be chosen. If the student is not quite sure of his qualitative identification of the compound, that derivative preparation should be tried which would most definitely eliminate all but one possibility. Thus, if a substance is known to be one of two compounds whose physical properties are so similar that definite identification is difficult or impossible, that preparation should be attempted which yields derivatives having melting points as far apart as possible. Again, if the unknown is found to be one of two non-homologous substances, a derivative preparation should be chosen, if possible, which gives widely different results with the two possibilities. It should be emphasized, however, that in the majority of cases there should be no doubt in the student's mind as to what his unknown is by the time he is ready to prepare a derivative.

In the preparation of a derivative it is advisable to use as little material as possible, not only from the point of view of economy, but also because it is much quicker to perform laboratory manipulations on small amounts of material. Unless otherwise directed, no more than 1 gram of unknown should be used in a derivative preparation. It is essential in handling small quantities of materials to develop a very different technique from that used in making the ordinary organic preparations. All apparatus used must be as small as possible. Test tubes can largely replace flasks for refluxing, although a 50-cc. Erlenmeyer flask is frequently useful. Recrystallizations should be carried out in test tubes, or in 25- or 50-cc. Erlenmeyer flasks or beakers. Filtrations should be performed with as small a piece of paper as possible and, when crystals are to be filtered off and dried, a Witt plate and funnel or a small Hirsch funnel should be used. These can be fitted into a side-arm test tube with a rubber stopper. A Gooch crucible may also be used for suction filtrations.

Weighing must be done more accurately than is possible with the ordinary platform balance, a horn-pan balance being suitable. Liquids are best measured with pipettes, a graduated 1-cc. pipette being particularly useful. In using a pipette an approximate knowledge of the density of the liquid is essential, as it may vary from 0.7 to 2.0, and stoichiometric quantities are always measured by weight.

In any case where the derivative melts at nearly the same temperature as the unknown, it is advisable to ascertain by a determination of the mixed melting point with the original unknown that the product obtained is not simply the unchanged unknown. A similar procedure should be followed if a reagent is used which melts at a temperature near the melting point of the desired product.

This chapter is not intended to be a complete treatment of the subject of the preparation of derivatives suitable for identification purposes. For example, the formation of semicarbazones from aldehydes and ketones has not been included. Much detailed information of this sort may be found in Mulliken's "The Identification of Pure Organic Compounds" and other books on qualitative organic analysis. Also satisfactory derivatives for many substances can be readily found in the literature, the first two places of reference usually being Beilstein's "Handbuch der organischen Chemie" and *Chemical Abstracts*. It is sometimes desirable to require advanced students or the better men in an elementary course to prepare derivatives other than those to be found in this chapter.

Warning! Caution should be used in preparing derivatives, since in many cases very drastic reagents such as fuming nitric acid are used with substances that may have been incorrectly identified.

The classes of compounds are listed in the following order:

Hydrocarbons

The aliphatic hydrocarbons will not be considered here since it is very difficult, or even impossible, to prepare derivatives from most of them. The aromatic hydrocarbons, however, usually offer no difficulties. Most of them either form picrates or can be nitrated to form satisfactory derivatives.

1. Picrates.—Picrate formation does not represent a chemical reaction in the ordinary sense, as the picric acid is joined to the second component by the so-called *secondary valence forces,* those used for instance in binding water to copper sulfate to form $CuSO_4 \cdot 5H_2O$. The proportion of picric acid to the second substance is generally 1:1, but many cases are known where it varies above and below this ratio.

Picrates are generally prepared by dissolving equivalent amounts of the substance and picric acid in the least possible amount of boiling alcohol. (In certain cases where the ratio is known to be different from 1:1, it will be indicated after the name of the compound in the table of melting points.) The picrate which separates on cooling the solution is recrystallized from alcohol. If the picrate does not separate on cooling, water may be added to the hot solution until a faint cloudiness persists. In such cases the product is recrystallized from dilute alcohol.

Important! Before taking the melting point of a picrate it is always advisable to heat a small sample on a spatula over a flame to see if the substance melts without exploding.

MELTING POINTS OF PICRATES

Hydrocarbon	M.P. of picrate	Hydrocarbon	M.P of picrate
Acenaphthene	161	β-Methylnaphthalene	117
Anthracene	139	Naphthalene....	151
α-Methylnaphthalene	142	Phenanthrene	143

2. Nitro Derivatives.—General directions for the preparation of nitro derivatives cannot well be given. A few of the more important cases will be considered.

Benzene is nitrated to give *m*-dinitrobenzene, M.P. 90°. Half a cubic centimeter of substance is added slowly with shaking and cooling to a mixture of 5 cc. each of concentrated nitric and sulfuric acids. The mixture is carefully heated to boiling and is then cooled and poured into cold water. The precipitate is filtered off, washed, and recrystallized from dilute alcohol.

Diphenyl.—A mixture of 1 g. of diphenyl, 2 cc. of glacial acetic acid, and 0.5 cc. of fuming nitric acid (**Caution!**) is refluxed for 10 minutes. The mixture is poured into water and the precipitate is filtered off, washed with water, and recrystallized from alcohol. *p*-Nitrodiphenyl, the product of this nitration, melts at 114°.

Diphenylmethane.—Five drops of substance is added slowly with shaking and cooling to a mixture of 3 cc. each of concentrated nitric and sulfuric acids. The mixture is then poured into cold water. The product, 2,4,2′,4′-tetranitrodiphenylmethane, M.P. 172°, is filtered off, washed with water, and recrystallized from alcohol.

Toluene is nitrated to 2,4-dinitrotoluene, M.P. 70°, as follows: To 1 cc. of substance is added gradually with shaking a mixture of 2 cc. of concentrated nitric acid and 3 cc. of concentrated sulfuric acid. The mixture is heated to 100° for 30 minutes and is then poured into cold water. The precipitate is filtered off, washed, and recrystallized from alcohol.

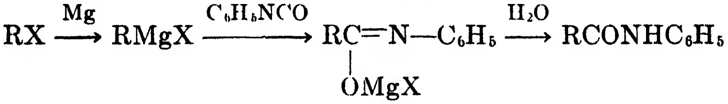
Triphenylmethane.—To 10 cc. of fuming nitric acid cooled in an ice-salt bath is added slowly with shaking 1 g. of triphenylmethane (**Caution!**). After all the solid has dissolved, the solution is poured into cold water and the precipitated p,p′,p″-trinitrotriphenylmethane, M.P. 207°, is filtered off, washed, and recrystallized from benzene.

m-Xylene.—Two drops of substance is added to a mixture of 2 cc. of concentrated sulfuric acid and 1 cc. of fuming nitric acid (**Caution!**), and after shaking, the mixture is boiled gently for a minute and then poured into cold water. The product, trinitro-*m*-xylene, M.P. 181°, is filtered off, washed with water, and recrystallized from alcohol.

3. Oxidation by Alkaline Permanganate.—Certain hydrocarbons are comparatively readily oxidized to yield derivatives convenient for identification purposes. *Dibenzyl, stilbene, styrene,* and the simple homologues of benzene such as *toluene* or *ethylbenzene* can be oxidized to benzoic acid, M.P. 122°, by means of alkaline permanganate. Disubstituted benzenes such as the *xylenes,* yield the corresponding phthalic acids. For melting points see page 193. The procedure follows: A slight excess of the compound is refluxed with potassium permanganate dissolved in 5 per cent sodium hydroxide solution until all the permanganate color has disappeared. (For difficulties encountered at this stage, consult page 73.) After filtering off the manganese dioxide, the cold filtrate is acidified with dilute hydrochloric acid and the precipitated organic acid filtered off and recrystallized from water or dilute alcohol. If no precipitate is formed on acidification of the filtrate, the solution should be extracted with several portions of ether, the extracts dried with anhydrous sodium sulfate, and the ether removed by evaporation (**Caution!**). The residual organic acid can then be recrystallized.

HALIDES

1. Anilides from Halides.—A procedure for converting alkyl or side-chain halides into anilides has been developed by Schwartz and Johnson.[1] The halide is first transformed to the Grignard reagent, which is then treated with phenylisocyanate, the resulting addition compound yielding an anilide on hydrolysis.



$$RX \xrightarrow{Mg} RMgX \xrightarrow{C_6H_5NCO} \underset{\substack{| \\ OMgX}}{RC}{=}N{-}C_6H_5 \xrightarrow{H_2O} RCONHC_6H_5$$

Because of the difficulty of keeping a Grignard reagent, this derivative preparation should be completed in one period. A test tube is attached by means of a *cork* to a reflux condenser equipped with a calcium chloride tube in the top. A *small* crystal of iodine and 0.4 g. of magnesium are placed in the tube and gently heated until the iodine has reacted. After the tube has cooled, 2 g. of the dry halide dissolved in 4 to 5 cc. of *dry* ether is added. If necessary the tube is cooled in ice water, but if the reaction does not start spontaneously it is warmed in a water bath. Disappearance of the iodine color is an indication that the reaction has started. After the reaction has begun, the ether is kept boiling gently for an hour. The mixture is then cooled, 10 cc. of *dry* ether is added and, after the magnesium has settled, the solution is decanted into a small dry Erlenmeyer flask and treated dropwise with shaking with a solution of 7 drops of phenylisocyanate in 5 cc. of *dry* ether. The flask is fitted with a calcium chloride tube and allowed to stand for 15 minutes with occasional shaking. The mixture is then *cautiously* poured into 20 cc. of ice water containing 1 cc. of

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[1] SCHWARTZ and JOHNSON, *J. Am. Chem. Soc.*, **53**, 1063 (1931).

concentrated hydrochloric acid, and the whole is thoroughly shaken. The ether is removed on a water bath (**Caution!**) and the residual anilide is filtered off and recrystallized from water or dilute alcohol. For the melting points of the resulting anilides see the table on page 194.

If dry reagents and dry apparatus have not been used, diphenylurea, M.P. 235°, will be formed.

2. Picrates.—Certain of the halogen derivatives of the higher aromatic hydrocarbons form picrates when treated as described on page 167.

MELTING POINTS OF PICRATES

Halide	M.P. of Picrate
α-Bromonaphthalene	134
β-Bromonaphthalene	86
α-Chloronaphthalene	137

3. Nitro Derivatives.—Certain halogenated benzenes yield mononitro derivatives when treated as follows: One cubic centimeter of substance is added with shaking to a solution of 1 g. of potassium nitrate dissolved in 10 cc. of concentrated sulfuric acid. The mixture is heated in a boiling water bath for 15 minutes with frequent shaking and, after cooling, is poured into cold water. The product is filtered off and recrystallized from alcohol or dilute alcohol to constant melting point.

MELTING POINTS OF NITROHALOBENZENES

	M.P.
p-Nitrobromobenzene	127
p-Nitrochlorobenzene	83
2-Nitro-1,4-dibromobenzene	85
2-Nitro-1,4-dichlorobenzene	54

4. Miscellaneous.—*Benzal chloride* is changed to benzaldehyde by refluxing 1 cc. with 5 cc. of 10 per cent sodium hydroxide and 15 cc. of water for an hour. At the end of this time the mixture is cooled and the benzaldehyde extracted with 10 cc. of ether. After evaporation of the solvent, 2 cc. of glacial acetic acid, 1 cc. of phenylhydrazine, and enough alcohol to effect solution are added and the mixture is boiled for a minute. The benzalphenylhydrazone is precipitated by dilution of the mixture with water and is purified by crystallization from 50 per cent alcohol, M.P. 156°.

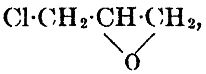
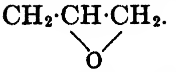
Benzotrichloride is classed as a derivative of an acid (see page 192).

Benzyl chloride yields β-naphthyl benzyl ether, M.P. 99°, when treated in the following manner: Two-tenths of a gram of freshly-cut sodium is dissolved, under a reflux condenser, in 10 cc. of alcohol. To this solution are added 1 g. of β-naphthol and 0.9 cc. of benzyl chloride, and the mixture is warmed to 70° for 15 minutes. The sodium chloride is removed by filtering the hot mixture and is washed with 3 cc. of hot alcohol. On cooling the combined filtrate and washings, the β-naphthyl benzyl ether separates. It is recrystallized from alcohol. This reaction is an illustration of the Williamson method for the preparation of ethers. Compare with the example on page 66.

Chloro- and bromotoluenes can be oxidized to chloro- and bromobenzoic acids by alkaline permanganate (page 168), though the oxidation is comparatively difficult. *Iodotoluenes* can be oxidized by prolonged refluxing with dilute nitric acid (1:1). The halobenzoic acids may be recrystallized from water or dilute alcohol.

