UNITIZED EXPERIMENTS IN ORGANIC CHEMISTRY

by

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Preface

Unitized Experiments in Organic Chemistry represents an embodiment of the conviction that a tremendous amount of organic chemistry can be taught—and learned—in the laboratory. Not only the techniques, skills, and philosophy involved in organic synthesis, but, if the experiments are well designed, much of the fundamental theory and factual material of organic chemistry, as well, can be mastered by the student during the several hours a week which he spends in the laboratory. This can be achieved for an entire class only if every student, the best as well as the poorest, works to capacity, thoughtfully and productively, and only if the lectures and laboratory work are coordinated into a single integrated unit. These are the goals which we hope the present manual will aid the teacher in achieving.

Carefully tested time schedules, along with thought-provoking questions, are provided with each experiment to challenge the student to maximum efficiency. Optional experiments are provided for superior students who are able to complete the regular work in less than the allotted time.

Every experiment has been designed, not only to teach the basic skills and techniques of organic laboratory work, but also to clothe in flesh and blood the skeleton of words to which lectures and textbooks are necessarily restricted. Each day's experiment is preceded by an introduction which places the work of the day in proper context in the scheme of organic chemistry and encourages the student to think about the important principles that are being illustrated. Together, the discussion and experimental work constitute a complete, finished unit which affords the student a real sense of accomplishment and leaves him with a sharply defined picture of what the day's assignment is designed to teach.

The first eight units cover the theory and practice of the most important fundamental techniques employed in the organic chemistry laboratory. Each discussion is followed immediately by an experimental section designed to drive home the underlying principles involved. The discussions are, however, sharply divided from the experimental sections so that the student may refer to them continuously without being forced to re-read detailed instructions for a specific experiment. The early introduction of these units on techniques, which may be performed in regular order or assigned individually at such times as will enable the teacher to keep the laboratory work completely synchronized with the lectures, provides a high degree of flexibility. Once the student has completed these early experiments, he should be prepared to perform the remaining experiment, both those on aliphatic and those on aromatic compounds, in any order the teacher may wish to follow.

Further flexibility is made possible by the inclusion of more units than can be performed normally in a two-semester course so that the instructor may exercise considerable selection. For a one-semester course, we have found highly successful the plan of assigning different experiments to different groups, with an opportunity provided for comparison of results. In this way, each student is given an insight into the experimental aspects of many more experiments than he can perform personally.

Every experiment has been carefully tested with hundreds of students under close supervision by the authors and we believe that all are eminently workable. Special emphasis has been placed on clear, accurate, and reliable experimental directions, given in sufficient detail to lead to successful and satisfying results in the hands of even the most inexperienced beginner; at the same time special skill and technique will be rewarded with sufficiently superior results to stimulate and challenge the best of students. Hazards and pitfalls have been either eliminated or properly recognized and pointed out. Often alternative procedures are described to allow for differences in equipment available to students at different institutions.

Students in the beginning courses in organic chemistry lack the experience to organize their work efficiently on their own. The present manual is based on the philosophy that at this stage the very best training for the future is that which shows the student how his work can be organized for maximum productivity.

Over the years, the authors have been led to the conviction that by far the most successful experiments in organic chemistry are those whose results the student can submit as an actual preparation or report as a numerical answer or an unknown. The interest and enthusiasm with which our own students have received the present manual have confirmed that conviction.

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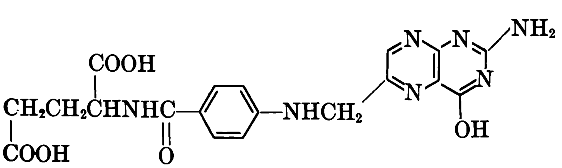
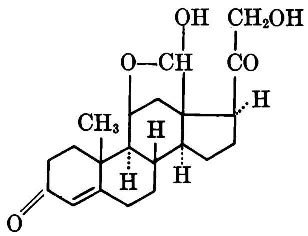
EXPERIMENT

Foreword to the Student

The practice of organic chemistry is both an art and a science. Complete elucidation of the structures of such complex compounds as, for example, the anti-anemia factor folic acid[1] and the steroidal hormone aldosterone,[2] on total samples of 500 and 57 mg., respectively, is sheer artistry. But underlying such brilliant work, and indispensable to it, is a thorough mastery of the fundamental scientific principles upon which the separation, purification, identification, and reactions of organic compounds are based.



Folic acid



Aldosterone

It is the purpose of your laboratory work in organic chemistry both to train you in the art and to school you in the scientific principles upon which the art is founded. It may perhaps be possible for you to muddle through the laboratory phase of your course in organic chemistry and achieve results of a sort without a clear understanding of what you are doing and why you are doing it. But truly distinguished achievement, characterized by rapid, efficient performance of each experiment with isolation of a high purity product in maximum yield, will require on your part a real understanding of the principles which underlie all laboratory techniques and procedures. Such achievement does not just happen. It will be possible only if you plan your work carefully in advance and work purposefully during each laboratory period.

Above all, it is important that you study the experiment of the day carefully before coming to the laboratory. *In advance* (1) master the theoretical principles involved, (2) in your notebook list in condensed form the equipment and chemicals (with amounts) required, so that a single trip to the stockroom or balance will suffice, and (3) write your own outline of the procedure in a form you can follow rapidly and write the balanced equations for the reactions involved.

In the laboratory, work with an open, inquiring mind, recording at once, not what you think is supposed to happen, but what you actually observe. A good scientist is, first of all, a careful observer. As you work, ask yourself questions; if, after a determined effort you cannot answer them, do not hesitate to ask your instructor. Many of the most provocative and interesting questions in organic chemistry are raised by beginning students.

Your experiments will be graded on the quality and quantity of your product, your technique, your notebook report, and your understanding of the practice and principles involved in the experiment as revealed by oral or written quizzes which your instructor will give from time to time. The quality of your product is judged from physical appearance and from such physical constants as melting point, boiling point, density, and refractive index. The quantity is expressed as the "percentage yield."

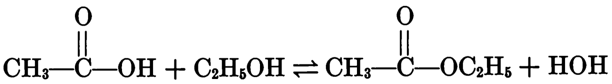
The percentage yield for any reaction represents the extent, expressed in per cent, to which the reactants were converted into the isolated product. It is calculated as follows:

$$\text{Percentage yield} = \left(\frac{\text{actual yield}}{\text{theoretical yield}}\right)(100)$$

where the actual yield = the weight or volume (for a gas) of product actually isolated

and the theoretical yield = the weight or volume (for a gas) of product that would be formed from the starting materials used if the reaction proceeded 100 per cent as indicated by the balanced equation.

For example, let us calculate the percentage yield of the ester, ethyl acetate, if 33.6 g. were isolated from the reaction of 35.0 g. of acetic acid with 75.0 g. of ethyl alcohol. According to the balanced equation (see Experiment 26),



$$\mathrm{CH_3{-}\overset{\overset{O}{\|}}{C}{-}OH + C_2H_5OH \rightleftharpoons CH_3{-}\overset{\overset{O}{\|}}{C}{-}OC_2H_5 + HOH}$$

60.1 g.	46.1 g.	88.1 g.
(1 mole)	(1 mole)	(1 mole)

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[1] E. L. R. Stokstad, B. L. Hutchings, S. H. Mowat, J. H. Boothe, C. W. Waller, R. B. Angier, J. Semb and Y. SubbaRow, *J. Am. Chem. Soc.*, **70,** 5 and 10 (1948).

[2] S. A. Simpson, J. F. Tait, A. Wettstein, R. Neher, J. von Euw, O. Schindler and T. Reichstein, *Experientia,* **10,** 132 (1954); *Helv. Chim. Acta,* **37,** 1163, 1200 (1954); *Ann. Reports,* **1954,** 223.

theoretically 60.1 g. (1 mole) of acetic acid reacts with 46.1 g. (1 mole) of ethyl alcohol to yield 88.1 g. (1 mole) of ethyl acetate.

Hence the theoretical yield of ethyl acetate from 35.0 g. of acetic acid is

$$\left(\frac{35.0\text{ g.}}{60.1\text{ g.}}\right)(88.1\text{ g.}) = 51.3\text{ g.}$$

and from 75.0 g. of ethyl alcohol,

$$\left(\frac{75.0\text{ g.}}{46.1\text{ g.}}\right)(88.1\text{ g.}) = 143.3\text{ g.}$$

In other words, the ethyl alcohol is present in theoretical excess, and the acetic acid is the limiting reagent in determining the theoretical yield. No matter how great an excess of ethyl alcohol is added, the maximum yield of ethyl acetate that can be obtained from 35.0 g. of acetic acid is 51.3 g. This, then, is the theoretical yield of ethyl acetate. The percentage yield is equal to

$$\left(\frac{33.6\text{ g.}}{51.3\text{ g.}}\right)(100\%) = 65.5\%$$

Esterification is an equilibrium reaction and addition of an excess of the cheaper reagent, ethyl alcohol, through the mass action effect, increases the weight of ethyl acetate produced per unit weight of the more costly reactant, acetic acid.

You may prefer to solve problems of this type by calculating the number of moles of the limiting reactant used and of the product isolated. Thus, in the synthesis of ethyl acetate, we see from the equation that, for every 1 mole of acetic acid which reacts, 1 mole of ethyl acetate is formed. But 35.0 g. of acetic acid is only

$$\frac{35.0\text{ g.}}{60.1\text{ g./mole}} = 0.582\text{ mole of acetic acid}$$

and the theoretical yield of ethyl acetate is therefore 0.582 mole of ethyl acetate.

The actual yield of ethyl acetate, 33.6 g., is

$$\frac{33.6\text{ g.}}{88.1\text{ g./mole}} = 0.381\text{ mole of ethyl acetate}$$

The percentage yield is therefore

$$\left(\frac{0.381\text{ mole}}{0.582\text{ mole}}\right)(100\%) = 65.5\%$$

If, in the synthesis of ethyl iodide (Experiment 16), 3.5 g. of phosphorus, 25.0 g. of iodine, and 19.7 g. of ethyl alcohol are used, it can be calculated from the balanced equation for the over-all reaction

$$\begin{array}{ccccc} 2P & + & 3I_2 & + & 6CH_3\text{—}CH_2OH \rightarrow \\ 61.96\text{ g.} & & 761.5\text{ g.} & & 276.4\text{ g.} \\ (2\text{ moles}) & & (3\text{ moles}) & & (6\text{ moles}) \end{array}$$

$$\begin{array}{c} 6C_2H_5I + 2H_3PO_3 \\ 935.9\text{ g.} \\ (6\text{ moles}) \end{array}$$

that the iodine, by far the most expensive of the reagents, is the limiting reagent. From 25.0 g. of iodine, the theoretical yield of ethyl iodide is

$$\left(\frac{25.0\text{ g.}}{761.5\text{ g.}}\right)(935.9\text{ g.}) = 30.7\text{ g.}$$

If the actual yield of ethyl iodide is 21.0 g., then the

$$\text{percentage yield} = \left(\frac{21.0\text{ g.}}{30.7\text{ g.}}\right)(100\%) = 68.4\%$$

Working the same problem on a mole basis, we can see from the equation that 3 moles of iodine yield theoretically 6 moles of ethyl iodide, or 1 mole of iodine yields 2 moles of ethyl iodide. But 25.0 g. of iodine is only

$$\frac{25.0\text{ g.}}{253.84\text{ g./mole}} = 0.0985\text{ mole of iodine}$$

and yields theoretically (2)(0.0985) = 0.197 mole of ethyl iodide.