MELTING POINTS OF HALOBENZOIC ACIDS

Acid	M.P.	Acid	M.P.
o-Bromobenzoic . . .	148	*p*-Chlorobenzoic	241
m-Bromobenzoic	152	*o*-Iodobenzoic	162
p-Bromobenzoic	251	*m*-Iodobenzoic	185
o-Chlorobenzoic	141	*p*-Iodobenzoic	266
m-Chlorobenzoic	155		

Epichlorohydrin,  $Cl\cdot CH_2\cdot\underset{O}{\underbrace{CH\cdot CH_2}}$, reacts with a variety of sodium salts of acids to form esters of glycide alcohol, HO· $CH_2\cdot\underset{O}{\underbrace{CH\cdot CH_2}}$. The following procedure yields glycidyl 3,5-dinitrobenzoate, M.P. 94°. One and a half grams of 3,5-dinitrobenzoic acid is dissolved in 20 cc. of warm 95 per cent alcohol. The solution is nearly neutralized with 25 per cent sodium hydroxide, and is then made just alkaline to phenolphthalein with 2 to 3 per cent sodium hydroxide. The mixture is placed in an ice bath until precipitation is complete, and the sodium salt is then filtered off and washed with a small amount of cold alcohol. The sodium salt is suspended in 20 cc. of 50 per cent alcohol, 0.5 cc. of epichlorohydrin is added, and the mixture is refluxed for an hour. The ester is precipitated by dilution with 3 or 4 volumes of cold water, and is filtered off and washed with a small amount of cold water. It is purified by recrystallization from a small volume of alcohol.

Iodobenzene is conveniently characterized as follows: Two grams of substance is dissolved in 10 cc. of chloroform and the solution, cooled in an ice bath, is saturated with chlorine (**Hood!**). The precipitate is filtered off and washed with chloroform. The product of this reaction, phenyl iodochloride, $C_6H_5I{\cdot}Cl_2$, is a loose addition product of iodobenzene and chlorine. It decomposes with loss of chlorine when heated, and readily liberates iodine from aqueous potassium iodide.

p-Iodotoluene yields *p*-ditolyl, M.P. 121°, on being refluxed gently for 15 minutes with twice its weight of copper powder. The ditolyl is separated from the copper by solution in boiling alcohol, from which solvent it separates on cooling. It should be recrystallized from the same solvent. The reaction is essentially a modification of the Fittig reaction, with copper replacing the sodium usually employed.

Phenacyl chloride yields esters with the same treatment as given on page 185 for *p*-bromophenacyl bromide. Phenacyl esters having satisfactory properties are given in the following table.

MELTING POINTS OF PHENACYL ESTERS

Phenacyl Ester of	M.P.
Benzoic acid	118
Cinnamic acid	140
Succinic acid	148

p-Nitrobenzyl chloride reacts with the sodium salts of acids to yield esters. The procedure is described on page 186.

ALCOHOLS

1. p-Nitrobenzoates and 3,5-Dinitrobenzoates.—Alcohols react with acid chlorides to form esters. If *p*-nitro- or 3,5-dinitrobenzoyl chloride is used, the esters formed in many cases are solids having convenient properties. One gram of the acid chloride is heated at 100° for 30 minutes with five times the equivalent amount of the alcohol to be identified. The reaction mixture is treated with 15 cc. of water, neutralized with solid sodium bicarbonate, and the product filtered off and recrystallized from dilute alcohol. If the product does not solidify on the addition of the water, the aqueous layer is decanted after neutralization, and the product dissolved in the least possible amount of boiling alcohol. On cooling the solution the product should separate.

MELTING POINTS OF *p*-NITROBENZOATES

Alcohol	M.P. of ester	Alcohol	M.P. of ester
Cinnamyl	78	Isopropyl	110
Ethyl	57	Methyl	96
Ethylene glycol	143	Trimethylene glycol	119
Glycerol (recrystallize the ester from acetone)	192		

MELTING POINTS OF 3,5-DINITROBENZOATES

Alcohol	M.P. of ester	Alcohol	M.P. of ester
Allyl..	48	Isoamyl	62
sec-Amyl	61	Isobutyl.	64
Benzyl	112	Isopropyl	122
n-Butyl	64	Methyl	112
sec-Butyl	75	*n*-Propyl	73
Ethyl	94	Propylene glycol	147

2. Iodoform.—All alcohols containing the CH_3—CHOH— grouping yield iodoform on treatment with iodine and sodium hydroxide or carbonate. For the mechanism of this reaction see page 144.

Two grams each of sodium carbonate and the alcohol are added to 15 cc. of water and the mixture is heated in a water bath to 70 to 80°. One gram of iodine is added in small portions with thorough shaking. If any iodine color remains after the addition is complete, sufficient carbonate is added to remove it. The mixture is cooled and the precipitated iodoform is filtered off, washed with water, and recrystallized from a small amount of alcohol. Iodoform melts at 119°.

In the treatment of hydroxy acids enough additional sodium carbonate must be used to neutralize the acid before the addition of the iodine.

3. Miscellaneous.—*Cholesterol*, $C_{27}H_{45}OH$, forms a benzoate on being gently warmed with the theoretical amount of benzoyl chloride. After the evolution of hydrogen chloride has ceased, the benzoate is recrystallized from a mixture of alcohol and ether (1:1). It melts to an opaque liquid at 146°, and after going through a change of color finally becomes clear at 178°. On cooling the same changes are observed in the reverse order.

Cyclohexanol is readily oxidized to adipic acid, $HOOC(CH_2)_4COOH$, M.P. 151°. Ten drops of the substance is added drop by drop to 2 cc. of boiling concentrated nitric acid (**Caution! Hood!**). The mixture is boiled for 5 minutes, cooled, and treated with 10 cc. of water. After cooling in an ice-salt bath, the adipic acid is filtered off and recrystallized from a small amount of water, this solution also being well cooled before the product is filtered.

Hydroxy acids are considered under Acids.

Triphenylcarbinol does not readily form esters, possibly because of "steric hindrance" resulting from the three large phenyl groups on the central carbon atom. Treatment of the carbinol with an equal weight of phosphorus pentachloride, with gentle heating for a minute or two after the initial reaction has subsided, leads to the formation of triphenylchloromethane, M.P. 112°. The cooled reaction mixture is treated with half-concentrated hydrochloric acid and the product is filtered off, dried, and recrystallized from petroleum ether.

PHENOLS

1. Benzoates.—Many phenols react readily with benzoyl chloride to form crystalline benzoates. The following procedure is satisfactory in most cases. The phenol is heated to 100° with the equivalent amount of benzoyl chloride until the evolution of hydrogen chloride ceases. After cooling, 5 per cent sodium hydroxide is added and after any unreacted benzoyl chloride has been decomposed the benzoate is filtered off, washed with water, and recrystallized, usually from alcohol.

MELTING POINTS OF BENZOATES OF PHENOLS

Phenol	M P of benzoate	Phenol	M P of benzoate
p-Bromophenol	108	Isoeugenol	104
Catechol (dibenzoate)	84	*α*-Naphthol	56
p-Chlorophenol	93	*β*-Naphthol	110
m-Cresol	55	*m*-Nitrophenol	95
p-Cresol	71	*p*-Nitrophenol	142
2,4-Dibromophenol	97	Phenol	71
2,4-Dichlorophenol	97	Phloroglucinol (tribenzoate)	173
2,4-Dinitrophenol	132	Pyrogallol (tribenzoate)	89
Eugenol	70	Resorcinol (dibenzoate)	117
Guaiacol	61	Tribromophenol	81
Hydroquinone (dibenzoate)	199		

2. Picrates.—Certain phenols form easily identifiable picrates. The procedure is the same as that given on page 167 for hydrocarbons. Some difficulty is frequently met in preparing the picrates of phenols of low molecular weight, since they are usually less stable than those of more complex phenols and tend to dissociate during the recrystallization. In such cases it is sometimes helpful to use benzene as the solvent in place of alcohol, and to omit recrystallization.

MELTING POINTS OF PICRATES OF PHENOLS

Phenol	M.P. of picrate	Phenol	M P. of picrate
o-Chlorophenol	81	*p*-Cresol	64
o-Cresol....	90	*α*-Naphthol	189
m-Cresol...	62	*β*-Naphthol	156

3. Bromo Derivatives.—The presence of the hydroxyl group in phenols facilitates substitution of the nuclear hydrogen atoms by halogen. Thus most phenols react readily and almost quantitatively with bromine water to form polybromides in which, as a rule, all available positions ortho and para to the hydroxyl group are brominated. To the phenol in aqueous solution or suspension, bromine water is added until a faint bromine color persists for several minutes, and the precipitated polybromophenol is filtered off, washed with water, and recrystallized from alcohol or dilute alcohol. In the following table are listed the melting points of some bromophenols obtainable in this way. It should be noted that *o*- or *p*-bromophenol or 2,4-dibromophenol will all yield tribromophenol.

MELTING POINTS OF BROMO DERIVATIVES OF PHENOLS

Substance	M P.	Substance	M.P.
2-Bromo-4,6-dichlorophenol	68	Dibromo-*o*-cresol	57
2-Bromo-4,6-dinitrophenol ..	118	Tribromo-*m*-cresol......	84
4-Bromo-2-nitrophenol .	88	Tribromo-orcinol........	104
2,4-Dibromo-6-chlorophenol	76	Tribromophenol.........	96
2,6-Dibromo-4-chlorophenol	92	Tribromophloroglucinol[1]	153
2,4-Dibromo-6-nitrophenol	117	Tribromoresorcinol	111

[1] This product should be recrystallized from water and dried at 100°

4. Ethyl Ethers.—Phenols form ethyl ethers readily when treated with diethyl sulfate and alkali. Only a few of the commoner phenols, however, form ethyl ethers which are solid at ordinary temperatures. One gram of the phenol is dissolved in 20 cc. of 10 per cent sodium hydroxide and 1.25 cc. of diethyl sulfate is added. If the phenol does not dissolve in the alkali, sufficient alcohol is added to effect solution. The mixture is heated to 100° with frequent shaking for 30 minutes, and is then acidified, cooled, and allowed to stand until crystallization is complete. The product is filtered off, washed with water, and recrystallized from alcohol or dilute alcohol.

MELTING POINTS OF ETHYL ETHERS OF CERTAIN PHENOLS

Ethyl ether of	M.P.	Ethyl ether of	M.P.
2,4-Dibromophenol.. . ..	50	*p*-Nitrophenol	59
2,4-Dinitrophenol... . .	86	Tribromophenol......... .	72

5. Miscellaneous.—Certain phenols may be conveniently nitrated to give derivatives suitable for characterization. The procedure in the case of *o-chlorophenol* illustrates the general method, though it is necessary to alter the conditions somewhat in other cases. One gram of *o*-chlorophenol is dissolved in 1 cc. of concentrated sulfuric acid and a mixture of 2 cc. each of concentrated nitric and sulfuric acids is added slowly. After being allowed to stand for 30 minutes, the reaction mixture is poured into cold water and the precipitate is filtered off, washed with water, and recrystallized from 50 per cent alcohol. The product of this reaction, 2-chloro-4,6-dinitrophenol, melts at 113°. It is to be noted that the directive influence of the hydroxyl completely overshadows that of the chloro group.

Hydroquinone (quinol) is readily oxidized to benzoquinone, which unites with unchanged hydroquinone to form the molecular compound quinhydrone, $C_6H_4O_2 \cdot C_6H_4(OH)_2$. One-half of a gram of hydroquinone is dissolved in 15 cc. of warm water. The solution is cooled and then treated slowly and with shaking with 15 cc. of 10 per cent ferric chloride solution. The product is filtered off and washed with 20 cc. of cold water. It is then warmed to 40° with 30 cc. of water, cooled, filtered, and again washed with water. The quinhydrone forms greenish black needles that melt at approximately 170° after beginning to sublime at 145 to 150°. (The bath should be heated rapidly in observing this melting point.)

Phenolic acids are treated under acids.

Picric acid may be characterized in the form of the picrate of naphthalene or of a naphthol, prepared as directed on page 167.

ETHERS

1. Dinitrobenzoates of Corresponding Alcohols.—Aliphatic ethers may be converted to the dinitrobenzoates of the corresponding alcohols by treatment with zinc chloride and dinitrobenzoyl chloride. It is evident that the method would generally be unsatisfactory in the case of a mixed ether, since two products would be formed in equivalent amounts. A mixture of 2 cc. of the ether, 0.25 g. of freshly-fused and powdered zinc chloride, and 1.0 g. of 3,5-dinitrobenzoyl chloride is refluxed for 30 minutes, a water bath being used in case the ether boils under 100°. The reaction mixture is poured into cold water and the precipitate filtered off and washed thoroughly. It is then warmed with 10 cc. of saturated aqueous sodium bicarbonate for 15 minutes to destroy excess acid chloride. The residue is recrystallized from dilute alcohol. The melting points of the dinitrobenzoates are given on page 173.

2. Nitro Derivatives.—Some aromatic ethers may be nitrated to give solid nitro derivatives. Specific directions for only a few cases are given.

Anisole yields 2,4-dinitroanisole, M.P. 95°, when treated as follows: To a solution of 1 g. of anisole in 1 cc. of concentrated sulfuric acid is added slowly and with cooling a mixture of 1 cc. each of concentrated nitric and sulfuric acids. The mixture is allowed to stand for 10 minutes, is then heated to 50 to 60° for 5 minutes, and is finally poured into cold water. The precipitate is filtered off, washed with water, and recrystallized from 50 per cent alcohol.

The three *cresyl ethyl ethers* and *diphenyl ether* may be nitrated according to the following directions: One gram of the substance is added slowly with shaking to 10 cc. of fuming nitric acid which is cooled in an ice bath. (**Caution! Hood!**) The mixture is then poured into cold water, the precipitate is filtered off, washed with water, and recrystallized from alcohol.

MELTING POINTS OF NITRO DERIVATIVES

Substance	M.P.
4,4′-Dinitrodiphenyl ether	143
3,5-Dinitro-2-ethoxytoluene	51
3,5-Dinitro-4-ethoxytoluene	75
2,4,6-Trinitro-3-ethoxytoluene	75

Phenetole yields a symmetrical trinitro derivative, M.P. 80°, as follows: Five drops of substance dissolved in 3 cc. of concentrated sulfuric acid is treated with shaking and cooling with 3 successive portions of 1 cc. each of concentrated nitric acid. The mixture is allowed to stand for 5 minutes at room temperature, the tube being cooled if it becomes hot during this time, and is then poured into cold water. The product is recrystallized from 50 per cent alcohol after being filtered off and washed with water.

Resorcinol dimethyl ether is nitrated to give 4,6-dinitroresorcinol dimethyl ether, M.P. 157°, as follows: One cubic centimeter of substance is added dropwise with shaking to an ice-cold solution of 1 g. of potassium nitrate in 10 cc. of concentrated sulfuric acid. The mixture is allowed to stand in the ice bath for 5 minutes and is then poured into cold water. After the precipitate has coagulated, it is filtered off and recrystallized from alcohol. If the nitration proceeds too far some of the trinitro derivative, dimethyl styphnate, M.P. 124°, will be formed.

3. Picrates.—Certain aromatic ethers form picrates according to the directions given on page 167.

MELTING POINTS OF PICRATES

Ether	M P of Picrate
α-Naphthyl ethyl ether	118
β-Naphthyl ethyl ether	104
Veratrole	56

4. The three **cresyl ethyl ethers** may be oxidized to the corresponding ethoxybenzoic acids by the method given on page 168 for hydrocarbons using alkaline permanganate.

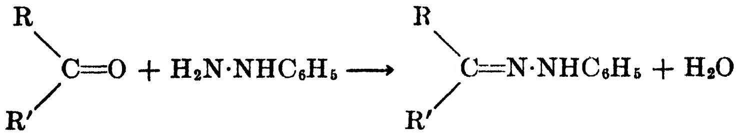
MELTING POINTS OF ETHOXYBENZOIC ACIDS

Substance	M.P
o-Ethoxybenzoic acid	22
m-Ethoxybenzoic acid	137
p-Ethoxybenzoic acid	195

Certain ethers which contain other characteristic groups are considered elsewhere. Thus, *vanillin* is listed as an aldehyde though it also contains a methoxy and an hydroxy group.

ALDEHYDES, KETONES, AND ACETALS

1. Phenylhydrazones.—One of the most important reagents for the characterization of aldehydes and ketones is phenylhydrazine. This reagent leads to the formation of phenylhydrazones in accordance with the following equation:



$$RR'C{=}O + H_2N{\cdot}NHC_6H_5 \longrightarrow RR'C{=}N{\cdot}NHC_6H_5 + H_2O$$

One-half gram of substance is added to a solution of 1 cc. of phenylhydrazine and 0.5 cc. of glacial acetic acid in 5 cc. of water, The mixture is heated to boiling and, after cooling, is thoroughly shaken to hasten the crystallization of the product. After it has completely precipitated, the product is filtered off and recrystallized from dilute alcohol.

MELTING POINTS OF PHENYLHYDRAZONES

Phenylhydrazone of	M.P	Phenylhydrazone of	M.P.
Acetophenone	105	Furfural	97
Anisaldehyde	120	*p*-Hydroxybenzaldehyde	177
Benzalacetone	157	*o*-Nitrobenzaldehyde	156
Benzaldehyde	158	*m*-Nitrobenzaldehyde	120
Benzil (diphenylhydrazone)	225	*p*-Nitrobenzaldehyde	159
Benzophenone	137	Piperonal	100
Cinnamaldehyde	168	Salicylaldehyde	142
Cyclohexanone	77	Vanillin	105

2. 2,4-Dinitrophenylhydrazones.—Many aldehydes and ketones which yield liquid or difficultly crystallizable phenylhydrazones form convenient derivatives with 2,4-dinitrophenylhydrazine.[1] One-half gram of 2,4-dinitrophenylhydrazine is dissolved by warming in a solution of 1 cc. of concentrated

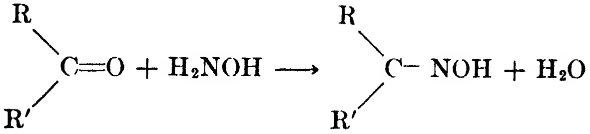
MELTING POINTS OF 2,4-DINITROPHENYLHYDRAZONES

Dinitrophenylhydrazone of	M.P.	Dinitrophenylhydrazone of	M.P
Acetaldehyde	164	Cyclohexanone	160
Acetone	128	Diethyl ketone	156
Acetophenone	237	Ethyl acetoacetate	96
Acrolein	165	Formaldehyde	167
Anisaldehyde	250	Isobutyraldehyde	182
Benzalacetone	223	Levulinic acid	92
Benzil (didinitrophenylhydrazone)	185	Menthone	145
Butanone	115	*o*-Nitrobenzaldehyde	192
n-Butyraldehyde	122	*m*-Nitrobenzaldehyde	268d
d-Camphor	175	*p*-Nitrobenzaldehyde	320
Citronellal	78	Propionaldehyde	155
Crotonaldehyde	190	Pyruvic acid	213

[1] For the preparation of this reagent see Allen, *J. Am. Chem. Soc.*, **52,** 2955 (1930).

sulfuric acid in 10 cc. of 95 per cent alcohol. To this solution is added a slight excess of the unknown dissolved in a few cubic centimeters of alcohol. The mixture is heated to boiling and set aside until crystallization is complete. If no precipitate forms, the mixture is diluted with 10 per cent sulfuric acid. The product is filtered off and recrystallized from alcohol or dilute alcohol.

3. Oximes.—Most aldehydes and ketones react with hydroxylamine to form oximes:



$$\begin{matrix} R \\ & C{=}O + H_2NOH \longrightarrow \\ R' \end{matrix} \quad \begin{matrix} R \\ & C{-}NOH + H_2O \\ R' \end{matrix}$$

The oximes are frequently convenient derivatives for the characterization of the original substances. One gram of hydroxylamine hydrochloride is dissolved in 4 cc. of water. To this solution is added enough 10 per cent sodium hydroxide to make the solution alkaline to phenolphthalein. Four-tenths of a gram of the unknown and just enough alcohol to effect solution at the boiling temperature are then added. The solution is refluxed for 15 minutes, or longer if necessary (*d*-camphor, for example, requires 60 minutes) and is then cooled. If crystals separate, they are filtered off and recrystallized from alcohol or dilute alcohol. If no solid separates on cooling the reaction mixture, it is diluted with 2 or 3 volumes of water and the precipitated solid filtered off and recrystallized.

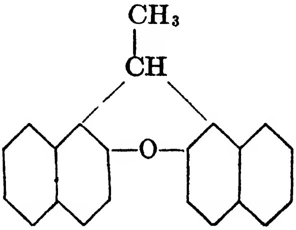
MELTING POINTS OF OXIMES

Oxime of	M.P.	Oxime of	M.P.
Acetophenone	59	Cyclohexanone	90
Acetone	59	Diacetone alcohol	57
Anisaldehyde	92	*o*-Nitrobenzaldehyde	102
Benzalacetone	115	*m*-Nitrobenzaldehyde	120
Benzoin	151	*p*-Nitrobenzaldehyde	129
Benzophenone	141	Piperonal	110
d-Camphor	118	Salicylaldehyde	57
Cinnamaldehyde	138	Vanillin	117

4. Iodoform.—Compounds containing the CH_3CO— group yield iodoform on treatment with iodine and sodium carbonate. For directions see page 173.

5. Acids from Aromatic Aldehydes.—Aromatic aldehydes are readily oxidized to the corresponding acids under the influence of dilute alkaline permanganate at ordinary temperatures. The resulting acid can be obtained by acidification of the solution after removal of the manganese dioxide. The melting points of important acids obtainable in this manner are given on page 193.

6. Miscellaneous.—*Acetaldehyde* condenses with β-naphthol to form ethylidene-β-dinaphthyl oxide, M.P. 173°,



One-half gram of the aldehyde is heated on a water bath for 10 minutes with 1 g. of β-naphthol and 1 drop of concentrated hydrochloric acid. After cooling, 5 cc. of chloroform is added and the mixture heated to boiling for a minute and then filtered while hot. After 15 cc. of alcohol has been added to the filtrate, it is cooled thoroughly. The precipitate is filtered off and washed with 50 per cent alcohol. *Paraldehyde,* a trimer of acetaldehyde which is depolymerized by heating with mineral acids, and *acetal,* which is readily hydrolyzed to yield acetaldehyde, may be treated in the same way. In the case of acetal the heating period should be increased to 1 hour.

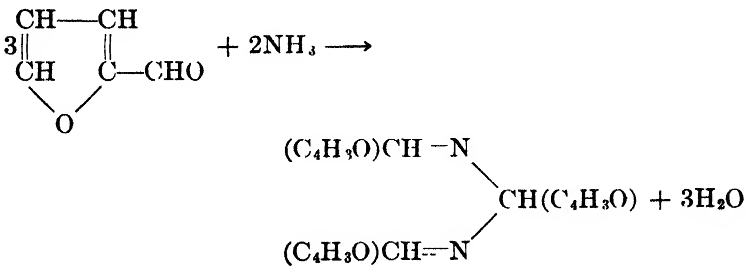
Acetone is readily condensed with benzaldehyde to give dibenzalacetone, $C_6H_5CH{=}CH{-}CO{-}CH{=}CHC_6H_5$, M.P. 112°. (Compare page 70.) To one-half cubic centimeter of acetone are added 2 cc. of water, 2 cc. of benzaldehyde, 10 cc. of alcohol, and 2.5 cc. of 10 per cent sodium hydroxide. The mixture is boiled gently for a minute and is then cooled. The product is filtered off, washed with a small amount of alcohol, and recrystallized from this solvent.

Benzoquinone is reduced by granulated zinc and warm dilute hydrochloric acid to hydroquinone, the latter substance reacting with an equal amount of benzoquinone to form quinhydrone (see page 177). If the solution is too hot, the quinhydrone does not precipitate out and the reduction goes completely to hydroquinone, in which case addition of an equivalent amount of benzoquinone yields the desired product.

Crotonaldehyde reacts with hydrogen chloride to form β-chlorobutyraldehyde, M.P. 96°, the negative part of the adding molecule going to the position farther away from the carbonyl group. One gram of the aldehyde is saturated with dry hydrogen chloride (see page 44) and is allowed to stand overnight. The product is dissolved in 10 cc. of boiling alcohol and solid calcium carbonate is added to the hot solution until the evolution of carbon dioxide ceases. A little norite is added and the mixture boiled for 2 or 3 minutes and filtered hot. The filtrate is cooled and water is added to it until it becomes quite turbid. After standing in an ice-salt bath until crystallization is complete, the product is filtered off and recrystallized from dilute alcohol.

Cyclohexanone may be oxidized to adipic acid according to the directions given on page 174.

Furfural condenses with ammonia to form the so-called furfuramide according to the equation:

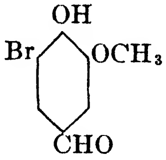


The product is unfortunately named since it is not an amide. One cubic centimeter of furfural is allowed to stand for 6 hours with 6 cc. of concentrated ammonium hydroxide. The product is filtered off and recrystallized from alcohol. M.P. 117°.

Certain *hydroxyketones* may be oxidized to diketones which are convenient derivatives in many cases. The directions given on page 97 for the oxidation of *benzoin* to benzil, M.P. 95°, may be conveniently adapted to a small scale preparation.

Keto acids or their *derivatives* are discussed under acids or acid derivatives.