The actual yield of ethyl iodide, 21.0 g., is

$$\frac{21.0\text{ g.}}{155.98\text{ g./mole}} = 0.135\text{ mole of ethyl iodide}$$

The percentage yield is then

$$\left(\frac{0.135\text{ mole}}{0.197\text{ mole}}\right)(100\%) = 68.4\%$$

The percentage yield obtained in a given reaction is an indication both of the suitability of the reaction for synthetic purposes and of the skill and technique of the investigator. Many organic reactions are reversible, most are accompanied by competing side reactions which lead to the formation of by-products, and almost all are relatively slow as compared, for example, to the familiar reaction of sodium hydroxide solution with hydrochloric acid or of silver nitrate with sodium chloride in solution. For these reasons, careful control of such factors as time of reaction, temperature, solvent, concentration, pH, product removal, and judicious use of catalysts are of the utmost importance in organic reactions. But even under optimum experimental conditions, very few organic reactions afford the desired product in 100 per cent yield.

For every reaction there is an inherent limitation on possible yield imposed by the nature of the reaction itself and competition from side reactions. Other factors being equal, a reaction in which a maximum yield of 95 per cent may be achieved is certainly to be preferred above one in which the maximum attainable yield is 25 per cent. But the percentage of this limiting yield that is actually realized in a given case depends upon the personal factor; it is at this point that the skill, technique, and ingenuity of the experimenter come into play. Nothing will be more personally rewarding or gratifying to you in the organic laboratory than the type of intelligent and skilled workmanship which exploits each reaction to its fullest extent.

Safe Working Procedures and Avoidance of Accidents

All too often chemical laboratories are the scene of accidents—mostly minor ones but some of serious nature. These so-called accidents do not merely *happen;* they *are caused* by improper or careless procedures. Close observance of the precautions, given in the following list, will prevent directly most such mishaps and indirectly will aid the student in acquiring those habits of safety which will be of inestimable value to him not only in the laboratory but elsewhere as well.

1. Avoid cuts and lacerations

Cuts from broken pieces of glass tubing are among the most frequent accidents in the laboratory. These may be avoided by observing the following rules when inserting a glass tube or thermometer into the hole in a stopper:

a) Bore the hole in the stopper to a suitable size.
b) Lubricate the tube with water, soap solution, or glycerol.
c) Protect your hands with a towel.
d) Rotate the tube slowly and apply pressure gently.
e) Do not use one arm of a bent tube as a lever for application of excessive pressure, but grip the side-arm close to the cork or stopper.
f) Soften a cork stopper in the cork roller before boring a hole in it. The rolling aids in boring a smooth hole which fits the tube securely. The same rules apply to the removal of a tube from a stopper.

2. Guard against fire

Remember that many solvents used in the organic chemistry laboratory are flammable. Observe the following precautions:

a) Flammable solvents of boiling point less than 100° should be distilled, heated, or evaporated on the steam bath, not over a Bunsen burner. This includes methanol, ethanol, acetone, benzene, petroleum ether, ligroin, etc.
b) Flammable solvents should be contained in flasks rather than in open beakers.
c) Keep flasks containing flammable solvents away from your own and also from your neighbor's Bunsen burner.
d) Bottles of flammable solvents should not be on your work bench near a lighted burner. Keep them on the side shelf.
e) Do not pour flammable liquids into the waste crocks.

3. Extinguishing fires

The laboratory is provided with fire extinguishers, a fire blanket, an emergency shower, a bucket of sand, and perhaps other items.

a) Know the location and use of these pieces of equipment.
b) Remember that burning sodium reacts with carbon tetrachloride with explosive vigor. Smother sodium fires with dry sand or sodium carbonate, scrape the material into a pan and carry it out of doors.

4. Protect your eyes

a) Wear goggles whenever you are performing an experiment in which there is danger of spattering.
b) Wearing protective spectacles in the laboratory at all times is an excellent safety measure.
c) Avoid looking into the open mouth of a test tube or flask in which a reaction is being conducted.

5. Shun explosive mixtures

Strong oxidizing agents and easily oxidized material (reducing agents) must be mixed with extreme caution and in small amounts. Never add nitric acid to a flask containing alcohol. The reaction is so violent that a bad explosion may result.

6. General Procedures

a) Absorb escaping obnoxious gases in water or other suitable medium or conduct the experiment in a fume hood.
b) Keep the gas and water valves closed except when these utilities are needed.
c) Insoluble waste such as filter papers, match stems, and kindred items must be thrown into the waste jars—not into the sinks.
d) Ordinary rubber stoppers are never used on apparatus where they can be subjected to the action of organic solvents. Most such solvents attack the rubber and cause contamination of the product.
e) Never work in the laboratory alone. A minor mishap that may be of little consequence if some one is at hand to help you, may be serious if you are alone.
f) Do not swing a graduated cylinder or similar piece of glassware in a circular arc to dry it by centrifugal force. Such spattering of your neighbors is inexcusable.

g) Do not put scraps of metallic sodium into the sinks or waste jars. Cover them with kerosene and ask the instructor for the local arrangements for disposing of them.

h) Be neat in your work. If you spill something, clean it up.

i) Never heat an enclosed system and never completely close an assembly of apparatus in which a gas is being evolved; always provide a vent of suitable size.

j) Work with bromine, phosphorous trichloride, acetyl chloride, benzoyl chloride, and other obnoxious materials in the hood. Each laboratory has its own provisions for handling such substances. Ask the instructor for directions.

k) Much of the sloppiness of laboratory tables is caused by a too rapid stream of water flowing through the condenser; a gentle stream is usually sufficient.

Writing Your Laboratory Notebook

We have stated in the Foreword and repeat here for emphasis that before coming to the laboratory you should:

(a) Read carefully the discussion and directions for the experiment in this manual.

(b) In your textbook, turn to the subject of the experiment and study the presentation given there.

(c) Write up the experiment in your notebook using the following outline and omitting only the observations and answers to questions that inherently cannot be supplied until the work has been done.

Careful observance of this plan for your laboratory work is the very essence of meaningful experimentation. By following such a prearranged plan you will have no trouble in completing the laboratory work according to the time schedule given with the experiment. On the contrary, you will wonder why the schedule is so slow.

Outline Reporting a Laboratory Preparation

EXPERIMENT NO. —

Title

Materials	Theoretical Yield Actual Yield Percentage Yield Boiling Range (or M.P.) B.P. or M.P. (from Handbook) Density (from Handbook)

Equations

Procedure. State or outline, briefly but clearly, the working methods so that the experiment may be repeated from your notebook without reference to the Manual. All statements should be impersonal. In many instances one page of your notebook will suffice for the report of the preparation of an organic compound. The description of the chemical properties of a compound, or a series of related compounds can usually be given best by short statements accompanied by chemical equations.

Answers to questions

Temperatures are in degrees centigrade.

A time schedule, in minutes, is given for completing each assignment within the three-hour laboratory period. This schedule is given in bold-face numbers in the margins.

EXPERIMENT 1

Calibration of a Thermometer

Introduction. Throughout your laboratory course in organic chemistry, you will be measuring temperatures —melting points, boiling points, reaction temperatures, bath temperatures, etc.—by means of a thermometer. For some purposes, you will wish to know only the approximate temperature, but often you will desire an exact reading. An ordinary mercury thermometer can be used for measuring temperatures from approximately −38° to 360° (mercury boils at 356.6° at 760 mm. pressure). This range will be adequate for your needs.

Laboratory thermometers, however, differ widely in accuracy. The very best are calibrated according to the specifications of the U. S. Bureau of Standards. For such precision thermometers, the maximum tolerance is 0.5° for temperatures up to 100° and 1.0° up to 250°. Ordinary laboratory thermometers are less reliable; a given thermometer may be quite accurate or may, especially at higher temperatures, be in error by as much as 3° or 4°.

For this reason, you will find it worthwhile to calibrate your own thermometer. For practical purposes, it is best to do so under conditions as nearly identical as possible to those under which the thermometer will be used. Any required corrections can then be applied to all of your precise readings throughout the course.

In the calibration of a thermometer its readings at a series of known temperatures are determined. The known temperatures are either (1) read from a standard comparison thermometer immersed in a bath along with the thermometer being calibrated or (2) provided by pure substances at some transition point, such as the melting point (solid–liquid transition point) or boiling point (liquid–vapor transition point).

The most convenient solid–liquid system is ice–water at 0°. Others are listed in Table 1. Pressure effects are negligible and can be disregarded.

A few of the many substances whose boiling points at 760 mm. pressure may be used as reference temperatures are listed in Table 1. For other pressures, a correction must be applied. When the pressure is not too far from 760 mm., the approximate correction for every 10 mm. of difference in pressure may be calculated by dividing the boiling point on the **absolute** scale by a factor of 1020 for associated liquids and 850 for nonassociated liquids. For example, at 740 mm. the boiling point of water, which is highly associated, is approximately $(373°/1020)(2) = 0.7°$ lower than at 760 mm. Nitrobenzene, which is nonassociated, boils approximately $483°/850 = 0.6°$ higher at 770 than at 760 mm.

Whenever a transition temperature is used as a reference standard, it is extremely important that equilibrium conditions are realized at the bulb of the thermometer. For solid–liquid systems (melting points) this sometimes requires vigorous stirring. For liquid–vapor systems (boiling points) the bulb of the thermometer should be above the surface of the boiling liquid (which is likely to be superheated) and wet with condensed liquid in equilibrium with vapor.

Experimental

1. Ice–Water at 0°. Fill a 600-ml. beaker with finely chopped ice and add distilled water to within 6 cm. of the top of the beaker. Stir the mixture vigorously with a stirring rod for a few moments. Then insert your thermometer into the mixture so that the zero point is just above the surface and note and record the minimum reading obtainable. **0-20**

2. Melting Point of Benzoic Acid at 122.5°. Add about 10 g. of C.p. benzoic acid to a 6-inch test tube. Mount the test tube on a ring stand above a wire gauze on a ring and heat gently until all of the benzoic acid has melted. In a cork of proper size to fit a 6-inch test tube, bore a hole to accommodate your thermometer. **20-90**

Then suspend the thermometer (by means of a clamp attached to the cork) into the liquid so that the top of the bulb extends a centimeter or two below the surface of the liquid (Figure 1a). Allow the liquid to cool,

TABLE 1. REFERENCE TEMPERATURES FOR CALIBRATION OF THERMOMETERS

Compound	M.P., °C., at 760 mm.	Compound	B.P., °C., at 760 mm.
Water-ice	0.0	Acetone	56.1
Diphenylamine	53.5	Benzene	80.2
Benzoic acid	122.5	Water	100.0
Salicylic acid	158.3	Chlorobenzene	132.0
Succinic acid	189.0	Bromobenzene	156.2
3.5-Dinitrobenzoic acid	205.0	Aniline	184.5
p-Nitrobenzoic acid	239.0	Nitrobenzene	210.9
-*p*-Tolyurea	268.0	Biphenyl	254.9
N,N-Diacetylbenzidine	317.0	Acetanilide	305.0

stirring vigorously about the bulb by raising and lowering an aluminum or nichrome wire (Note 1)[1] looped so as to fit loosely around the thermometer bulb.

When about one half of the benzoic acid has solidified, observe the thermometer reading, still stirring vigorously. Record the temperature and calculate the thermometer correction from the known m.p. (122.5°) of benzoic acid (Note 2). Clean and dry the test tube thoroughly before it is used in another determination.

Repeat with two or three other solids whose melting points are listed in Table 1 and are distributed somewhat uniformly over the entire temperature range (Note 3). Calculate the required thermometer correction at each melting point temperature.

90-110 *3. Water–Water Vapor at 100°.* Place about 6 ml. of distilled water and a boiling chip (see p. 11) in a clean, dry 6-inch Pyrex test tube. Mount the test tube on a ring stand above a wire gauze on a ring and by means of a vented one-holed cork suspend a thermometer in the tube so that the bulb is about 3 cm. above the surface of the water (Figure 1b).

Heat the tube until the water boils gently. You will then observe a sharply defined ring of condensate around the wall of the test tube indicating where condensation of the ascending vapor begins. This ring rises as heating is increased. Apply heat until the condensation ring is about 2 cm. above the bulb of the thermometer, and the bulb is wet with condensed vapor. Continue gentle boiling until the thermometer reading is constant; then observe and record the temperature (Note 2) and the atmospheric pressure.

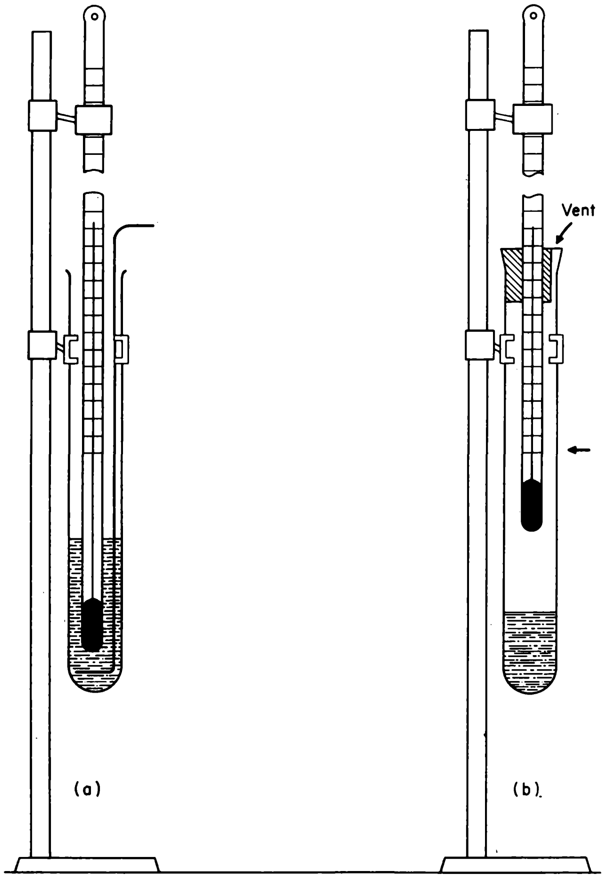
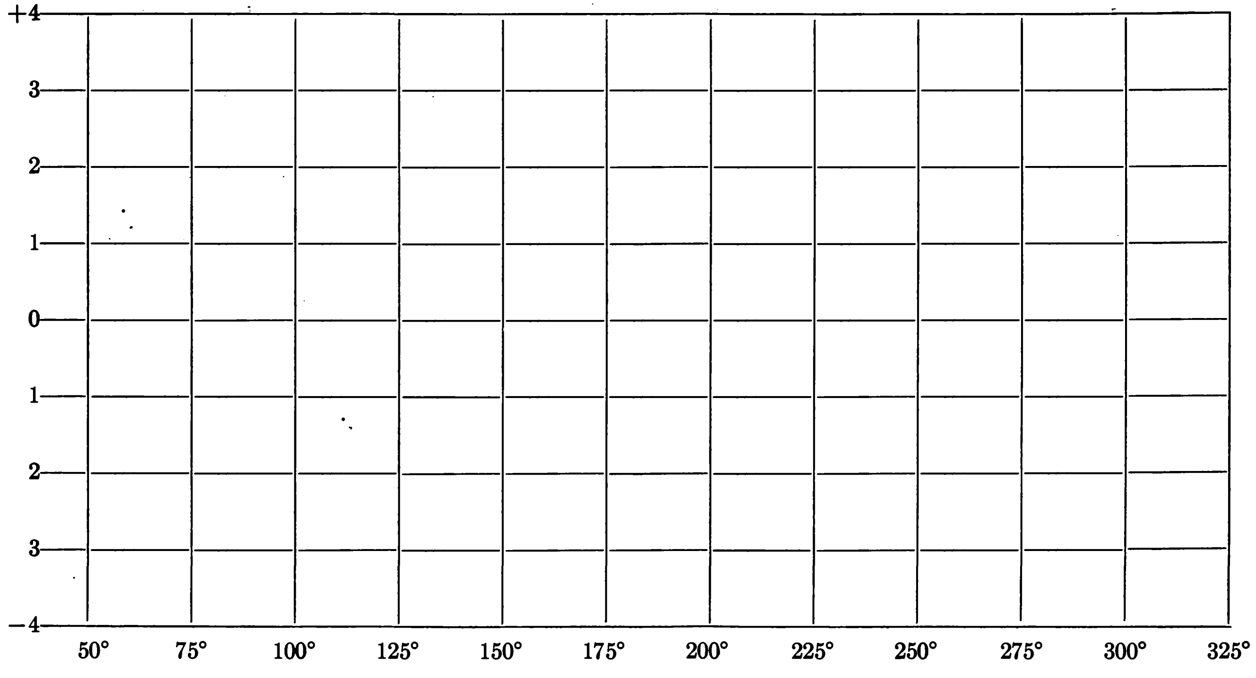


FIG. 1. Apparatus for the calibration of a thermometer.



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[1] Notes are listed at end of the experiment.

Repeat this process for three additional pure compounds listed in Table 1 (Note 3). Select these compounds so that they supplement the reference temperatures provided by your melting-point calibrations. Calculate the corrections which must be applied to the readings at different temperatures. Then plot in the figure provided on page 2 a correction curve for your thermometer for use throughout this course. **110-160**

NOTES

1. Copper and iron wire corrodes somewhat in the molten acid. You may prefer to make a glass stirrer by bending a circular or triangular loop at the end of a length of 5- or 6-mm. glass rodding or sealed glass tubing. If so, be certain to use a wing-tip on your burner. Be careful not to touch the glass at the heated section and always lay the heated glass on a wire gauze or a strip of asbestos paper—never on the desk top.

2. The method described here simulates sufficiently closely the conditions actually used in the determination of boiling points and melting points so that the stem correction (see p. 7) is automatically included in the calibration.

3. Three students may wish to cooperate, each calibrating all three thermometers at one temperature.

QUESTIONS

1. What is meant by an associated liquid? What type of bonds are ordinarily involved in the association of the molecules of liquids?

2. What advantage would result from the calibration of a thermometer in such a way that the boiling vapor surrounded the entire mercury column of the thermometer? What is the practical advantage of the method you used?

3. Even if your thermometer is not accurate, it will give the same reading at the same temperature consistently. What, then, is the purpose in calibrating it?

4. Calculate the approximate boiling point of benzene at 710 mm.; of acetanilide at 724 mm.; of chlorobenzene at 775 mm. What would be the corresponding temperature readings on your thermometer?

5. Suggest how temperatures below −40° and above 360° may be measured.

6. Can you suggest any explanation for the fact that a change in pressure has a greater effect on the boiling point of a nonassociated liquid than it does on that of an associated liquid?

EXPERIMENT 2

I. Melting Points

II. Sublimation

I. MELTING POINTS

A. Theory

a. Definition of Melting Point. No physical constant of solids is more widely used by organic chemists than the melting point. In a practical sense, the melting point of a crystalline solid is simply the temperature at which the solid changes to a liquid under a pressure of one atmosphere. For a pure substance, the change is usually quite sharp and the temperature is characteristic and not significantly affected by moderate changes in pressure. Hence, the melting point is a convenient constant commonly used in the identification of solids. In addition, because the melting point is almost always markedly altered by the presence of impurities,[1] it is a valuable criterion of purity.

The liquid form of a pure substance, when cooled in such a way that supercooling is prevented, solidifies at the same temperature at which the pure solid phase melts. For a pure substance, then, the melting and freezing points are identical. The melting (and freezing) point of a substance is best defined as the temperature at which the liquid and solid phases can exist in equilibrium with each other under a total pressure of one atmosphere.

b. Vapor Pressure–Temperature Diagram. The reason for the constancy and sharpness of the melting point of a pure crystalline substance can be shown by means of a generalized vapor pressure–temperature diagram which is developed in Figure 2. *AB* (Figure 2a) gives the experimentally determined vapor pressure of a pure solid, *x*, at temperatures from T_A to T_B. *BC* (Figure 2a) shows the vapor pressures for pure liquid *x* at temperatures from T_B to T_C.[2] At T_B, the vapor pressures of both solid and liquid phases of pure *x* are equal to P_B; in other words, the vapor pressure curves for solid and liquid intersect at *B*. T_B is therefore the melting point of *x*.

Now, let us evaluate the effect of a small amount of an impurity, *y* (which is soluble in liquid *x*), on the melting point of *x*. At the precise moment when the last minute crystal of *x* is melting, all of the impurity *y* will be dissolved in essentially all of *x*. But the presence of this dissoved impurity will lower the vapor pressure due to liquid *x* throughout the whole temperature range, as shown by curve B_1C_1. It is clear, then, that the vapor pressure of solid *x* becomes equal to that of the liquid at temperature T_{B_1}, which is below the melting point (T_B) of pure *x*.

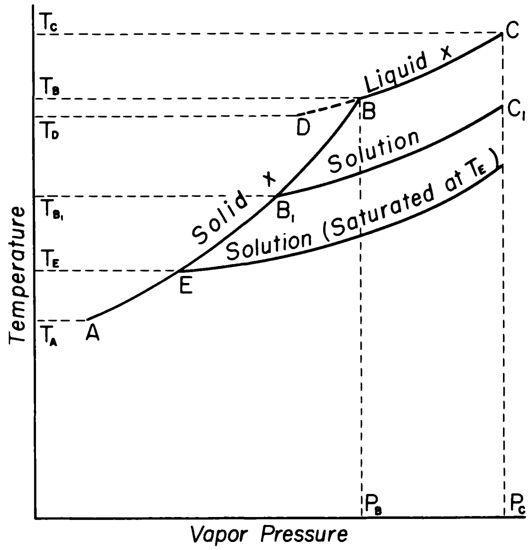

FIG. 2a. Generalized vapor pressure-temperature diagram.

In other words, in the presence of this amount of impurity, *y*, the temperature at which the last trace of *x* melts is lowered to T_{B_1}, and the effect of the impurity *y* is clearly to lower the melting point of *x*, just as salt or alcohol lowers the melting point of ice.

c. Eutectic Point. Continued addition of higher percentages of *y* progressively lowers the melting point of *x*. Finally, however, a limiting situation is reached in which *y* is present in a concentration just sufficient to saturate the solvent liquid *x* even as the last trace of *x* melts. The temperature at which this occurs is shown on the graph as T_E. It may be thought of as the temperature at which a saturated solution of *y* in liquid *x* (the eutectic composition) is in equilibrium with solid *x*.

Any additional *y* does not dissolve and hence cannot depress the melting point of *x* below T_E. This limiting temperature is known as the **eutectic temperature.** The **eutectic temperature** is the temperature below which a mixture of *x* and *y* cannot exist as a liquid under one atmosphere pressure. It follows, also, that a mixture of *x* and *y* having the eutectic composition melts con-

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[1] In order to affect the melting point of a solid substance, the impurity must be at least somewhat soluble in the liquid melt. In practice, this condition is almost always met.

[2] The extension of the liquid curve, *BD*, shows the vapor pressure of supercooled liquid *x* at temperatures from T_B to T_D. The line *BD* is dotted because it represents a metastable condition which can exist only in the absence of any solid phase. If solid *x* is added to the supercooled liquid, immediate crystallization of *x* occurs, and the heat of crystallization raises the temperature to T_B, where solid and liquid phases can exist in equilibrium.

stantly at the eutectic temperature, as if it were a pure compound.

d. Effect of an Impurity on Melting Range. In order to evaluate the effect of an impurity on the melting-point *range* of a pure substance, let us consider the effect of heating the mixture of *x* with a small amount of impurity *y* in which the last trace of *x* melted at T_{B_1}. To establish the range, we must know where the mixture will begin to melt. If stirring is sufficiently thorough to assure equilibrium conditions while the solid mixture is heated, as soon as a minute amount of liquid *x* is formed, it will become saturated with dissolved *y*, to form a liquid phase of eutectic composition. But such a saturated solution of eutectic composition is in equilibrium with solid *x* at the eutectic temperature, T_E, and melting would therefore actually begin at T_E.