Vanillin reacts with an excess of bromine water to give a monobromo derivative



M P. 160°. This product may be recrystallized from alcohol. Vanillin may also be acetylated by the following method: One gram of vanillin dissolved in 7 cc. of 5 per cent sodium hydroxide is treated in a small separatory funnel with 0.8 cc. of acetic anhydride in 5 cc. of ether, the mixture being shaken frequently during a period of 1 hour. Sufficient ether is then added to bring any solid material into solution, the ether layer separated, and the ether removed. The residue is recrystallized from dilute alcohol. Vanillin acetate melts at 77°. Other *phenolic aldehydes* may be treated in a similar manner.

Carboxylic Acids and Their Salts

1. p-Bromophenacyl Esters.— *p*-Bromophenacyl bromide[1] is a very useful reagent for forming characteristic derivatives of many carboxylic acids. The side-chain bromine group is comparatively reactive because of the presence of the adjacent carbonyl group, so that esters are readily formed from the sodium salts of acids. Furthermore, the esters so formed usually have sufficiently high melting points and favorable solubilities so that purification and characterization offer no great difficulties.

The reaction between *p*-bromophenacyl bromide and the sodium salt of an acid may be written in the general form:

$$RCOONa + BrC_6H_4COCH_2Br \longrightarrow BrC_6H_4COCH_2OCOR + NaBr$$

This is an example of a generally applicable method for preparing esters from alkyl or side-chain halides.

---

[1] The preparation of *p*-bromophenacyl bromide is described on page 111.

One-half gram of the substance under examination is dissolved in a small volume of 75 per cent alcohol, with warming if necessary. If the substance is a free acid, the solution is *carefully* neutralized with dilute sodium hydroxide, a drop of phenolphthalein being used as indicator. Slightly less than the theoretical amount of *p*-bromophenacyl bromide is then added, and the mixture refluxed for an hour. An equal volume of water is added, the mixture is cooled, and the product is filtered off and recrystallized from alcohol.

If the salt of an unidentified acid is being used, satisfactory results may be obtained by employing equal amounts of the salt and *p*-bromophenacyl bromide.

MELTING POINTS OF *p*-BROMOPHENACYL ESTERS

Acid	M.P.	Acid	M.P.
Acetic	85	Isovaleric	68
Anisic	152	Lactic	112
Benzoic	119	Lauric	76
n-Butyric	63	Palmitic	86
n-Caproic	71	Phenoxyacetic	150
n-Caprylic	67	Phenylacetic	89
o-Chlorobenzoic	107	Phthalic	153
Cinnamic	146	Propionic	63
Citric	148	Stearic	90
Crotonic	96	Succinic	211
Diphenylacetic	109	*o*-Toluic	57
Formic	102	*m*-Toluic	108
Hippuric	151	*p*-Toluic	153
		n-Valeric	75

In case a product having a melting point between 100 and 120° is obtained, it is necessary to ascertain whether the product is unchanged *p*-bromophenacyl bromide by means of determining a mixed melting point with that substance. *p*-Bromophenacyl bromide melts at 109°.

2. p-Nitrobenzyl Esters.—The salts of acids react with *p*-nitrobenzyl bromide in a manner similar to their reaction with *p*-bromophenacyl bromide:

$$RCOONa + NO_2C_6H_4CH_2Br \longrightarrow NO_2C_6H_4CH_2OCOR + NaBr.$$

One-half gram of the sodium salt of an acid is dissolved in 5 cc. of water. If the substance to be treated is a free acid, an amount of the acid equivalent to 0.5 g. of the salt is dissolved or suspended in 3 cc. of water and the mixture *carefully* neutralized (phenolphthalein indicator) with 10 per cent sodium hydroxide. Ten cubic centimeters of 95 per cent alcohol and the amount of *p*-nitrobenzyl bromide equivalent to the salt are added and the mixture is refluxed for 30 minutes. If an insoluble ester separates from the solution during the refluxing, a little more alcohol is added. Finally the mixture is cooled and the precipitated ester filtered off and recrystallized from alcohol or dilute alcohol. In some cases it may be necessary to add water to the hot reaction mixture to the point of incipient cloudiness to obtain sufficient recovery of the ester.

MELTING POINTS OF *p*-NITROBENZYL ESTERS

Acid	M.P. of ester	Acid	M.P. of ester
Acetic	78	Malic (monoester)	87
Anisic	132	Malic (diester)	124
Benzilic	99	Malonic	85
Benzoic	89	*o*-Nitrobenzoic	112
m-Bromobenzoic	105	*m*-Nitrobenzoic	141
p-Bromobenzoic	139	*p*-Nitrobenzoic	168
o-Chlorobenzoic	106	*m*-Nitrocinnamic	174
p-Chlorobenzoic	129	Oxalic	204
Cinnamic	116	Phenoxyacetic	65
Citric	102	Phenylacetic	65
2,4-Dinitrobenzoic	142	Phthalic	155
Diphenylacetic	104	Salicylic	98
Fumaric	151	Succinic	88
Hippuric	136	*d*-Tartaric	163
Hydrocinnamic	36	Terephthalic	263
m-Hydroxybenzoic	107	*o*-Toluic	91
p-Hydroxybenzoic	181	*m*-Toluic	86
Maleic	89	*p*-Toluic	104
		Vanillic	140

If a product having a melting point in the neighborhood of 100° is obtained, a mixed melting point with *p*-nitrobenzyl bromide, M.P. 100°, should be determined to insure that the product is not the unchanged reagent. If the unchanged reagent is recovered, the reaction should be repeated with the addition of a slight excess of sodium hydroxide.

In the case of a *hydroxybenzoic acid* the presence of two reactive groups complicates matters. It is theoretically possible in such a case to obtain in addition to an ester, an ether, or an ether ester. The melting points of these derivatives are given below.

MELTING POINTS OF *p*-NITROBENZYL DERIVATIVES OF HYDROXYBENZOIC ACIDS

Substance	M.P. of ether	M.P. of ether ester
m-Hydroxybenzoic acid	195	143
p-Hydroxybenzoic acid	260	196
Salicylic acid	167	138

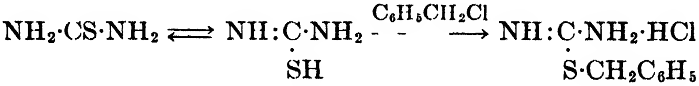
3. Methyl or Ethyl Esters.—Some acids, particularly substituted aromatic acids, form solid methyl or ethyl esters which

MELTING POINTS OF ESTERS

Acid	M.P. of methyl ester	M.P. of ethyl ester
Anisic	45	
Benzilic	74	34
p-Bromobenzoic	81	
p-Chlorobenzoic	44	
2,4-Dinitrobenzoic	70	41
3,5-Dinitrobenzoic	112	94
Fumaric	102	
m-Hydroxybenzoic	70	72
p-Hydroxybenzoic	131	116
Mandelic	57	
β-Naphthoic	77	
m-Nitrobenzoic	78	47
p-Nitrobenzoic	96	57
m-Nitrocinnamic	123	78
Terephthalic	140	44
Vanillic	62	44

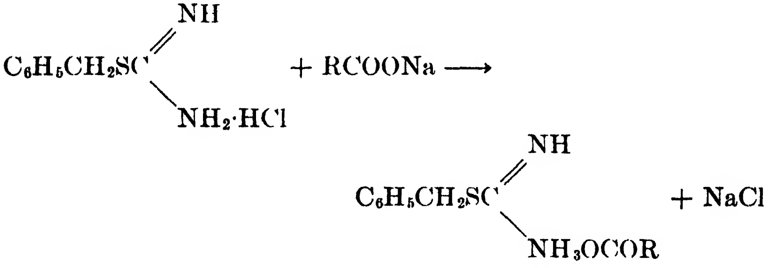
are suitable for characterization. These esters may be formed by the following simple esterification procedure: A gram of the acid is dissolved in 10 cc. of absolute methyl or ethyl alcohol, 1 cc. of concentrated sulfuric acid is added, and the mixture is refluxed for 30 minutes. The ester is precipitated by cooling the reaction mixture or by addition of water if necessary and is recrystallized from alcohol or dilute alcohol. In some cases, notably oxalic acid, the refluxing period may be shortened.

4. Pseudobenzylthiourea Salts.[1]—The sodium salts of most acids, including sulfonic acids, react with pseudobenzylthiourea hydrochloride to form salts which are generally nicely crystalline compounds. The reagent is formed by the reaction of benzyl chloride with the pseudo form of thiourea:



$$NH_2{\cdot}CS{\cdot}NH_2 \rightleftharpoons NH{:}\underset{SH}{C}{\cdot}NH_2 \xrightarrow{C_6H_5CH_2Cl} NH{:}\underset{S\cdot CH_2C_6H_5}{C}{\cdot}NH_2{\cdot}HCl$$

The resulting salt enters into a double decomposition with the salt of an organic acid to form a pseudobenzylthiourea salt which is less soluble than the hydrochloride:



This is an ionic reaction and is therefore practically instantaneous.

One-half gram of the acid is dissolved or suspended in 10 cc. of warm water and *carefully* neutralized to phenolphthalein with 10 per cent sodium hydroxide. The resulting solution is added

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[1] The authors are indebted to Professor J. J. Donleavy for pointing out to them the convenience of the pseudobenzylthiourea salts and for supplying the necessary data in advance of publication in *J. Am. Chem. Soc.*, **58**, 1004 (1936).

to a slight excess of pseudobenzylthiourea hydrochloride dissolved in a small amount of warm alcohol. The product which separates on cooling is filtered off and recrystallized from alcohol.

In the case of the salt of an acid, half a gram is dissolved in warm water and added directly to the reagent as described above.

MELTING POINTS OF PSEUDOBENZYLTHIOUREA SALTS

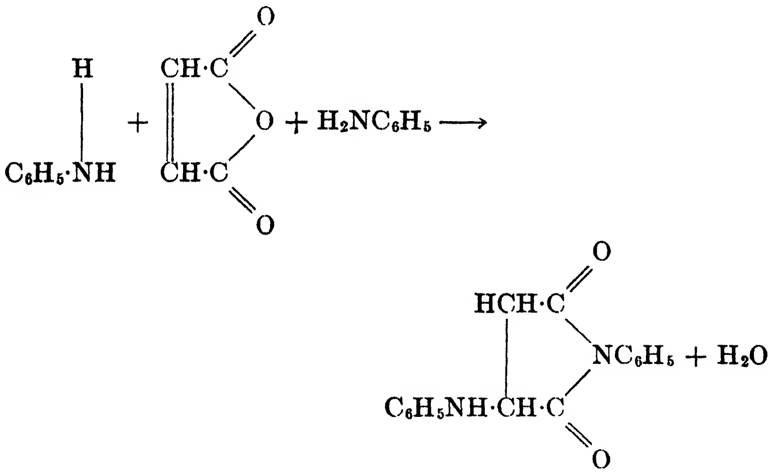
Acid	M.P. of salt	Acid	M.P. of salt	Acid	M.P. of salt
Acetic	134	Lactic	153	Phthalic	151
Benzoic	166	Maleic (acid salt)	163	Propionic	148
n-Butyric	146	Mandelic	166	Salicylic	146
Cinnamic	175	*o*-Nitrobenzoic	159	Stearic	143
Crotonic	162	*m*-Nitrobenzoic	163	Succinic	149
Diphenylacetic	145	*p*-Nitrobenzoic	182	*o*-Toluic	140
Formic	146	Oxalic	193	*m*-Toluic	164
Fumaric	178	Palmitic	141	*p*-Toluic	190
Isobutyric	143				

5. Miscellaneous.—*Chloroacetic acid* is conveniently identified as the anilide. To 1 g. of the acid is added drop by drop 2 cc. of thionyl chloride. **(Hood!)** The mixture is refluxed gently for 2 minutes, cooled, and carefully treated with 2 cc. of aniline, after which it is gently warmed for a few minutes. After cooling, 25 cc. of water is added, the mixture acidified, and the product filtered and recrystallized twice from water. *α*-Chloroacetanilide melts at 134°. For the use of thionyl chloride in the preparation of acid chlorides see page 110.

Cinnamic and mandelic acids are readily oxidized by potassium permanganate to yield benzaldehyde, which in turn may be characterized in the form of its phenylhydrazone. The substance is treated with the required amount of a 2 per cent solution of potassium permanganate (with mandelic acid the products of oxidation are benzaldehyde and potassium carbonate; with cinnamic acid, benzaldehyde and potassium oxalate or carbonate) and, after precipitation of the manganese dioxide is complete, the benzaldehyde is removed by distillation of the reaction mixture (essentially a steam distillation). The distillate is treated with the required amount of phenylhydrazine, and, after shaking for 1 or 2 minutes, is acidified with dilute hydrochloric acid. The phenylhydrazone is filtered off and recrystallized from 50 per cent alcohol. It melts at 158°.