As heating is continued, more *x* melts and more *y* dissolves *at the eutectic temperature* until there is enough liquid *x* to dissolve all of *y*. Then as more *x* melts, the liquid becomes less concentrated in impurity *y* and the melting point rises, as shown along curve *EB*, until the whole mixture is liquid at T_{B_1}. Hence, if perfect equilibrium conditions are maintained, the melting point range for such a mixture would be from T_E to T_{B_1}.

In theory, for any mixture of *x* with impurity *y*, melting will begin at T_E and will be complete at some temperature below T_B. Theoretically, as the concentration of impurity *y* is increased progressively, the upper limit of the melting-point range is lowered, and therefore the range itself is decreased.

In practice, however, equilibrium conditions are almost never achieved and, in addition, the melt is not observed until an appreciable amount has been formed. If only a small amount of impurity is present, the amount of liquid formed at the eutectic is very small; in fact, liquid may not be observed until considerably above the eutectic temperature.

Therefore, as actually observed, a nearly pure solid shows a narrow melting range with an upper limit near the true melting point. A rather impure solid usually gives a broad melting range with the maximum temperature attained considerably below the true melting point. Hence, the purification of a solid is often followed by melting point; a sharp melting point, which remains constant from one recrystallization to another, even when different solvents are used, is a good indication of purity.

e. Temperature–Composition Diagram. Another way of looking at melting-point theory may be helpful, especially in expanding our definition of the eutectic point. Figure 2b is a generalized equilibrium temperature–composition diagram for a typical two-component system such as we have been discussing.[3] The curve *BE* represents the temperature at which solutions of *y* in *x*[4] of different concentrations are in equilibrium with solid *x*. Pure *x* melts and freezes at the temperature corresponding to *B*. For any other mixture of composition between 100 per cent *x* and that represented at *E*, the curve indicates the temperature at which the first trace of *x* will crystallize when the liquid mixture is cooled or the last trace of *x* will melt when the solid mixture is heated.

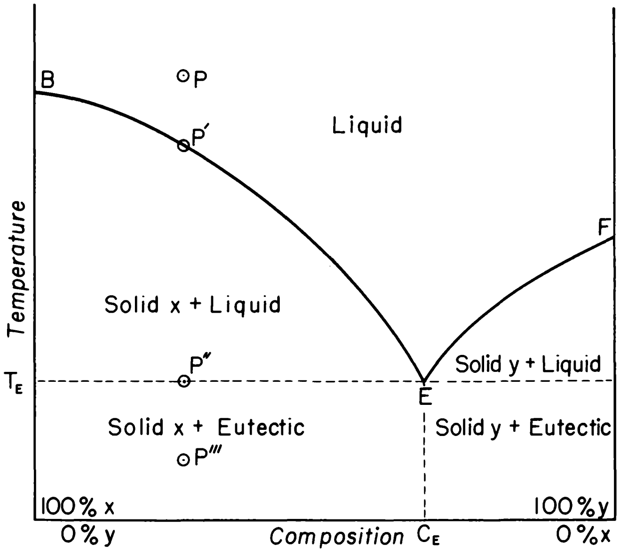

FIG. 2b. Generalized temperature-composition diagram.

Similarly, *FE* represents the temperature at which solutions of *x* in *y* of different concentrations are in equilibrium with solid *y*. At the point of intersection of the two curves, *E*, both solid components can exist in equilibrium with a liquid solution of the definite composition C_E. This point is, once again, the **eutectic point,** and the corresponding temperature T_E is the eutectic temperature. In a broad sense, we might think of the liquid at the eutectic point either as a saturated solution of solute *y* in solvent *x* or of solute *x* in solvent *y*. Cooling of the eutectic liquid will bring about crystallization of both *x* and *y* at a constant temperature, the **eutectic temperature,** and at a constant composition, the **eutectic composition.**

If a liquid mixture of *x* and *y* of the composition and at the temperature represented by *P* is cooled, when the temperature represented by *P′* is reached, pure *x* will begin to crystallize. As cooling is continued, more *x* will crystallize; the solution will then become more concentrated in *y* and the temperature will drop, both as indicated by curve *BE*.

As soon as the eutectic temperature and composition

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[3] The system is understood to be one in which the components are completely miscible in the liquid phase and the solid phases consist of pure components.

[4] The designation of one component as solvent and the other as solute is actually arbitrary.

are reached, both x and y will crystallize at constant (eutectic) composition and at constant (eutectic) temperature until the entire mass is solidified. The temperature and composition of the solid are then those represented by P''. Further cooling simply lowers the temperature of the solid mass to some point P'''.

Now if the solid mixture of x and y, as represented at P''', is heated, the system will retrace the route just outlined, provided perfect equilibrium conditions are maintained. Melting will begin at T_E and will be complete at the temperature corresponding to P'. In practice, however, unless a sample is very impure, the first sign of melting is not observed until the temperature is considerably above T_E.

B. Experimental Determination of Melting Points

a. Apparatus and Procedure. To determine the melting point of a solid, you will introduce a small sample into a capillary tube, attach the capillary to the stem of a thermometer, heat the bath slowly, and observe the temperatures at which melting begins and is complete. Because at least some time is required for the melting to occur and because the heating is uniform, even a pure substance will show a melting-point range, as measured in this manner. As a rule, however, pure samples will melt sharply, with an observed range of only 0.5°-1.0°.

The sample of solid should be dry and finely divided. If necessary, it should be ground with mortar and pestle or powdered on a piece of filter paper with a small spatula. For economy, and in order to ensure a reliable melting point, only enough solid to fill the capillary to a height corresponding to the length of the thermometer bulb should be used. The temptation is always to use too much.

The melting-point tubes should be thin-walled capillary tubes, 1-2 mm. in diameter, sealed at one end. They may be made from glass tubing or test tubes 10-15 mm. in diameter. The glass must be heated until quite soft and then drawn, slowly at first, then quite rapidly, until it is of the desired diameter.

A good trick is to seal off (with the flame) the long capillary at intervals so as to give individual tubes of twice the desired length, sealed at both ends. They may then be cut into half, just before use, by means of a file or small piece of carborundum, to give two tubes of desired length. This method avoids contamination of the inside of the tubes with moisture or dust.

To fill the melting-point tube, invert it and scoop up a small amount of the solid with the open end of the tube. Then revert the tube and tamp the solid to the bottom by (1) gently rubbing with a file, (2) tapping the tube on the desk gently while holding it with your thumb and forefinger or (3) dropping the tube through a 2-ft. length of glass tubing onto the desk. Repeat this entire process until the desired amount of sample has been introduced. The melting tube can be held to the thermometer by capillary attraction or by means of a narrow band of rubber tubing placed above the surface of the liquid bath.

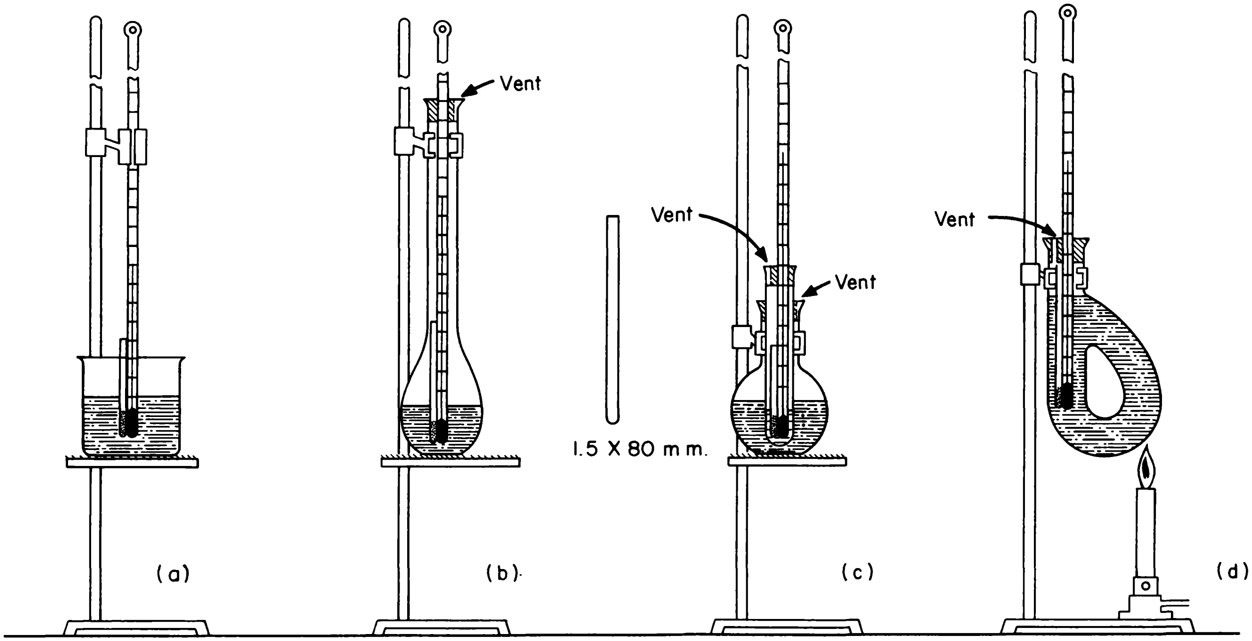

FIG. 3. Various types of melting point baths. (a) Simple beaker. (b) Kjeldahl flask. (c) Double liquid bath. (d) Thiele apparatus.

Liquids that may be used for the bath should be high boiling and stable; glycerol, paraffin oil, cottonseed oil, butyl phthalate, and silicone oil are popular. Glycerol is highly hygroscopic and should be stored in a stoppered bottle; the other liquids may be left in the apparatus.

Various baths (Figure 3) for melting-point determinations are designed for uniform heating. The simplest bath consists of a beaker (100 ml.) mounted on a wire gauze above a small burner (Figure 3a). The thermometer may be suspended in the liquid by means of a clamp and a fitted one-holed cork, a small lengthwise section of which is cut away so that the thermometer scale is visible throughout. The liquid is stirred by the up-and-down motion of a wire, looped to encircle the thermometer bulb and provided with a convenient handle.

A Kjeldahl or similar type long-necked, round-bottomed flask (Figure 3b) may be substituted for the beaker; in this case convection currents provide uniform heating of the thermometer bulb, and the stopper bearing the thermometer is fitted loosely into the neck of the flask. Still other baths are the Thiele apparatus (Figure 3d), which depends upon convection currents for uniform heating, and the double liquid bath (Figure 3c).

To save time, it is wise to heat the bath rapidly until the temperature is about 10° below the melting point of the sample. Then heating should be slow so that the bath temperature rises uniformly and not faster than 2° per minute.

If you do not know the melting point of the solid, you will find it time-saving to fill two capillaries and take a rough, preliminary melting point with rapid heating on one sample. Then allow the bath to cool to about 30° below the melting point, insert the second capillary, and make an accurate determination.

b. Mixed Melting Points. You should always observe and record the melting-point range, from the temperature of first softening to the temperature of complete liquefaction. In the identification of an unknown compound, you will find it useful to run a mixed melting-point determination. If a pure unknown x is suspected of being a known compound y, a melting point is run on a mixture of x with a small amount of y. If x and y are identical, the mixture will melt sharply at the same temperature as pure x. If the x and y are different, the mixture will, as a rule, melt unsharply below the melting point of x.[5] This test is based upon the principles discussed under the *Theory Section* of this Experiment.

c. Stem Correction. For readings of above 100°, the mercury in the stem of the thermometer above the bath is considerably cooler than that in the bulb. For this reason, the observed temperature is slightly lower than the actual bath temperature, and if your thermometer has not been calibrated (see Experiment 1) a "stem correction" should be added.