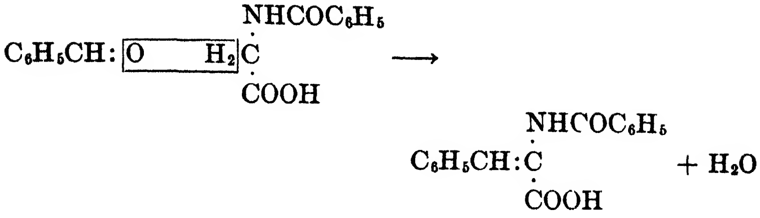
Fumaric, maleic, and malic acids and *maleic anhydride* are converted into phenylaspartic anil by being refluxed for an hour with twice their weight of aniline. The anil is extracted from the cooled reaction cake with boiling alcohol, from which solvent it separates on cooling. The product thus obtained should be recrystallized from alcohol, with the use of norite. The pure anil melts at 212°.

The first step in the reaction in each case can be considered to be dehydration to form maleic anhydride, which then combines with two molecules of aniline:



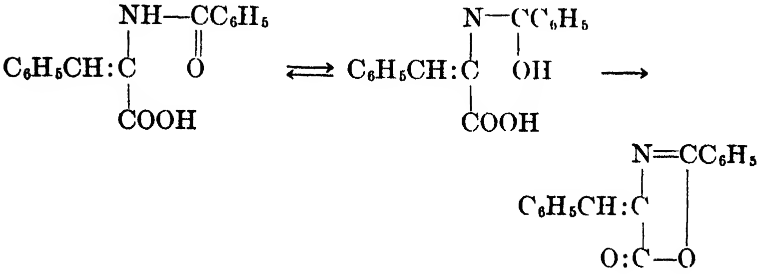
Hippuric acid is readily converted to a satisfactory derivative as follows: A mixture of 2 g. of hippuric acid, 1 g. of benzaldehyde, 1 g. of fused sodium acetate, and 3 cc. of acetic anhydride is heated to 100° for 45 minutes. The solution is then cooled and the crystals which separate are filtered off and washed with cold alcohol. The product, the lactimide of benzalhippuric acid, is recrystallized from benzene. It melts at 165°.

The first step in this reaction is the condensation of benzaldehyde with hippuric acid:



$$C_6H_5CH{:}\boxed{O\quad H_2}\overset{NHCOC_6H_5}{\underset{COOH}{C}} \longrightarrow C_6H_5CH{:}\overset{NHCOC_6H_5}{\underset{COOH}{C}} + H_2O$$

The hydrogen on the nitrogen then migrates to the carbonyl group and an inner ester, in this case a lactimide or azlactone, is formed by loss of water with the carboxyl group:



Hydroxy and keto acids containing the $CH_3CHOH—$ or $CH_3CO—$ group may be treated with iodine and sodium carbonate to yield iodoform. Directions for this reaction are given on page 173. For the preparation of the 2,4-dinitrophenylhydrazones of *levulinic* and *pyruvic* acids see page 180.

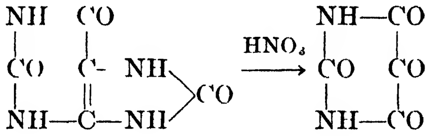
Phenolic acids may be acetylated by being refluxed for 10 minutes with an excess of acetic anhydride. When the reaction is complete the reaction product is poured into hot water and the mixture is stirred until the excess anhydride has been decomposed. The acetate separates on cooling and is recrystallized from water or dilute alcohol.

Melting Points of Acetates of Phenolic Acids

Acid	M.P.	Acid	M.P.
Gallic	170	Salicylic	135 (aspirin)
m-Hydroxybenzoic	131	Vanillic	142
p-Hydroxybenzoic	187		

Salicylic acid may be nitrated as follows: To a solution of 0.3 g. of substance in 15 cc. of boiling water is added slowly 3 cc. of concentrated nitric acid. After boiling for 5 minutes, the mixture is cooled and diluted and the precipitate filtered off and recrystallized from water. The product, 5-nitro-2-hydroxybenzoic acid, melts at 228° after sintering at 220°.

Uric acid is oxidized by nitric acid to alloxan in accordance with the following equation:



Alloxan is the ureide of mesoxalic acid, $CO(COOH)_2$.

One gram of uric acid is added slowly with constant stirring to 20 cc. of concentrated nitric acid. The mixture is allowed to stand until crystallization is complete (24 hours or longer) and is then filtered. The alloxan is washed with a *small amount of ice water*. A drop of an aqueous solution of the substance produces a red color when placed on the skin. Alloxan loses its water of crystallization and darkens between 150 and 170° but does not melt.

Carboxylic Acid Derivatives

ESTERS, AMIDES, IMIDES, ANHYDRIDES, ACID HALIDES, AND CYANIDES

1. Insoluble Solid Acids from Their Derivatives.—Many derivatives of insoluble solid acids are conveniently characterized by hydrolysis to the corresponding acid. A typical procedure follows: One gram of the substance is refluxed with 10 cc. of 10 per cent sodium hydroxide until it has completely gone into solution or, if one of the products is insoluble in boiling water, for 1 hour. The solution is cooled, acidified with hydrochloric acid, and the precipitated organic acid filtered off and recrystallized from water or dilute alcohol.

Some comparatively stable substances, such as certain esters, are more rapidly saponified by being refluxed with a smaller amount of 40 per cent sodium hydroxide and enough alcohol to give a clear solution at the refluxing temperature.

There are some acid derivatives, such as certain substituted benzamides, which are very resistant to hydrolysis. Such compounds can usually be converted to nitro or other derivatives by methods described below.

In the treatment of derivatives of acids comparatively soluble in water (see classified lists in Chap. VI for qualitative solubilities) some care must be exercised to keep the volume of solutions as small as possible and to cool them thoroughly to precipitate the products.

Melting Points of Acids

Acid	M P	Acid	M P.
Anisic	184	Isophthalic	330
Benzilic	150	α-Naphthoic	162
Benzoic	122	β-Naphthoic	185
o-Bromobenzoic	150	*o*-Nitrobenzoic	147
m-Bromobenzoic	155	*m*-Nitrobenzoic	141
p-Bromobenzoic	251	*p*-Nitrobenzoic	242
o-Chlorobenzoic	141	Palmitic	64
m-Chlorobenzoic	158	Phenoxyacetic	99
p-Chlorobenzoic	242	Phenylacetic	77
Cinnamic	133	Phthalic	190 to 200d
2,4-Dinitrobenzoic	179	Salicylic	159
3,5-Dinitrobenzoic	205	Stearic	69
Fumaric	200 + (sublimes)	Succinic	188
Gallic	240d	Terephthalic	Sublimes
Hippuric	187	*o*-Toluic	102
Hydrocinnamic	49	*m*-Toluic	110
m-Hydroxybenzoic	201	*p*-Toluic	177
p-Hydroxybenzoic	213	Vanillic	207

2. Insoluble Solid Amines from Substituted Amides.— The procedure in the preceding paragraph may be applied to the hydrolysis of substituted amides in cases where the corresponding amine is to be isolated. The amine is isolated simply by cooling the reaction mixture at the completion of the refluxing period, the precipitated amine being recrystallized from water or dilute alcohol. Note the remark in the preceding paragraph concerning the stability of some amides.

MELTING POINTS OF INSOLUBLE AMINES

Amine	M.P.	Amine	M.P.
p-Anisidine	58	*o*-Nitroaniline	71
Benzidine	128	*m*-Nitroaniline	112
p-Bromoaniline	66	*p*-Nitroaniline	148
p-Chloroaniline	70	*m*-Phenylenediamine	63
2,4-Dichloroaniline	63	*p*-Toluidine	45
Diphenylamine	54	*s*-Tribromoaniline	119
α-Naphthylamine	50	*s*-Trichloroaniline	77
β-Naphthylamine	112		

3. Anilides from Acid Halides and Anhydrides.—Anilides are amides having one of the hydrogen atoms on the amide nitrogen replaced by a phenyl or substituted phenyl group. They are in general prepared in the same manner as unsubstituted amides, but in many cases are preferable to the latter for purposes of characterization because of their smaller solubility in water. The substance to be tested is cautiously treated with a slight excess of aniline and the mixture is heated to 100° for 5 minutes. It is then cooled, diluted with water, and acidified with hydrochloric acid. The precipitated anilide is filtered off, washed with cold water, and recrystallized from water or dilute alcohol.

MELTING POINTS OF ANILIDES

Acid	M.P. of anilide	Acid	M.P. of anilide
Acetic	114	Isopropylacetic	114
Anisic	168	*o*-Nitrobenzoic	155
Benzoic	160	*m*-Nitrobenzoic	153
Bromoacetic	131	*p*-Nitrobenzoic	204
n-Butyric	92	Palmitic	90
n-Caproic	95	Phenoxyacetic	99
Chloroacetic	134	Phenylacetic	117
o-Chlorobenzoic	114	Propionic	104
m-Chlorobenzoic	123	Stearic	93
p-Chlorobenzoic	194	Succinic	226
3,5-Dinitrobenzoic	234	*o*-Toluic	125
n-Heptoic	71	*p*-Toluic	140
Hydrocinnamic	92	Trichloroacetic	94
Isobutyric	105	*n*-Valeric	63

4. p-Bromophenacyl Esters from Acid Derivatives.—The procedure described below furnishes a convenient method of obtaining easily purified and characterized *p*-bromophenacyl esters from acid derivatives such as esters and anhydrides. In the case of esters and other comparatively difficultly hydrolyzed substances, 1 g. of the substance is refluxed for an hour with 5 cc. of 40 per cent sodium hydroxide and enough alcohol to give a clear solution at the boiling temperature. The solution is then made just neutral to phenolphthalein with dilute hydrochloric acid, is treated with slightly less than the calculated quantity of *p*-bromophenacyl bromide and sufficient alcohol to give a clear solution at the refluxing temperature, and refluxed for 30 minutes. An equal volume of water is added and the ester, which separates on cooling, is filtered off and recrystallized from alcohol.

Ethyl lactate and lactamide should be saponified in the following manner: One gram of the substance is dissolved in 5 cc. of water containing a drop of phenolphthalein solution, and 10 per cent sodium hydroxide is then slowly added to the boiling solution until a faint pink color which persists is produced.

In the case of anhydrides and other easily hydrolyzed compounds, hydrolysis is accomplished by refluxing with water until the reaction is complete, after which the solution is neutralized with alkali (phenolphthalein being used as the indicator) and is then treated with *p*-bromophenacyl bromide as directed above.

The melting points of the *p*-bromophenacyl esters of common acids are listed on page 185.

5. p-Nitrobenzyl Esters from Acid Derivatives.—Compare with the preceding paragraph. The directions given there can be taken over completely for the preparation of *p*-nitrobenzyl esters, *p*-nitrobenzyl bromide being used in place of *p*-bromophenacyl bromide. The remarks on page 186 on the isolation and purification of these esters should be noted. The melting points of the esters are given on page 186.

6. Pseudobenzylthiourea Salts from Acid Derivatives.—The substance may be saponified as directed in Paragraph 4 above, and after being made faintly alkaline to phenolphthalein, is treated with pseudobenzylthiourea hydrochloride as directed on page 188.

7. Miscellaneous.—Some *aliphatic amides* such as *acetamide* may be converted into anilides by refluxing with aniline. This reaction involves the replacement of the volatile base, ammonia, by one less volatile. The substance is refluxed with an equal weight of aniline for an hour, and the reaction mixture is then poured into dilute hydrochloric acid. The anilide is filtered off and recrystallized from water or dilute alcohol. For melting points see Paragraph 3.

Substituted amides, such as *acetanilide, p-acetotoluide,* and *benzanilide,* may be nitrated to give crystalline derivatives. In the three cases mentioned, 1 g. of substance is added in small portions with shaking to a cooled mixture of 5 cc. each of concentrated sulfuric and nitric acids. After 2 minutes the reaction mixture is poured into cold water and the precipitate filtered off, washed with water, and recrystallized from alcohol. *Phenacetin* (*p*-ethoxyacetanilide) must be treated with a milder reagent. One-half gram of phenacetin is added to a solution of 5 cc. of concentrated nitric acid in 15 cc. of water. The mixture is heated to 70 to 80° for half a minute and is then poured into cold water. The precipitated nitro compound is filtered off and recrystallized from 50 per cent alcohol.