An approximate correction for stem correction can be calculated from the formula:

$$\text{Stem correction } (^\circ\text{C.}) = (0.000154)\, l\, (T_o - T_m)$$

in which the constant 0.000154 = the apparent coefficient of expansion of mercury in glass,

l = the length of exposed thread in degrees,
T_o = observed temperature,
T_m = median temperature of exposed thread.

This last value, T_m, is taken as the temperature read on a second thermometer hung along the exposed stem.

II. Sublimation

Occasionally one encounters a solid, such as hexachloroethane, $Cl_3C—CCl_3$, or solid carbon dioxide (Dry Ice), whose vapor pressure reaches 760 mm. before the melting point is attained; i.e., below the temperature at which the vapor pressure of the solid substance becomes equal to that of its liquid modification. For such solids, the vapor pressure–temperature curve (*AM* in Figure 4a) shows a pressure of 760 mm. at a temperature below T_M, or, stated in another way, the vapor pressure, P_M, at the melting point, T_M, is above 760 mm.

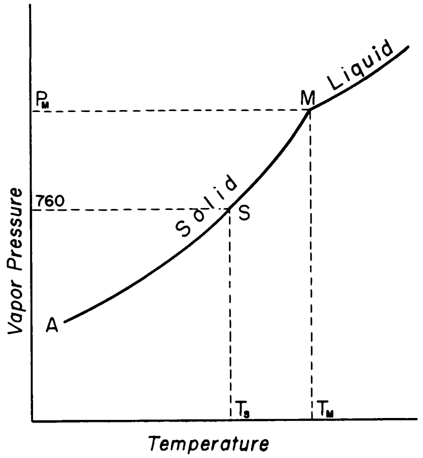

FIG. 4a. Generalized vapor pressure—temperature diagram of a solid which sublimes readily.

When such a solid is heated under one atmosphere pressure, as soon as a vapor pressure of 760 mm. is reached, the solid will pass directly from the solid to the vapor phase at constant temperature. Now, if the vapors are cooled, they will pass back directly into the

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[5] This will not necessarily be true when solid x and solid y are soluble in each other. Fortunately for our purposes, such cases, which are in theory more complex than the general type we have been discussing, are not frequently encountered in organic laboratory work.

solid phase. This total process of direct conversion of a solid to vapor and back again is called **sublimation.** It is a most useful and increasingly important method for the purification of organic compounds.

A study of Figure 4a will show that many solids which melt at atmospheric pressure can be sublimed successfully under vacuum. Theoretically, in order to sublime any solid, we need only reduce the external pressure to some value below the pressure P_M, the vapor pressure at the melting point. In fact, a wide variety of solids which ordinarily melt when heated at atmospheric pressure may still be made to sublime under reduced pressure.

In order to see how this is possible, let us inspect the vapor pressure–temperature diagram for camphor (Figure 4b). *AB* represents the vapor pressure of solid camphor from 0 to 179°; *BC* represents the vapor pressure of liquid camphor from 179° to 208°; *BD* represents the melting point of camphor at various pressures. Point *B* (179° and a pressure of 370 mm.) represents the normal melting point of camphor.[6]

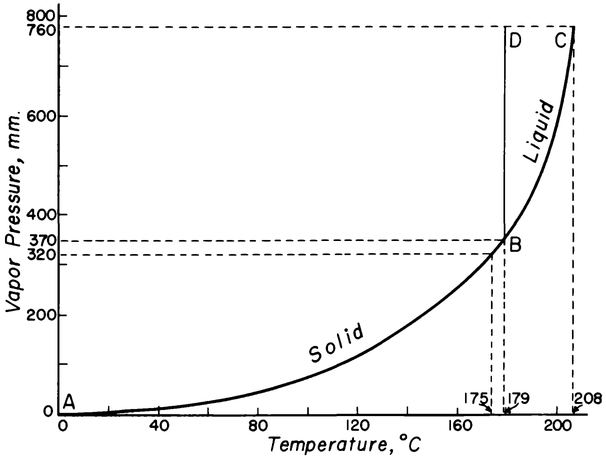

FIG. 4b. Vapor pressure—temperature diagram of camphor.

When heated at atmospheric pressure, camphor melts at 179° and boils at 208°. But if the external pressure is reduced below 370 mm. (and this can very easily be accomplished by means of a water or mechanical pump), solid camphor will pass directly into the vapor phase. Hence sublimation would be carried out readily at any pressure below 370 mm.

But the sublimation could also be carried out at one atmosphere pressure. Suppose that solid camphor in an evaporating dish were maintained at 175° with a condensing surface kept at 25° just above it. At 175° the vapor pressure of camphor is 320 mm.; at 25° it is only 0.7 mm. Then camphor would sublime from the beaker to the condensing surface, because the vapor, leaving the surface of the solid camphor at 175° and 320 mm. pressure, would be cooled at the condensing surface to 25°, where its vapor pressure cannot exceed 0.7 mm. Thus the bulk of the camphor vapor would be converted directly into solid camphor.

Various types of apparatus, from simple to highly elaborate, have been devised for carrying out the purification of solids by sublimation, both at atmospheric and reduced pressure. One of the simplest consists of an evaporating or a Petri dish covered with an ice-cooled watch glass. This will be used in today's experiment on the sublimation of camphor. Other organic solids, besides camphor and hexachloroethane, which can be sublimed fairly readily, are anthracene and various quinones.

Experimental

I. Melting Points

The purpose of this experiment is to determine the melting points of a series of compounds and then to carry out the partial identification of an organic compound by means of mixed melting-point tests.

0-20 Arrange a Thiele tube melting-point apparatus as shown in Figure 3d. Make a small lengthwise slit in the stopper used for supporting the thermometer so that the stem is exposed throughout. Add cottonseed[7] oil to a level just above the top of the side arm.

20-45 Obtain from the side shelf small samples of five of the compounds whose melting points are listed in Table 2. If necessary, powder the sample by means of a mortar and pestle or by crushing on a small filter paper with a spatula.

Introduce a *small amount* of the first sample into a melting-point tube. Attach the tube to the thermometer by means of a small rubber band cut from rubber tubing so that the filled portion of the tube is alongside the thermometer bulb (the two should be approximately equal in length). Be sure that the rubber band is well above the surface of the liquid.

Heat rapidly until the temperature is within 10° of
the recorded melting point for the sample. Then heat
slowly so that the temperature of the bath rises uni-
formly at a rate of not more than 2° per minute. Ob-
serve and record the melting-point range, from the time
the sample first softens and pulls away from the walls
of the capillary until it becomes a clear liquid. Deter- **45-90**
mine and record the melting-point ranges for the four
other samples in the same way.

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[6] Actually 179° is the melting point of camphor at 370 mm. pressure. The melting point at 760 mm. would differ from this value very slightly because increased pressures change the melting point to only a small extent. The behavior of camphor is unusual in that there is no break in the vapor pressure curve in the transition from liquid to solid camphor at the melting point.

[7] Any of the common vegetable oils available at a grocery store may be used.

TABLE 2

Compound	M.P., °C.	Compound	M.P., °C.
Acetanilide	115	Benzoin	137
Benzoic acid	123	*o*-Chlorobenzoic acid	140
Benzamide	128	3-Nitrosalicylic acid	144
Phthalic anhydride	131	Anthranilic acid	146
Urea	132	Adipic acid	152
trans-Cinnamic acid	133	Salicylic acid	158
Phenacetin	135	Benzanilide	161

90-130 Apply to the instructor for an unknown, which may be one of the 14 compounds listed in Table 2, or some other compound. Determine the melting-point range of your unknown. Then select from the list in Table 2 each compound which may possibly be identical with your unknown. As a general rule, all compounds whose melting points are within 5° of that observed for an unknown are considered as possibilities.

Now run a mixed melting point with your unknown and each of these known compounds. To do so, make an intimate mixture of a small quantity of your unknown with roughly one fifth as much of the known sample, either by means of small mortar and pestle or by crushing the material on filter paper with a small spatula. Determine and record the melting-point range.

If the compounds are identical, the melting point of the unknown will be unchanged. If the compounds are different, the known sample will constitute an impurity in the unknown and, except in unusual cases, the mixture will melt lower and over a broader range. Sometimes it is helpful to run melting points on the pure and the mixed samples simultaneously, one on either side of the thermometer, so that their melting behavior may be compared directly.

On the basis of the mixed melting-point determinations, decide which, if any, of the known compounds corresponds to your unknown. Report the melting point of your unknown, and, if possible, its identity.

Since the melting-point apparatus will be used frequently in future experiments, it may be advisable, if possible, to store it in assembled form.

II. Sublimation

Purification of Camphor by Sublimation. Take from the side shelf or prepare a 1-g. sample of an intimate mixture of roughly 19 parts of camphor with 1 part of succinic acid. Determine simultaneously and compare the melting points of camphor,[8] alone, and the camphor–succinic acid mixture. Record these values. Fill a third melting-point tube with a sample of the camphor–succinic acid mixture and set it aside for comparison with the sublimed material.

130-160 Place the remainder of the sample in a small evaporating or Petri dish supported over a wire gauze on a ring stand. Place over the dish a watch glass containing a few pieces of crushed ice. Gently heat the bottom of the dish, keeping the temperature below the temperature at which any liquid is formed.

After a significant amount of camphor has collected on the bottom of the watch glass, very gently pour out the water and ice, and scrape off the camphor with a spatula. Wrap the sample tightly in a small piece of filter paper and allow it to dry until the next period. Then determine simultaneously and compare the melting points of the sublimed material and of the camphor–succinic acid mixture. Record the values.

QUESTIONS

1. What effect would each of the following have on the observed melting point and melting point range of a sample:

(a) Use of a thick-walled melting point tube.

(b) Use of a 3-5 mm. capillary tube.

(c) Rapid heating.

(d) Use of so much sample that the filled portion of the capillary tube extends considerably beyond the thermometer bulb.

(e) Presence of a pin-hole in the bottom of the capillary tube which allows the bath liquid to enter the capillary.

(f) Poor circulation of the bath liquid.

2. Can you suggest any reason why it might be advisable to run a mixed melting point on samples of two different compositions before concluding that the two compounds used were identical?

3. Which gives more accurate melting points, the capillary tube method or the equilibrium method used in the calibration of your thermometer (Experiment 1)? Explain.

4. Ordinarily you will determine melting points in glass apparatus. This means that glass constitutes an impurity in the system. Why does the glass have no noticeable effect on the melting points? Does sand lower the melting point of ice appreciably? Why or why not?

5. A student suspected that an unknown was undergoing a chemical change at its melting point. Suggest a simple method for testing his hypothesis.

6. How do you explain that acetone and ethyl alcohol lower the melting point of ice as well as the boiling point of water, whereas salt and sugar raise the boiling point and lower the melting point?

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[8] For solids, such as camphor, which sublime readily, the melting point is best determined in a sealed capillary.

7. How can liquid carbon dioxide and liquid hexachloroethane be obtained?

8. Cite specific data to prove that camphor may be separated from succinic acid by sublimation.

9. An organic compound has a melting point of 156°; its vapor pressure at that temperature is 231 mm. How can it be sublimed?

10. (For Specially Interested Students) According to Raoult's Law, addition of one mole of any nonionizing solute to 1000 g. of solvent lowers the melting point of the solvent by a constant value, characteristic of that solvent, called the freezing-point constant, K_f, for that solvent. This constitutes the basis for a convenient method for the determination of the molecular weights of organic compounds in solvents such as benzene and camphor. The molecular weight (M) of any compound, x, may be calculated from the equation

$$M = \frac{1000\, K_f w}{\Delta T W}$$

where K_f is the freezing-point constant of the solvent, and ΔT is the observed freezing-point depression observed for a solution which contains w g. of x dissolved in W g. of solvent. Derive this equation.