MELTING POINTS OF NITROAMIDES

Substance	M.P.	Substance	M.P.
3,5-Dinitro-*p*-acetotoluide....	195	*p*-Nitrobenzanilide..........	199
p-Nitroacetanilide...........	214	2-Nitro-4-ethoxyacetanilide..	103
3-Nitro-*p*-acetotoluide......	148		

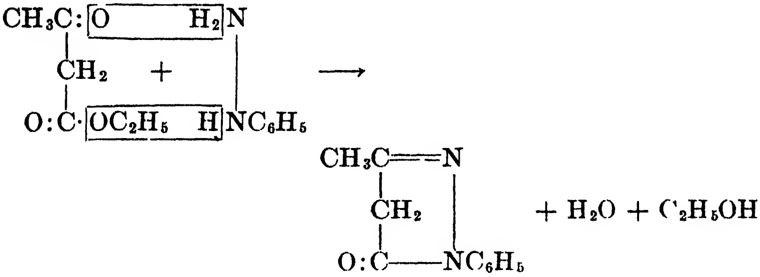
o-Bromoacetanilide and o-chloroacetanilide may be hydrolyzed according to the directions given on page 193 for substituted amides. In these two cases the resulting amines should be steam distilled and brominated as described on page 201.

Certain esters may be characterized by conversion into amides. Thus *diethyl carbonate* and *diethyl oxalate* yield crystalline half amides, urethane and ethyl oxamate, respectively, when treated with ammonia. In the case of diethyl carbonate an equal volume of concentrated ammonium hydroxide and sufficient alcohol to give a clear solution are added to the ester, and the mixture is allowed to stand in a stoppered test tube for at least 2 days. The urethane is obtained from the reaction mixture by evaporation to dryness under reduced pressure and recrystallization of the residue from petroleum ether. M.P. 48°.

Ethyl oxamate is prepared by cooling a solution of 1 cc. of diethyl oxalate in 2 cc. of alcohol in an ice-salt bath and adding dropwise a similarly cooled solution of 0.5 cc. of concentrated ammonium hydroxide in 2 cc. of alcohol. The mixture is allowed to stand in the bath until crystallization is complete, and the ethyl oxamate is then filtered off and recrystallized from alcohol. M.P. 115°.

Esters of phenols can usually be converted into polybromophenols. The ester is saponified as directed in Paragraph 1 above, the resulting solution is acidified, and a slight excess of bromine water is added. The product is recrystallized from alcohol or dilute alcohol. For the melting points of the polybromophenols see page 176.

Ethyl acetoacetate reacts readily with phenylhydrazine to form 1-phenyl-3-methyl pyrazolone, according to the equation:



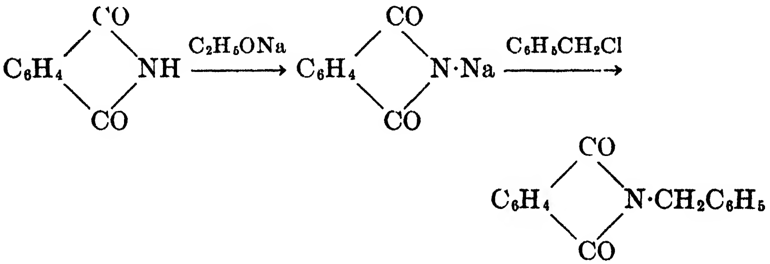
One gram each of phenylhydrazine hydrochloride and ethyl acetoacetate, and 6 drops of concentrated hydrochloric acid are heated in a boiling water bath for 15 minutes. Twenty cubic centimeters of water and a little norite are then added while the mixture is still hot, and after boiling for 1 or 2 minutes the insoluble material is filtered off. The filtrate is *carefully* neutralized with ammonium hydroxide and the slowly crystallizing precipitate is filtered off and recrystallized from alcohol. M.P. 127°.

Maleic anhydride may be converted into phenylaspartic anil by the directions given on page 190. It may also be hydrolyzed to give maleic acid, M.P. 130°, by heating with water, though some care must be exercised in isolating the acid since it is quite soluble in water.

p-Nitrobenzoyl chloride and *3,5-dinitrobenzoyl chloride* yield esters with suitable properties according to the method described on page 173.

Phenylurea is decomposed by being heated for a few minutes to a temperature slightly above its melting point. Ammonium carbonate (odor of ammonia) is evolved, the residue being diphenylurea, M.P. 235°. The diphenylurea is purified by recrystallization from alcohol.

Phthalimide is readily changed to a crystalline benzyl derivative by the following reactions:



This series of reactions represents the preliminary steps in an important method of preparing pure primary amines. Hydrolysis of *N*-substituted imides yields primary amines uncontaminated with secondary and tertiary amines. Directions for the above reactions follow: One gram of phthalimide is dissolved in 40 cc. of boiling absolute alcohol. A solution of 0.15 g. of freshly cut sodium (**Caution!**) in 10 cc. of absolute alcohol is added, followed by 1 cc. of benzyl chloride. The mixture is then refluxed for an hour. The mixture is filtered hot and the filtrate is treated with 20 cc. of water; the *N*-benzylphthalimide that separates on cooling is filtered off and recrystallized from 50 per cent alcohol. It melts at 115°.

Urea is conveniently changed into its nitrate, $NH_2CONH_2{\cdot}HNO_3$. To a solution of 0.5 g. of urea in 5 cc. of water is added an equal volume of concentrated nitric acid. The nitrate is precipitated when the solution is thoroughly cooled, and is filtered off and washed with a small amount of ice-cold water. It melts at 153° with decomposition. Urea also forms a picrate, M.P. 142° d., prepared according to the directions given on page 167.

Diphenylurea (carbanilide) is decomposed by heating with acetic anhydride to give carbon dioxide and acetanilide. This reaction is essentially the displacement of a volatile acid from its amide by one less volatile. (Compare with the reaction of an amide with aniline described on page 196.) One gram of diphenylurea is refluxed for 2 hours with 6 cc. of acetic anhydride and 0.7 g. of fused sodium acetate. The reaction product is poured into 10 cc. of hot water and stirred until the acetic anhydride has been decomposed. The mixture is then made alkaline, cooled, and the precipitated acetanilide filtered off and recrystallized from water. M.P. 114°.

Vinyl acetate can be converted into iodoform according to the directions given on page 173.

SULFONIC ACIDS AND THEIR DERIVATIVES

1. Pseudobenzylthiourea Salts.—Sulfonic acids and their salts form pseudobenzylthiourea derivatives in exactly the same way as the corresponding carboxylic compounds (page 188). Sulfonic acid derivatives such as esters and chlorides, after saponification by the method described on page 195, also yield pseudobenzylthiourea salts.

MELTING POINTS OF PSEUDOBENZYLTHIOUREA SALTS

Sulfonic Acid	M P. of Salt
Benzenesulfonic........	144
α-Naphthalenesulfonic.	136
β-Naphthalenesulfonic	188
m-Nitrobenzenesulfonic	140
p-Toluenesulfonic......	178

2. Sulfonamides from Sulfonyl Chlorides.—To 1 cc. of sulfonyl chloride is added, drop by drop, 10 cc. of concentrated ammonium hydroxide. When the reaction has subsided the mixture is heated to boiling, and after cooling, the product is filtered off and recrystallized from water. If the ammonia is replaced by 2 cc. of aniline and the reaction mixture is heated to 100° for 5 minutes, an anilide is formed.

MELTING POINTS OF SULFONAMIDES AND SULFONANILIDES

Sulfonic acid	M.P. of amide	M.P. of anilide
m-Benzenedisulfonic	229	150
Benzenesulfonic	156	110
α-Naphthalenesulfonic	153	112
β-Naphthalenesulfonic	217	132
m-Nitrobenzenesulfonic	166	131
o-Toluenesulfonic	156	136
p-Toluenesulfonic	137	103

Free sulfonic acids or their salts can also be changed to amides or anilides if the chloride is first prepared by reaction with phosphorus pentachloride (page 107; the heating period can usually be shortened in small scale work). It is unnecessary to purify the chloride before adding ammonia or aniline.

3. *N*-Benzyl Derivatives from Sulfonamides.—Sulfonamides are considerably more acidic in nature than amides of carboxylic acids, and they are more stable towards alkaline hydrolysis. Thus they form comparatively stable sodium salts which react with benzyl chloride to form *N*-substituted derivatives:

$$RSO_2NH_2 \xrightarrow{NaOH} RSO_2NHNa \xrightarrow{C_6H_5CH_2Cl} RSO_2NHCH_2C_6H_5$$

A mixture of 1.5 g. of sulfonamide, the equivalent amount of benzyl chloride, 10 cc. of 10 per cent sodium hydroxide, and 5 cc. of alcohol is refluxed for 2 hours. After cooling, the precipitate is filtered off, washed with cold water, and recrystallized from alcohol or dilute alcohol.

MELTING POINTS OF *N*-BENZYL SULFONAMIDES

Sulfonamide	M.P. of Derivative
Benzenesulfonamide	88
α-Naphthalenesulfonamide	137
β-Naphthalenesulfonamide	124
p-Toluenesulfonamide	116

4. o- and p-Aminobenzenesulfonic acids yield *s*-tribromoaniline, M.P. 119°, on treatment with an excess of bromine water. After making the mixture ammoniacal, the product is filtered off and recrystallized from 50 per cent alcohol.

NITRO COMPOUNDS

Derivatives of nitro compounds are usually formed by further nitration, or by reduction to amines followed, in some cases, by further treatment of the amines.

1. Polynitro Derivatives.—Two examples of this procedure will be given. Many other nitro compounds form convenient derivatives on nitration, but the specific directions must usually be altered somewhat in each case.

Nitrobenzene is nitrated to give *m*-dinitrobenzene, M.P. 90°, according to the directions given for benzene on page 167.

o-Nitrotoluene yields 2,4-dinitrotoluene, M.P. 70°, when nitrated according to the directions given for toluene, page 168. In this case, however, only one-half of the amount of mixed acid should be used.

2. Reduction of Mononitro Compounds.—A mixture of 1 g. of substance, 3 g. of tin, and 20 cc. of concentrated hydrochloric acid is warmed to 100°, with vigorous shaking, until the original nitro compound has dissolved (in some cases a somewhat vigorous reaction starts after a short warming period). The mixture is cooled and cautiously made alkaline with 40 per cent sodium hydroxide.

In the case of aliphatic nitro compounds the volatile amine formed is converted to a substituted phenylurea as described on page 205.

If the resulting amine is aromatic and volatile with steam, half the mixture is distilled off, the amine separating from the distillate. If the amine is a solid it is filtered off, purified, and its melting point determined. If it is a liquid, it is dissolved by the addition of dilute hydrochloric acid, treated with an excess of bromine water, and then made alkaline with ammonia. The precipitated polybromoamine is filtered off, washed, and recrystallized from alcohol or dilute alcohol. As in the case of phenols, bromine water usually causes substitution in all free positions ortho or para to the amine group.

If the amine is not volatile with steam, it is extracted from the alkaline reaction mixture with ether, and the ether extract is washed with water and dried over sodium sulfate. After removal of the ether, the amine, which will be a solid in all important cases, is recrystallized from water or dilute alcohol.

The melting points of suitable amines are given on page 194.

MELTING POINTS OF POLYBROMO DERIVATIVES OF AMINES

Substance	M.P.	Substance	M.P.
2-Amino-3,5-dibromotoluene	50	2,3,4,6-Tetrabromoaniline	116
3-Amino-2,4,6-tribromotoluene	97	2,4,6-Tribromoaniline	119
2,6-Dibromo-4-chloroaniline	97	2,4,6-Tribromo-3-chloroaniline	123
4,6-Dibromo-2-chloroaniline	103		

3. Reduction of Dinitro Compounds.—This reduction is conveniently accomplished by means of sodium polysulfide, the product in each case being a nitroamine. The directions on page 88 can be adapted to a small scale procedure. The melting points of the nitroanilines, which can be prepared from the dinitrobenzenes by this method, are given on page 194.

4. Oxidation of Side-Chains.—The nitrotoluenes can be oxidized with alkaline permanganate to the corresponding nitrobenzoic acids according to the procedure given for hydrocarbons on page 168. The melting points are given on page 193.

5. Addition Compounds.—Certain polynitro compounds form addition products with naphthalene similar to naphthalene picrate. The directions given on page 167 for the preparation of picrates hold here, except that in some cases a solvent other than alcohol must be used. 2,4,6,-*Trinitrotoluene* (TNT) and *s-trinitrobenzene* form addition compounds with naphthalene in alcohol solution which melt at 97 and 152°, respectively, while 2,4-*dinitrotoluene* forms one in benzene solution which melts at 60°.

AMINES AND THEIR SALTS

1. Acetyl Derivatives.—All primary and secondary amines react with acetic anhydride to form substituted acetamides:

$$RNH_2 + (CH_3CO)_2O \longrightarrow CH_3CONHR + CH_3COOH$$

Many of these acetyl derivatives are crystalline substances having properties which make them excellent for identification purposes. The general procedure is as follows: One gram of the amine is heated to boiling for a few minutes with a 10 per cent excess of acetic anhydride. The reaction mixture is poured into 20 cc. of hot water and is then heated to boiling until the excess acetic anhydride is decomposed. The product which separates from the solution on cooling is filtered off, washed with cold water, and recrystallized from water or dilute alcohol.

MELTING POINTS OF ACETYL DERIVATIVES OF AMINES

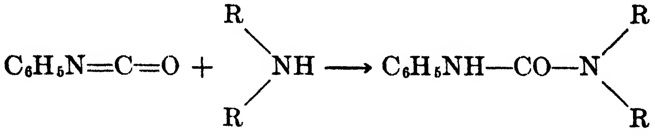
Acetyl derivative of	M P.	Acetyl derivative of	M P.
p-Aminodimethylaniline	130	Ethylaniline	54
p-Aminoazobenzene	144	Methylaniline	103
Aniline	114	α-Naphthylamine	159
o-Anisidine	84	β-Naphthylamine	132
p-Anisidine	127	*o*-Nitroaniline	92
Benzidine (diacetyl derivative)	317	*m*-Nitroaniline	155
o-Bromoaniline	99	*p*-Nitroaniline	214
m-Bromoaniline	87	*o*-Phenetidine	79
p-Bromoaniline	165	*p*-Phenetidine	135
o-Chloroaniline	87	*o*-Phenylenediamine (diacetyl derivative)	185
m-Chloroaniline	72	*m*-Phenylenediamine (diacetyl derivative)	191
p-Chloroaniline	179	*p*-Phenylenediamine (diacetyl derivative)	304
2,4-Dimethylaniline	129	*o*-Toluidine	112
3,5-Dimethylaniline	144	*m*-Toluidine	65
		p-Toluidine	153

2. Benzoyl Derivatives.—The formation of benzoyl derivatives with primary and secondary amines is similar to the formation of acetyl derivatives described above. In this case the more reactive benzoyl chloride is used rather than benzoic anhydride. The amine is heated with the theoretical amount of benzoyl chloride to 100° for 10 to 30 minutes; after cooling, excess 10 per cent sodium hydroxide is added and, if the odor of the benzoyl chloride is apparent, the mixture is shaken until this odor disappears. The precipitate is filtered off, washed with water, and recrystallized from water or dilute alcohol.

MELTING POINTS OF BENZOYL DERIVATIVES OF AMINES

Benzoyl derivative of	M P	Benzoyl derivative of	M P
p-Aminodimethylaniline	228	α-Naphthylamine	160
Aniline	160	β-Naphthylamine	162
p-Anisidine	154	o-Nitroaniline	94
Benzylamine	105	m-Nitroaniline	155
o-Bromoaniline	116	p-Nitroaniline	199
m-Bromoaniline	120	p-Phenetidine	173
p-Bromoaniline	204	o-Phenylenediamine (dibenzoyl derivative)	301
o-Chloroaniline	99	m-Phenylenediamine (dibenzoyl derivative)	240
m-Chloroaniline	120	p-Phenylenediamine (dibenzoyl derivative)	>300
p-Chloroaniline	192	n-Propylamine	84
Dibenzylamine	112	o-Toluidine	143
Dimethylamine	41	m-Toluidine	125
Diphenylamine	180	p-Toluidine	158
Ethylamine	71	s-Tribromoaniline	198
Ethylenediamine (dibenzoyl derivative)	249		
Methylamine	80		

3. Substituted Ureas.—Most primary and secondary amines react readily with phenylisocyanate to form substituted ureas. The amine adds to the nitrogen-carbon double bond of the isocyanate:



$$C_6H_5N{=}C{=}O + R_2NH \longrightarrow C_6H_5NH{-}CO{-}NR_2$$

In using this reaction it is important to note that the reagent also reacts with water to form diphenylurea. This product results from hydrolysis of part of the isocyanate with subsequent addition of the aniline formed to the unreacted reagent:

$$C_6H_5N{=}C{=}O + H_2O \longrightarrow C_6H_5NH_2 + CO_2$$
$$C_6H_5N{=}C{=}O + C_6H_5NH_2 \longrightarrow C_6H_5NH{-}CO{-}NHC_6H_5$$

Diphenylurea melts at 235°.

Phenylisocyanate has very pronounced lachrymatory properties, and care must be exercised in using it.

One-half cubic centimeter of phenylisocyanate is dissolved in 5 cc. of dry benzene, and the equivalent amount of amine is added slowly with cooling if necessary. After standing for 10 minutes, the reaction product is filtered off and recrystallized from alcohol or dilute alcohol. The following table lists the substituted ureas according to the substituents present other than the original phenyl group.

MELTING POINTS OF SUBSTITUTED PHENYL UREAS

Substituents present in addition to phenyl	M P	Substituents present in addition to phenyl	M P
n-Amyl	238	*o*-Methoxyphenyl	144
Benzyl	168	Methyl	151
Benzyl, benzyl	127	α-Naphthyl	222
n-Butyl	131	β-Naphthyl	220
n-Butyl; *n*-butyl	86	Phenyl	235
o-Ethoxyphenyl	169	Piperidyl	171
p-Ethoxyphenyl	178	*n*-Propyl	114
Ethyl	99	*o*-Tolyl	207
Ethyl, ethyl	85	*m*-Tolyl	173
Isobutyl; isobutyl	105	*p*-Tolyl	213
Isopropyl	142		

If a product is obtained which has a melting point in the neighborhood of that of diphenylurea, a mixed melting point with this substance should be determined unless this is the desired product.

The *salts of volatile amines* may be treated in the following manner. One gram of the amine salt is placed in a dry test tube fitted with a glass tube leading into a solution of 0.5 cc. of phenylisocyanate in 5 cc. of dry benzene. A few drops of 40 per cent sodium hydroxide is added to the test tube and the delivery tube is quickly replaced. As soon as evolution of the free amine has ceased, more alkali is added. This process is repeated until precipitation of the product from the benzene solution is complete. If no evolution of gas is apparent after the first addition of alkali, a total of 1 cc. is added and the mixture is gently boiled until the precipitation is complete. The product is filtered off and recrystallized from water or dilute alcohol.

Non-volatile amines are usually also insoluble in water so that the treatment of their salts offers no difficulties.

4. Picrates.—Many amines form picrates when treated according to the directions on page 167.

MELTING POINTS OF PICRATES OF AMINES

Amine	M.P. of picrate	Amine	M.P. of picrate
Di-*n*-butylaniline	125	Methylaniline	147
4,4′-Di (dimethylamino)-diphenylmethane[1]	185	α-Naphthylamine	182 d
Diethylaniline	142	β-Naphthylamine	182 d (decomposition noticeable at about 180°)
Dimethylamine	158		
Dimethylaniline	163	Piperidine	151
Ethylamine	170	Pyridine	167
Ethylaniline	139	Triethylamine	173
Ethylenediamine	234 d	Trimethylamine	216
Methylamine	207	Triphenylguanidine	184

[1] Also forms a picrate from 1 mol of amine and 2 mols of picric acid, M.P. 178°.

5. Benzal Derivatives.—Primary aromatic amines generally condense directly with benzaldehyde to form Schiff bases:

$$RNH_2 + C_6H_5CHO \longrightarrow RN{=}CH{-}C_6H_5 + H_2O$$

The Schiff bases, or benzal derivatives, frequently have properties which make them satisfactory for purposes of characterization. They may usually be prepared by heating the amine with the theoretical amount of benzaldehyde to 100° for a few minutes, and are purified by recrystallization from alcohol or dilute alcohol.

MELTING POINTS OF BENZAL DERIVATIVES OF AMINES

Benzal derivative of	M.P.	Benzal derivative of	M.P.
p-Aminoazobenzene	128	β-Naphthylamine	102
Aniline	54	*p*-Phenetidine	76
p-Anisidine	72	*o*-Phenylenediamine (dibenzal derivative	106
Benzidine (dibenzal derivative)	234	*m*-Phenylenediamine (dibenzal derivative	104
p-Bromoaniline	67	*p*-Phenylenediamine (dibenzal derivative)	138
p-Chloroaniline	62		
α-Naphthylamine	73		

6. Azo Derivatives from Tertiary Aromatic Amines.—Tertiary aromatic amines couple in the para position with phenyl diazonium chloride to give azo dyes, some of which are suitable for characterization. The phenyl diazonium chloride is prepared by dissolving 0.5 cc. of aniline in 10 cc. of water and 1 cc. of concentrated hydrochloric acid, and by treating this solution, cooled to 0°, with 0.4 g. of sodium nitrite, which is added in small portions with shaking. After all the nitrite has dissolved, the diazonium salt solution is added slowly to a solution prepared from 12 drops of tertiary amine, 1 cc. of glacial acetic acid, 2 g. of sodium acetate, and 10 cc. of water. The mixture is allowed to stand with frequent shaking for 15 minutes and the precipitate is then filtered off, washed well with water, and recrystallized from alcohol. Two of the most important compounds obtainable in this way are: *p*-diethylaminoazobenzene—dark orange—M.P. 97°, from *diethylaniline;* and *p*-dimethylaminoazobenzene—brilliant orange—M.P. 117°, from *dimethylaniline.*

7. Hydrazones from Substituted Hydrazines.—*Phenylhydrazine* and 2,4-*dinitrophenylhydrazine* can be converted into appropriate hydrazones by the directions given on pages 179–181.

AMINO CARBOXYLIC ACIDS AND THEIR DERIVATIVES

1. Acetyl Derivatives.—Acetyl derivatives of many amino acids and compounds derived from them may be prepared by the method described on page 203. The melting points of some of these derivatives are given below.

MELTING POINTS OF ACETYL DERIVATIVES OF AMINO ACIDS AND ESTERS

Amino acid or ester	M.P.	Amino acid or ester	M.P.
m-Aminobenzoic acid	250	Ethyl *p*-aminobenzoate	110
p-Aminobenzoic acid	256	Ethyl anthranilate	64
Anthranilic acid	185	Methyl anthranilate	101

2. Benzoyl Derivatives.—Amino acids are usually benzoylated by the so-called Baumann-Schotten method, which is also applicable to phenols in place of the method described on page 174. In the Baumann-Schotten method the reaction is carried out in an aqueous alkaline medium; the benzoyl chloride reacts much more readily with the amino acid or phenol salt than it does with the sodium hydroxide. The theoretical amount of benzoyl chloride and two equivalents of 10 per cent sodium hydroxide are added to 0.5 g. of the amino acid, the mixture is shaken vigorously for 30 minutes and is then acidified with hydrochloric acid. The precipitate is filtered off by suction and washed with several small portions of ether to remove benzoic acid. It is then recrystallized from water or dilute alcohol. It is obvious that this method should not be applied to esters or other alkali-unstable derivatives of amino acids.

MELTING POINTS OF BENZOYL DERIVATIVES OF AMINO ACIDS

Amino Acids	M.P.
dl-Alanine	165
p-Aminobenzoic acid	278
Anthranilic acid	181
l-Cystine (dibenzoyl derivative)	181
Glycine	187
l-Leucine	118
dl-Phenylalanine	187
l-Tyrosine (dibenzoyl derivative)	211

3. α-Naphthyluramino Acids.—Amino acids are conveniently transformed by means of α-naphthylisocyanate into substituted α-naphthyluramino acids, which are essentially ureas (see page 204). One gram of amino acid is dissolved or suspended in 50 cc. of water and treated with one equivalent each of α-naphthylisocyanate and sodium hydroxide, using two equivalents of the latter for dibasic acids. The mixture is then shaken vigorously for 45 minutes and filtered to remove di-α-naphthylurea. The filtrate is acidified with dilute hydrochloric acid and the precipitated α-naphthyluramino acid is filtered off, washed with water, and recrystallized from alcohol.

MELTING POINTS OF α-NAPHTHYLURAMINO ACIDS

Amino Acid	M.P.
dl-Alanine	198
d-Glutamic acid	236
Glycine	191
l-Leucine	164
l-Tyrosine	205

4. Bromination of Aminobenzoic Acids.—The presence of the amine group makes these compounds very easy to brominate with bromine water. The substance is dissolved in dilute hydrochloric acid and bromine water is added in slight excess. The mixture is made alkaline with ammonia and filtered to remove tribromoaniline (obtained by partial displacement of COOH by Br; compare bromination of sulfanilic acid, page 201). The filtrate is acidified with hydrochloric acid and the polybromide is filtered off and recrystallized from 50 per cent alcohol. The melting points of the products obtainable from *o-* and *p-aminobenzoic acids* are: 3,5-dibromo-2-aminobenzoic acid, 236°; 3,5-dibromo-4-aminobenzoic acid, 260 to 270° d.

Esters of o- and p-aminobenzoic acids may be saponified by the method described on page 192, and the above bromination procedure applied to the saponification mixture after acidification.

ISOCYANATES AND ISOTHIOCYANATES (MUSTARD OILS)

1. Substituted Ureas and Thioureas.—The preparation of substituted derivatives of urea by the reaction of amines with phenylisocyanate has been described on page 204. The same directions can be used for the preparation of derivatives of isocyanates and mustard oils by reaction with aniline. In the case of mustard oils the reaction mixture should be warmed to 100° for 10 minutes, and the product should be recrystallized from 75 per cent alcohol that contains a little hydrochloric acid. The melting points of several substituted ureas are given on page 205.