EXPERIMENT 3

Boiling Points—Distillation—Fractional Distillation

Introduction

A. Simple Distillation

Distillation is the most common and most important method for the purification of liquids. For the separation of a liquid from nonvolatile impurities, it is the obvious method of choice.

A simple distillation apparatus, such as that pictured in Figure 5, is used for this purpose. The entire apparatus should be mounted securely to ring stands by means of clamps. The latter should preferably be supplied with rubber or asbestos sleeves to reduce thermal and mechanical shock to the glass.

The liquid is distilled from the distilling flask which rests on a wire gauze supported by means of a ring. A fraction of the vapor condenses on the thermometer and on the walls of the flask, but most of the vapor passes through the side arm of the flask into the condenser where it is condensed by means of an ascending stream of cold water in the jacket of the condenser. The condensate is conveniently channeled into a receiving flask by means of a curved adapter. The nonvolatile material is left as a **residue** in the distilling flask.

The top of the thermometer bulb should extend just to the lower level of the side arm (see Figure 5, inset) so that the entire bulb is definitely bathed in a flow of vapor. Distillation should always be conducted slowly but steadily so that the thermometer bulb at all times bears a drop of condensate. This favors the maintenance of equilibrium between liquid and vapor at the bulb. In the distillation of water, rubber stoppers may be used throughout. For many organic liquids which cause swelling of rubber, neoprene or tightly fitting cork stoppers are usually preferred.

Almost all liquids tend to superheat (rise to a temperature somewhat above the boiling point) to some extent.[1] This is a metastable condition and is interrupted periodically by a sudden violent surge of vapor from the liquid called **bumping.** When this occurs, the vapor is superheated, also, and the observed boiling point may be high. All this may be largely avoided by the addition of 2 or 3 small boiling chips to the distilling flask.

Various types of commercially available carborundum[2] or hard, porous porcelain or tile chips are suitable for the purpose, or the boiling stones may be made by chipping of a porous plate with a hammer or pair of pliers. The small pores of the boiling stones provide a site for the formation of bubble nuclei and thereby induce even boiling. If the boiling liquid drops below its boiling point at any time, liquid fills the pores of the boiling aid and it is no longer effective. The liquid should definitely be cooled below its boiling point

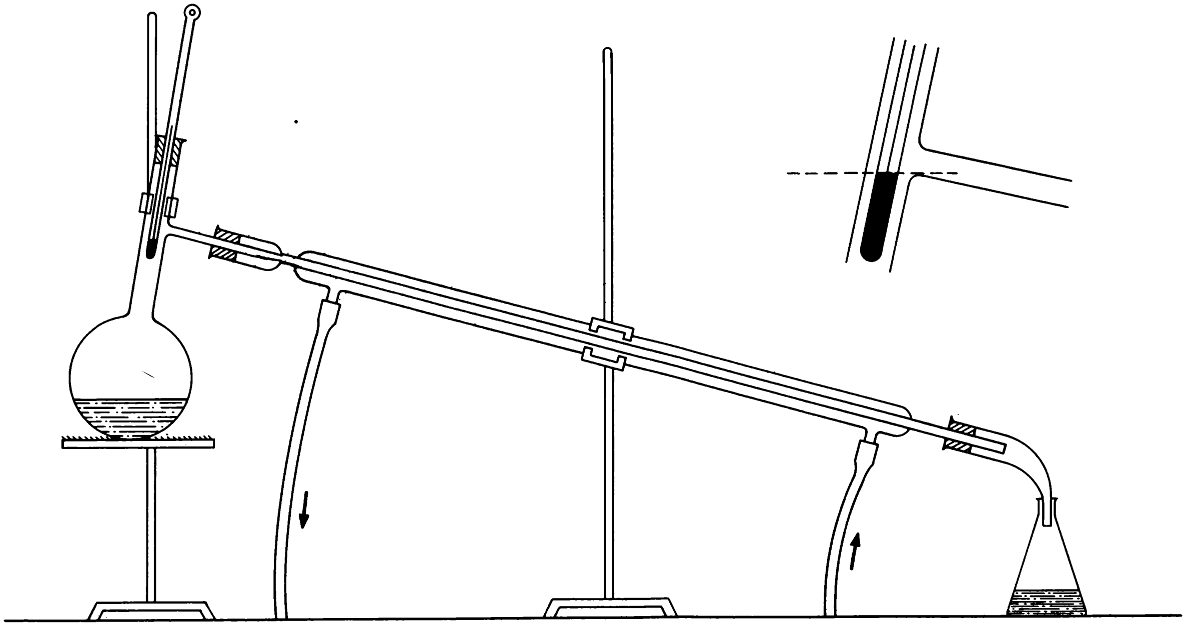

FIG. 5. Simple distillation apparatus.

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[1] Water freed from all dissolved air has been superheated to 137° at 1 atmosphere before it boiled.

[2] No. 12 carborundum stones available from the Carborundum Company, Niagara Falls, N. Y., are inexpensive and effective.

before the addition of a fresh chip; addition of a boiling stone to a superheated liquid initiates boiling that may proceed with violence.

A layer of solid at the bottom of the distillation flask may be the cause of violent bumping during a distillation, especially if intense local heating at the bottom of the flask is used. Heating of a flask in which a solid has deposited should always be carried out in a liquid bath of some type.

If a liquid is contaminated with a volatile impurity, separation of the two may usually still be effected by distillation. In fact, theoretically any two substances which do not have identical vapor pressures over the entire temperature range at which they are stable are separable by distillation. Practical achievement of the theoretical possibility is limited only by the patience of the investigator and his skill and ingenuity in the design and use of the proper equipment.

As a general rule, a mixture of any two components which boil at least 80° apart may be separated by a single simple distillation. For materials whose boiling points differ by 30° to 80°, separation may still be effected by repeated simple distillations.

Such mixtures are much more conveniently separated by **fractional distillation,** and, in fact, efficient fractionating equipment is used continually in industrial work and in research laboratories for the separation of liquids which boil but a few degrees or even a fraction of a degree apart. In order to understand the principles underlying such separation, we should review some of the theory of the relationship between vapor pressure and boiling point.

B. Boiling Points of Pure Liquids

Any given liquid, when admitted into a closed evacuated space, evaporates until the vapor attains a certain definite pressure, which depends only upon the temperature. This pressure, which is the pressure exerted by the vapor in equilibrium with the liquid, is the **vapor pressure** of the liquid at that temperature. As the temperature increases, the vapor pressure of a typical liquid, x, increases regularly as shown by the generalized vapor pressure–temperature curve BC, in Figure 6.

At the temperature, T_p, where the vapor pressure reaches 760 mm., x begins to boil and T_p is called the **normal boiling point** of x. Every liquid which does not decompose before its vapor pressure reaches 760 mm. has its own characteristic boiling point. In general, the boiling point of a substance depends upon the mass of its molecules and the strength of the attractive forces between them. For a given homologous series, the boiling points of the member compounds rise fairly regularly with increasing molecular weight.

Polar liquids tend to boil higher than nonpolar liquids of the same molecular weight, and associated polar liquids usually boil considerably higher than nonassociated polar compounds. Thus ethyl alcohol, C_2H_5OH, boils considerably higher (78.8°) than methyl ether, $CH_3—O—CH_3$ (−23.7°), which is somewhat polar but nonassociated, and both boil higher[3] than propane, C_3H_8, (−42.1°), which is both nonpolar and nonassociated.

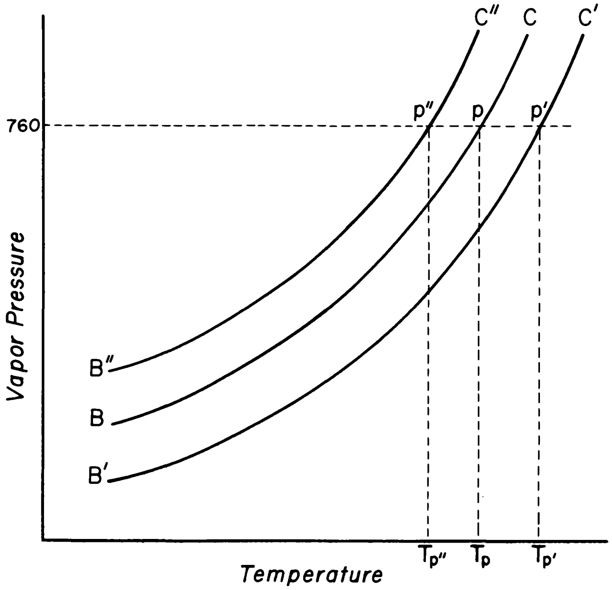

FIG. 6. Generalized vapor pressure diagrams for a pure liquid (BC), for a solution in which the solute is less volatile than the solvent (B′C′), and for a solution in which the solute is more volatile than the solvent (B″C″).

The boiling point is a characteristic constant that is widely used in the identification of liquids. Because of its marked dependence upon pressure and its rather erratic response to impurities, however, it is generally less reliable and useful in characterization and as a criterion of purity than is the melting point for solids.

C. Boiling Points of Solutions

The normal boiling point of any solution is the temperature at which the *total* vapor pressure of the solution is equal to 760 mm. The effect of any solute, y, on the boiling point of x will depend, then, upon the nature of y. If y is less volatile than x, then the total vapor pressure of the solution is lower, at any given temperature, than the vapor pressure of pure x.

Such a case is represented by curve $B'C'$, in which the experimentally determined values for the vapor pressures of a solution are plotted against temperature. The vapor pressure of the solution does not reach 760 mm. until a temperature $T_{p'}$ is attained. In other words, the presence of the less volatile solute raises the boiling point of x from T_p to $T_{p'}$. A solution of sugar or salt in water is a familiar example of this type of solution.

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[3] The comparison is being made between compounds of approximately the same molecular weight.

On the other hand, if y is more volatile than x, then the total vapor pressure of the solution is higher than that of pure x, as shown by curve $B''C''$. The vapor pressure of such a solution reaches 760 mm. at temperature $T_{p''}$; hence the effect of the more volatile solute is to lower the boiling point of x from T_p to $T_{p''}$. A solution of acetone in water is an example of this type.

In any solution of two liquids x and y, the molecules of x are diluted by molecules of y, and, conversely, the molecules of y are diluted by molecules of x. You would therefore expect the vapor pressure due to x to be less than that of pure x; in fact, you might predict that the **partial pressure** due to x would be proportional to the molecular concentration of x.

Similarly, the partial pressure of y might be expected to be proportional to the molecular concentration of y. This is, in fact, the relationship which holds for so-called ideal solutions. It is expressed in Raoult's Law: *the partial pressure of a component in a solution at a given temperature is equal to the vapor pressure of the pure substance multiplied by its mole fraction in solution.* In symbols, for a solution of components x and y,

$$P_x = P_x{}^0 N_x$$

where P_x = the partial pressure of x in solution,
$P_x{}^0$ = the vapor pressure of pure x at that temperature,
N_x = the mole fraction of x in the solution.

Similarly,

$$P_y = P_y{}^0 N_y$$

where P_y = the partial pressure of y in the solution,
$P_y{}^0$ = the vapor pressure of pure y at that temperature,
N_y = the mole fraction of y in solution.

The total pressure, P_T, of the solution would be the sum of the partial pressures of x and y.

$$P_T = P_x + P_y$$

For example, at 25° the vapor pressure of benzene is 94 mm. and that of toluene is 29 mm. In a solution containing 2 moles of benzene and 1 mole of toluene, therefore, the partial pressure, P_x, of benzene is calculated as follows:

$$P_x = (94 \text{ mm.}) (\tfrac{2}{3})$$
$$P_x = 63 \text{ mm.}$$

For the partial pressure of toluene, P_y:

$$P_y = (29 \text{ mm.}) (\tfrac{1}{3})$$
$$P_y = 10 \text{ mm.}$$

and for the total pressure, P_T,

$$P_T = P_x + P_y$$
$$P_T = 63 \text{ mm.} + 10 \text{ mm.}$$
$$P_T = 73 \text{ mm.}$$

At 87.7° the partial pressure of benzene in a 2:1 molar mixture of benzene and toluene is 637 mm. and that of toluene is 123 mm. Therefore at 87.7°, the total vapor pressure would be 760 mm., and the solution would begin to boil. The vapor which is in equilibrium with a solution containing $66\frac{2}{3}$ mole per cent benzene and $33\frac{1}{3}$ mole per cent toluene is 637/760 or 83.8 mole per cent benzene and 123/760 or 16.2 mole per cent toluene. In other words, the vapor is richer than the liquid in the more volatile component, benzene.

As applied to fractional distillation, two important practical generalizations emerge from Raoult's Law: (1) the boiling points of all solutions of x and y will lie between the boiling points of x and y, and (2) the vapor will always be richer in the lower boiling component than the liquid with which it is in equilibrium.

D. Temperature–Composition Diagram for Solutions which Follow Raoult's Law

These facts are represented graphically in Figure 7 which shows a typical temperature–composition diagram. This diagram is a temperature–composition plot of the experimentally determined values for the system benzene-toluene, but it is representative of the plot for all solutions which are described by Raoult's Law.

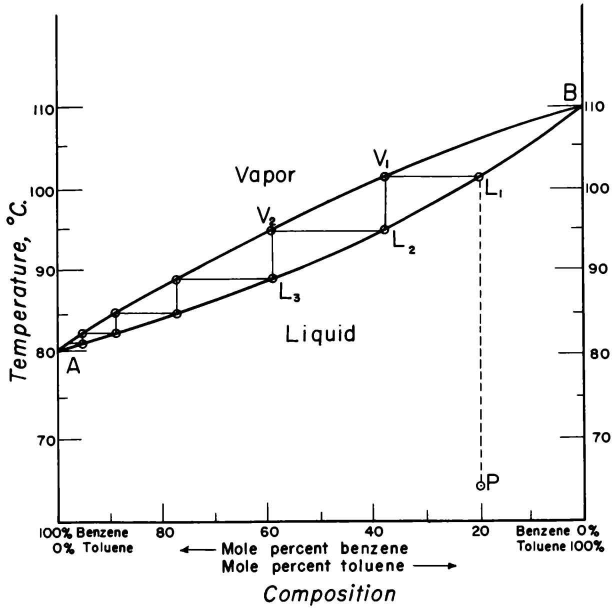

FIG. 7. Temperature-composition diagram of the system benzene-toluene.

Boiling points (ordinates) are plotted against composition expressed as mole fractions (abscissae). Pure benzene boils at 80.1° (point A) and pure toluene (100 per cent y) at 110.6° (point B). All mixtures of the two boil at intermediate temperatures, as shown by the liquid (lower) curve. This curve shows the temperature at which a mixture of benzene and toluene of any given composition begins to boil. The vapor (upper) curve represents the composition of the vapor in equilibrium with the liquid at any given temperature.

For example, consider the changes which occur when a 20 mole per cent benzene—80 mole per cent toluene solution (represented by point P) is heated. At 101.6°, corresponding to point L_1, the liquid begins to boil. The first trace of vapor which is formed is, of course, in equilibrium with the liquid at 101.6°. It has the composition 38 mole per cent benzene—62 mole per cent toluene, as represented by point V_1, and is therefore considerably richer than the liquid in benzene.

As the distillation proceeds, the concentration of toluene in the liquid phase and the boiling point increase continuously, following the values represented by L_1B. Finally, at the end of the distillation, the liquid phase is pure B boiling at 110.6°. Similarly, the vapor becomes progressively richer in toluene also, following V_1B. Always, however, it is richer in benzene than is the liquid with which it is in equilibrium, as shown by the points of intersection of any horizontal line with the vapor and liquid curves.

Obviously, a single simple distillation could never separate a 20:80 molar mixture of benzene and toluene into the pure components. But now consider what would be accomplished if the first trace of vapor formed by distillation of the mixture were cooled and condensed. It would, of course, form liquid corresponding to point L_2 of composition 38 mole per cent benzene —62 mole per cent toluene at 94.5°.

Now, if liquid L_2 were distilled, the first trace of vapor formed would have the composition 59 mole per cent benzene—41 mole per cent toluene (point V_2) and when cooled would condense to liquid at 88° (point L_3). This, in turn, may be further enriched in benzene as indicated on the graph.

E. Fractional Distillation

Obviously, by repeated simple distillation with combination and recombination of various distillate and condensate fractions, one could eventually separate a mixture of benzene and toluene into pure benzene and pure toluene. Ultimately, the distillate would become pure low-boiling component (benzene) and the residue pure high-boiling component (toluene).

Fractional distillation is simply a technique for accomplishing a whole series of such miniature separations in a single, continuous operation. In principle, a fractional distillation column provides an extensive surface for heat interchange, at equilibrium conditions, between ascending vapor and descending condensate. This makes possible a whole series of partial vaporizations and partial condensations along the length of the column.

In a simple packed[4] column, such as shown in Figure 8a, for example, there is a continuous interchange of

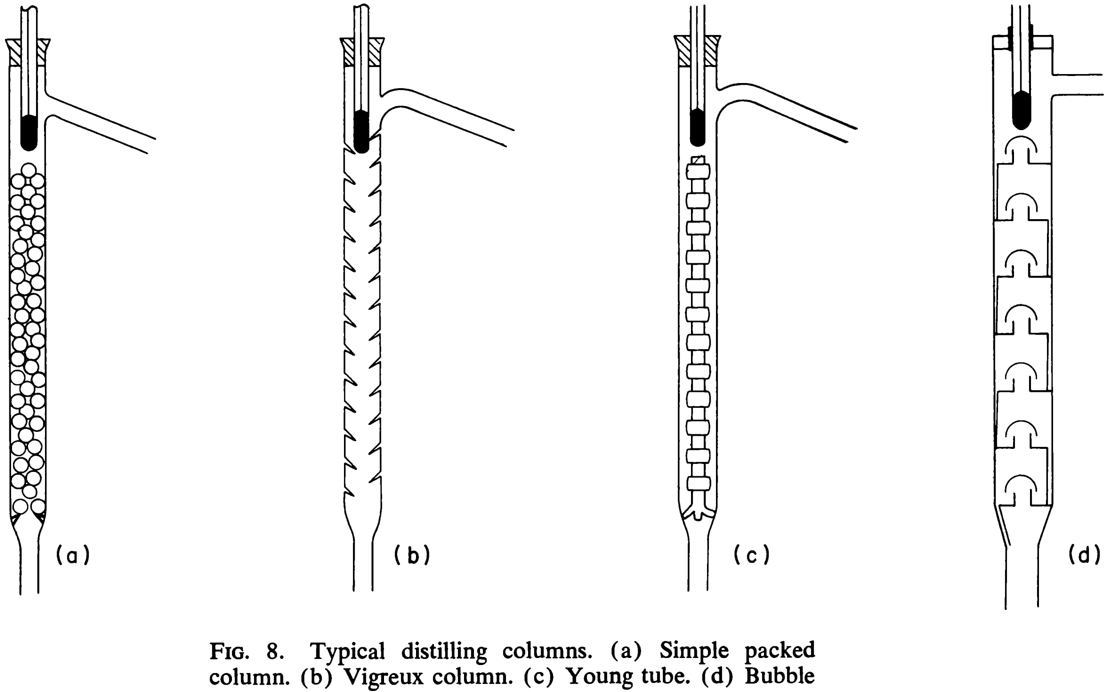

FIG. 8. Typical distilling columns. (a) Simple packed column. (b) Vigreux column. (c) Young tube. (d) Bubble plate column.

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[4] The packing may consist of any of a wide variety of inert materials with extensive surface area—glass beads or helices, metal helices, carborundum or porcelain stones, etc.

heat between the cooler descending condensate and the warmer ascending vapor at the surface of the packing. As the condensate at any point in the column accepts heat from the vapor, part is revaporized, and the vapor formed is richer in the more volatile component than the condensate. At the same time, as the vapor loses heat to the condensate, part of it condenses, the condensate being richer than the vapor with which it is in equilibrium in the high boiling component. Hence, the vapor eventually appearing and being removed at the top of the column is pure low-boiling component; the residue in the flask is pure high-boiling material.

Throughout the entire length of the column, there is a temperature gradient from the boiling point of y to the boiling point of x. This gradient represents a whole series of separate equilibria between liquid and vapor with the concentration of x in the equilibrium mixtures increasing progressively from bottom to top in the column.

Other simple types of fractionating columns are pictured in Figure 8. The Vigreux column (b) has indentations to provide increased surface, the Young tube (c) has a glass or metal spiral wound around a central core, and the bubble plate column (d) has small liquid traps spaced at regular intervals. Elaborate vacuum jacketed and externally heated columns (to prevent heat loss to the outside and thereby confine heat interchange to the liquid-vapor system) are in wide use in industry and in research laboratories.

Such columns accomplish the equivalent of several hundred separate simple distillations and are effective even in the separation of liquids whose boiling points differ by only a fraction of a degree. In these columns, most of the condensate from the condenser is allowed to trickle back over the packing in the column, with only a small fraction being taken off as distillate. The ratio of condensate returned to the column to that removed is called the **reflux ratio.** Efficiency of fractionation increases with increase in reflux ratio.

F. Temperature–Composition Curves for Nonideal Systems

Unfortunately, many systems are not ideal (their vapor pressure–composition behavior is not that described by Raoult's Law). Some liquid pairs form minimum boiling mixtures. Ethyl alcohol (b.p. 78.3°) and water, for example, form a minimum boiling mixture (95.57 per cent by weight alcohol and 4.43 per cent water) which boils constantly at 78.2°, a value below the boiling point of either water or alcohol. Water and formic acid (b.p. 100.8°), on the other hand, form a maximum boiling mixture (22.5 per cent by weight water and 77.5 per cent formic acid), which distills constantly at 107.1°, a temperature above the boiling point of either component.

Boiling point–composition curves of such systems are interpreted simply as if they consisted of two separate systems. Figure 9, for example, shows a typical temperature–composition diagram for a system of two components, x and y, which form a minimum boiling mixture, represented at M, with composition C_M and boiling point, T_M. The minimum boiling mixture distills completely at constant temperature since, at the boiling point, the vapor has the same composition as the liquid.

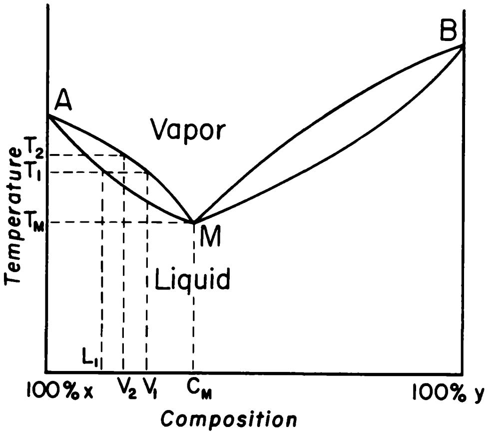


FIG. 9. Temperature-composition curve for a system which forms a minimum boiling mixture.