MELTING POINTS OF SUBSTITUTED PHENYLTHIOUREAS

Substituents Present Other Than Original Phenyl Group	M.P.
Allyl	98
Phenyl	153
o-Tolyl	141
m-Tolyl	91
p-Tolyl	139
α-Naphthyl	162

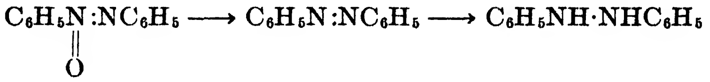
MISCELLANEOUS

Amino alcohols **are usually most easily identified as their picrates, prepared according to the directions given on page 167.**

MELTING POINTS OF AMINO ALCOHOL PICRATES

Amino alcohol	M.P.	Amino alcohol	M.P.
Ethanolamine	159 d	Dipropylaminoethanol	81
Diethanolamine	110	Ethylaminoethanol	126
Diethylaminoethanol	80	Propylaminoethanol	105
Dimethylaminoethanol	97	Triethanolamine	126

Azobenzene and *azoxybenzene* are reduced by means of zinc dust and alkali to hydrazobenzene, M.P. 131°. The reduction of azoxybenzene gives azobenzene as an intermediate product.



$$C_6H_5\underset{\underset{O}{\|}}{N}{:}NC_6H_5 \longrightarrow C_6H_5N{:}NC_6H_5 \longrightarrow C_6H_5NH{\cdot}NHC_6H_5$$

One-half gram of either of the above compounds is dissolved in 10 cc. of ethyl alcohol and treated with 2 cc. of 40 per cent sodium hydroxide and 1 g. of zinc dust. The mixture is heated to boiling for 5 minutes to complete the reaction. It is then filtered hot, allowed to cool, and the precipitated hydrazobenzene filtered off and recrystallized.

Carbon disulfide reacts with aniline in the presence of alkali to form *s*-diphenylthiourea (thiocarbanilide), M.P. 154°. This reaction is discussed on page 108. One cubic centimeter of aniline, 3 cc. of 40 per cent sodium hydroxide, and 0.3 cc. of carbon disulfide are mixed and shaken vigorously for 2 minutes. The mixture is then gently warmed (**Caution!** Carbon disulfide is highly inflammable!) and shaken for 2 minutes longer. After cooling, the mixture is diluted, acidified with concentrated hydrochloric acid, and the diphenylthiourea filtered off, washed, and recrystallized from alcohol.

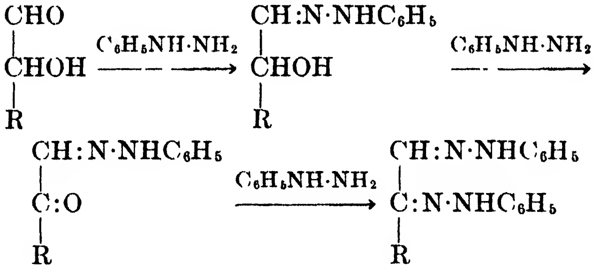
Diphenyl sulfide is readily oxidized by being gently boiled with 10 volumes of concentrated nitric acid until the evolution of brown fumes ceases. The product diphenyl sulfone, M.P. 129°, is obtained by diluting the reaction mixture with 4 volumes of water, filtering, washing, and recrystallizing from 33 per cent alcohol.

Diphenyl sulfone.—One-quarter gram of substance is heated to 150° for 2 minutes with a solution of 1 g. of potassium nitrate in

10 cc. of concentrated sulfuric acid. The mixture is then poured into ice water and the precipitated *m,m'*-dinitrodiphenyl sulfone is filtered off, washed with water and recrystallized from 95 per cent alcohol. The product is only slightly soluble in hot alcohol. M.P. 201°.

Diphenylthiourea (thiocarbanilide) yields diphenylurea, M.P. 235°, when boiled for 5 minutes with a tenfold excess of mercuric oxide suspended in alcohol. When the reaction is complete the hot mixture is filtered. The product separates from the filtrate on cooling and is recrystallized from alcohol.

Sugars.—All the common reducing sugars yield osazones on treatment with an excess of phenylhydrazine. In the formation of an osazone from an aldose the first step involves the formation of a hydrazone; this is followed by oxidation of the secondary alcohol group to a carbonyl group which then reacts with more of the reagent to form an osazone:



$$\begin{array}{l}CHO\\ |\\ CHOH\\ |\\ R\end{array} \xrightarrow{C_6H_5NH{\cdot}NH_2} \begin{array}{l}CH{:}N{\cdot}NHC_6H_5\\ |\\ CHOH\\ |\\ R\end{array} \xrightarrow{C_6H_5NH{\cdot}NH_2}$$

$$\begin{array}{l}CH{:}N{\cdot}NHC_6H_5\\ |\\ C{:}O\\ |\\ R\end{array} \xrightarrow{C_6H_5NH{\cdot}NH_2} \begin{array}{l}CH{:}N{\cdot}NHC_6H_5\\ |\\ C{:}N{\cdot}NHC_6H_5\\ |\\ R\end{array}$$

A similar series of reactions takes place with ketoses. Obviously, sugars having identical R groups will give the same osazone. Thus the aldoses, glucose and mannose, and the ketose, fructose, all yield glucosazone.

Two grams of phenylhydrazine and 3 cc. of glacial acetic acid are dissolved in 20 cc. of water. One gram of the carbohydrate is added; the tube is loosely stoppered and, after thorough shaking, is heated in a bath of boiling water for 30 minutes, or longer if necessary. After cooling, the osazone is filtered off, washed with water, and recrystallized twice from alcohol, using norite.

Sucrose, which is a non-reducing sugar, will yield phenyl glucosazone if it is first hydrolyzed to glucose and fructose by boiling for a few minutes with dilute hydrochloric acid. After neutralization of the solution with dilute sodium hydroxide (phenolphthalein used as indicator), the volume is made up to about 20 cc. and the phenylhydrazine and acetic acid are then added.

MELTING POINTS OF PHENYL OSAZONES

Sugar	M.P.
Arabinose	157
Fructose	205
Galactose	195
Glucose	205
Lactose	200
Maltose	206
Xylose	160

Thioacetic acid reacts vigorously with aniline to give acetanilide, M.P. 114°, and hydrogen sulfide, equal weights of the two substances being allowed to react. (**Hood!**) After the evolution of hydrogen sulfide ceases the reaction mixture is diluted with water, acidified with dilute hydrochloric acid, and the precipitated acetanilide is filtered off, washed and recrystallized from water.

Thiophenol yields a benzoyl derivative by the Baumann-Schotten method described on page 207. It should be observed that the product in this case will not be soluble in alkali so that it is unnecessary to acidify the reaction mixture and remove benzoic acid by washing with ether. The precipitate should be washed with water before it is recrystallized from alcohol. Thiophenyl benzoate melts at 56°.

Thiourea.—A mixture of 1 g. of substance, 1.6 g. of benzyl chloride, and 10 cc. of alcohol is refluxed for 30 minutes. The mixture is then evaporated to dryness on a steam bath and the residue is recrystallized from a small amount of dilute hydrochloric acid (1:1). The product, pseudobenzylthiourea hydrochloride, melts at 172°. For a discussion of the mode of formation of this substance see page 188.

APPENDIX I

A. Atomic Weights

Barium	137.36	Manganese	54.93
Bromine	79.92	Mercury	200.6
Calcium	40.08	Nitrogen	14.01
Carbon	12.00	Oxygen	16.00
Chlorine	35.46	Phosphorus	31.02
Chromium	52.01	Potassium	39.10
Copper	63.57	Silver	107.88
Hydrogen	1.008	Sodium	23.00
Iodine	126.92	Sulfur	32.06
Iron	55.84	Tin	118.7
Lead	207.22	Zinc	65.38
Magnesium	24.32		

B. Densities of Aqueous Solutions

Solution	Percentage by weight	Density at 20°C
Concentrated ammonium hydroxide	29 (NH_3)	0.895
Concentrated hydrochloric acid	36	1.18
Dilute hydrochloric acid	10	1.05
Concentrated nitric acid	72	1.42
Dilute nitric acid	10	1.05
Sodium hydroxide	40	1.43
Sodium hydroxide	20	1.22
Sodium hydroxide	10	1.11
Sodium hydroxide	5	1.05
Concentrated sulfuric acid	96	1.84
Dilute sulfuric acid	50	1.39
Dilute sulfuric acid	10	1.07

APPENDIX II

LIST OF REAGENTS[1] USED IN PART II

Acetic anhydride
Acetyl chloride
Aniline
Benzaldehyde
Benzoyl chloride
Benzyl chloride
Bromine water
Bromine (5 per cent in carbon tetrachloride)
p-Bromophenacyl bromide[2]
Calcium hydroxide (saturated aqueous solution)
Chlorine water
Copper (powder)
Cupric sulfate (1 per cent aqueous solution)
Diethyl sulfate
3,5-Dinitrobenzoyl chloride
2,4-Dinitrophenylhydrazine[3]
Ether (anhydrous)
Fehling's solutions A and B
Ferric chloride (2½ per cent aqueous solution)
Ferric chloride (solid)
Ferrous ammonium sulfate (solid)
Ferrous sulfate (saturated aqueous solution)
Hopkins-Cole reagent
Hydrochloric acid (0.2N aqueous solution)
Hydrochloric acid (10 per cent aqueous solution)
Hydrogen peroxide (3 per cent aqueous solution)
Hydroxylamine hydrochloride (solid)
Iodine (5 per cent in 25 per cent potassium iodide solution)
Iodine (solid)
Lead acetate (5 per cent aqueous solution)
Magnesium
Mercuric chloride (5 per cent aqueous solution)
Mercuric oxide
Methyl alcohol (absolute)

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[1] This list does not include the usual acids, solvents, and other reagents needed in all laboratory work.

[2] For preparation see page 111.

[3] For preparation see Allen, *J. Am. Chem. Soc.*, **52**, 2955 (1930).

Millon's reagent
Naphthalene
β-Naphthol
α-Naphthylisocyanate
p-Nitrobenzoyl chloride
p-Nitrobenzyl bromide
Orcinol reagent
Phenylhydrazine
Phenylhydrazine hydrochloride
Phenylisocyanate
Phosphorus pentachloride
Phthalic anhydride
Picric acid
Potassium hydroxide (0.5N alcoholic solution)
Potassium nitrate (solid)
Potassium permanganate (2 per cent aqueous solution)
Potassium permanganate (solid)
Pseudobenzylthiourea hydrochloride[1]
Resorcinol (solid)
Schiff's reagent
Schwanoff's reagent
Silver nitrate (1 per cent aqueous solution)
Sodium (metal)
Sodium acetate (anhydrous)
Sodium bicarbonate (saturated aqueous solution)
Sodium carbonate (5 per cent aqueous solution)
Sodium hydroxide (0.2N aqueous solution)
Sodium hydroxide (5 per cent aqueous solution)
Sodium hydroxide (10 per cent aqueous solution)
Sodium hydroxide (40 per cent aqueous solution)
Sodium nitrite (solid)
Sodium nitroprusside (solid)
Sodium sulfide (solid)
Sulfur
Tin (granulated)
Zinc (dust)
Zinc (granulated)
Zinc chloride (anhydrous)

Preparation of Special Reagents

Fehling's Solutions.—Solution A contains 70 g. of cupric sulfate ($5H_2O$) per liter. Solution B contains 250 g. of potassium hydroxide and 345 g. of Rochelle salts (sodium potassium tartrate) per liter.

Hopkins-Cole Reagent.—Forty grams of magnesium powder is covered with water and treated slowly with 1 l. of a saturated aqueous solution of

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[1] For preparation see J. J. Donleavy, *J. Am. Chem. Soc.*, **58**, 1004 (1936).

oxalic acid, with cooling if necessary. The mixture is filtered, acidified with glacial acetic acid, and diluted to 4 l. with water.

Millon's Reagent.—One part by weight of mercury is dissolved in 2 parts of concentrated nitric acid, and the solution is diluted with 2 volumes of water. Any precipitate is allowed to settle and the clear solution is decanted.

Orcinol Reagent.—One volume of half-saturated aqueous orcinol solution is added to 5 volumes of concentrated hydrochloric acid. The mixture is then diluted to 9 volumes with water.

Schiff's Reagent.—One-half gram of fuchsin (pararosaniline hydrochloride) is dissolved in 500 cc. of water and any insoluble material is filtered off. An equal volume of a saturated aqueous solution of sulfur dioxide is added. The reagent should be allowed to stand for several hours before use.

Seliwanoff's Reagent.—This reagent is a 1 per cent solution of resorcinol in 20 per cent hydrochloric acid.

INDEX OF ORGANIC COMPOUNDS

SUBJECT INDEX