Fractional distillation of any mixture of composition from pure x to C_M is separated eventually into distillate of composition C_M (constant boiling mixture) and residue pure x. Similarly, any mixture of composition from C_M to pure y will separate into distillate of composition C_M (constant boiling mixture) and residue pure y. In other words, this system behaves throughout the whole composition range as if the minimum boiling mixture is the low-boiling component.

Conversely, a system which forms a maximum boiling mixture behaves throughout its whole composition range as if the maximum boiling mixture is the high-boiling component. Figure 10 represents a typical system of

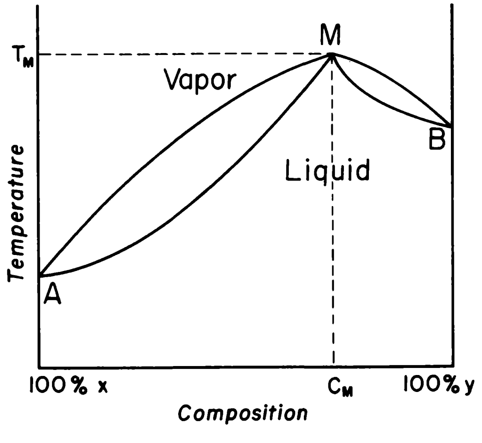


FIG. 10. Temperature-composition diagram for a system which forms a maximum boiling mixture.

this type, in which x and y form a maximum boiling mixture, with composition C_M and boiling point T_M. Fractional distillation of any mixture from composition pure x to C_M separates the mixture eventually into a distillate of pure x and residue of composition C_M (constant boiling mixture). Similarly, any mixture of composition from C_M to pure y is separated eventually into a distillate of pure y and residue of the constant boiling mixture, C_M.

Constant boiling mixtures are called **azeotropic** (Greek: to boil unchanged) mixtures. The composition, as well as the boiling point, of an azeotropic mixture varies somewhat with changes in the external pressure. Often azeotropic mixtures can be separated into their pure components by a type of distillation in which a third component which alters the vapor pressure ratio in the azeotrope is added (see Experiment 37).

G. Vacuum Distillation

Many substances cannot be purified by distillation at ordinary pressures because they decompose below their normal boiling points. Others have boiling points that make distillation inconvenient or even difficult. Often such liquids (and solids, also) can still be distilled if the distillation is conducted under reduced pressure.

A liquid begins to boil at the temperature at which its vapor pressure becomes equal to the external pressure. A study of Figure 6 will show that the boiling point of a liquid decreases regularly with decrease in the external pressure. Hence, by the use of a special apparatus for the distillation (including fractional distillation) of liquids under reduced pressure, from just below atmospheric pressure to pressures of 10^{-8} mm., chemists have been able to distill most organic liquids and many solids. Such distillation at pressures below atmospheric pressure is called **vacuum distillation.** A simple apparatus for vacuum distillation is shown in Figure 28 (Experiment 33).

Experimental

In this experiment you will compare the efficiency of (1) simple distillation without a column, (2) distillation through an unpacked column, and (3) distillation through a packed column. Students will work in groups of three. One student in each trio will conduct the distillation described below with the simple apparatus (Figure 5), the second using an unpacked air condenser or fractionating column (Figure 8), and the third an air condenser or fractionating column packed with a copper sponge. In order to pack the condenser or column, pull out an ordinary dime-store copper sponge (such as a "Chore Girl") to a strand about 3 ft. long and work it into the column with a quarter-inch dowel.

At the end of the experiment, compare your results with those obtained by each of the other two students in your trio.

Introduce into a 150-ml. distilling flask, or a 200-ml. round-bottomed flask, 35 ml. of water and 35 ml. of acetone and 2 or 3 small boiling chips. Clamp the distilling flask securely to a ring stand above a wire gauze supported on a ring. Arrange the rest of the apparatus as specified in the previous paragraph, according to your assignment in your trio. Rubber stoppers or tightly fitting corks should be used throughout. Force a *gentle* stream of water from the tap up through the condenser by means of a rubber tube from the tap to the water inlet. The emergent stream of water should be conducted to the drain by a length of rubber tubing attached to the water outlet. Number and label five small flasks for collecting various fractions as follows:

I 56°-62°
II 62°-72°
III 72°-82°
IV 82°-95°
V Residue

Heat the flask by means of a low flame so that the condensate collects steadily, without interruption, at the rate of approximately 1 drop a second. Change the receivers rapidly at the specified temperature intervals. When the temperature reaches 95°, interrupt the distillation and cool the distillation flask, allowing any condensate in the fractionating column to trickle back into the flask.

Measure with the graduated cylinder the volumes of distillate obtained in each fraction, and of the residue in the flask. Record these volumes and draw a distillation curve by plotting the volume of distillate vs. the temperature. The first fraction is essentially pure acetone, the residue pure water. You may wish to test a small sample of each fraction on a watch glass to see if it will burn. Record the data obtained by each of your two partners and compare the three sets of data.

Now, if you have been assigned the simple distillation without use of a column, introduce into the empty distilling flask the contents of receiver II and reassemble the apparatus for distillation. Distill until the temperature reaches 72°, adding the fraction distilling from 56°-62° to receiver I, and that from 62°-72° to receiver II.

Again interrupt the distillation, allow the distilling flask to cool below 50°, and pour into it, by means of a small funnel, the contents of receiver III. Resume the distillation and add the various fractions to receivers I, II, III, as indicated by the thermometer reading.

Stop the distillation at 82°, allow the flask to cool somewhat, and introduce the contents of receiver IV. Repeat the distillation, adding each fraction to the appropriate receiver. When the temperature reaches 95°, cease the distillation and add residue in the flask to receiver V. Again measure and record the total volume of each fraction.

QUESTIONS

1. Summarize the data for the distillation of the acetone–water mixture obtained by each member of your trio. Explain the differences in the results.

2. Why does not all of the liquid in the distilling flask vaporize at once when the boiling point is reached?

3. Why should a distilling flask not be filled much more than half full?

4. What is the disadvantage of using a distilling flask whose capacity is four or five times or more the volume of the liquid being distilled?

5. Draw a general temperature–composition diagram similar to that of Figure 7, but with a boiling point of 56.6° for component x and of 100° for component y. This diagram now represents, at least approximately, the acetone–water system. At approximately what temperature will a 1:1 molar mixture of acetone and water begin to distill? A 3:1 molar mixture? A 1:3 molar mixture? What is the approximate composition of an acetone–water mixture which begins to distill at 70°? At 80°?

6. If liquids x and y both have a boiling point of 160° and do not form an azeotrope, what will be the boiling point of a mixture of x and y? In a general sense, how does this fact limit the value of boiling points as a criterion for determining the purity of liquids?

7. An organic liquid decomposes at 80°. Its vapor pressure at that temperature is 36 mm. How would you distill the liquid?

8. If the thermometer bulb is not kept moist with condensate during a distillation, will the boiling-point reading tend to be high or low? Explain.

9. Why does condensate continually flow back into the distillation flask from a fractionating column that does not have a reflux condenser? Does this have any effect on the distillation? Explain.

10. If the rate of distillation through a packed column is too rapid, flooding occurs (liquid is forced up through the column). What effect would flooding have on the efficiency of distillation?

EXPERIMENT 4

Crystallization

Introduction

General Methods of Crystallization. Since the days of the earliest alchemists, solids have been purified by crystallization from suitable solvents. Today this technique still stands as the most useful method for the purification of solid substances.

As commonly practiced, purification by crystallization depends upon the fact that most solids are more soluble in hot than in cold solvents. The solid to be purified is dissolved in the hot solvent at its boiling point, the hot mixture is filtered to remove all insoluble impurities, and then crystallization is allowed to proceed as the solution cools. In the ideal case, all of the desired substance separates in nicely crystalline form and all the soluble impurities remain dissolved in the mother liquor. Finally, the crystals are collected on a filter and dried. If a single crystallization operation does not yield a pure substance, the process may be repeated with the same or another solvent.

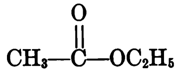
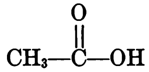
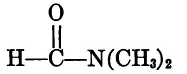
The great beauty of crystallization as a purification technique lies in the fact that the orientation of molecules in a crystal lattice is an extremely delicate and selective process. Only infrequently do different substances crystallize in the same lattice. At times, the desired solid can be crystallized selectively from a solution also saturated with other solid impurities simply by the careful introduction of a tiny seed crystal. In such cases, the molecules of the desired compound leave the solution to take positions in the crystal lattice, while the mother liquor remains saturated, or even becomes supersaturated, with respect to the foreign materials.

A solid solute may, of course, be crystallized by spontaneous evaporation of solvent from a saturated solution. Occasionally, this is used as a method of purification. Evaporation should proceed very slowly to avoid formation of a crust of impure solid at the evaporating surface. In general, this method is less effective than the classical crystallization technique.

Selection of Solvent. Similia similibus solvunter (like dissolves like) was a watchword among the alchemists and medieval iatrochemists. It is still perhaps the best three-word summary of solvent behavior; a detailed study of the relationship between structure and solvent action becomes highly complex. In the final analysis, the best way to find a suitable recrystallization solvent for a given substance is by experimental trial (see Experimental section). A few helpful and reasonably valid generalizations may, however, speed the process. The most useful of the common organic crystallization solvents, together with some of their properties, are listed in Table 3.

No nonionic compound dissolves appreciably in water unless its molecules are ionized in water solution or can co-associate with water molecules through hydrogen bonding.[1] Thus, hydrocarbons and their halogen derivatives are virtually insoluble in water. Compounds

TABLE 3. COMMON RECRYSTALLIZATION SOLVENTS

Solvent	Formula	Boiling Point, °C.	Freezing Point, °C.	Miscibility with Water	Fire Hazard
Petroleum ether	Mixture of C_5H_{12} and C_6H_{14}	35-65	<0	−	++++
Ether	$(C_2H_5)_2O$	34.6	−116	−	++++
Acetone	$(CH_3)_2CO$	56.1	−95	+	+++
Ligroin	C_nH_{2n+2}	60-80	<0	−	++++
Chloroform	$CHCl_3$	61.3	<0	−	0
Methyl alcohol	CH_3OH	64.7	−98	+	++
Carbon tetrachloride	CCl_4	76.7	<0	−	0
Ethyl acetate	 $CH_3-\overset{O}{\overset{\|}{C}}-OC_2H_5$	77.2	−84	−	++
95% ethyl alcohol	C_2H_5OH	78.1	−116	+	++
Benzene	C_6H_6	80.2	5.5	−	++++
Acetic acid	 $CH_3-\overset{O}{\overset{\|}{C}}-OH$	118.1	16.6	+	+
Dimethylformamide	 $H-\overset{O}{\overset{\|}{C}}-N(CH_3)_2$	153.0	−61	+	+
Nitrobenzene	$C_6H_5NO_2$	210.9	5.7	−	+

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[1] The hydrogen bonds or hydrogen bridges with which we are concerned in dealing with the water solubilities of organic compounds are almost exclusively those in which hydrogen links oxygen atoms to oxygen or nitrogen atoms.

whose molecules contain functional groups [such as alcohol (OH), aldehyde ($-\overset{H}{\overset{|}{C}}=O$),[2] ketone ($R-\overset{O}{\overset{\|}{C}}-R$), carboxylic acid ($-\overset{O}{\overset{\|}{C}}-OH$), and amide ($-\overset{O}{\overset{\|}{C}}-NH_2$) groups], which can form hydrogen bonds with water, are soluble in water unless the ratio of the total number of carbon atoms to such functional groups in the molecule exceeds 4 or 5. Then the solubility falls off rapidly. Thus, acetamide ($CH_3-\overset{O}{\overset{\|}{C}}-NH_2$) is soluble in water, but caproamide ($CH_3-(CH_2)_4-\overset{O}{\overset{\|}{C}}-NH_2$) is not. In fact, it is a very general rule that as any homologous series is ascended, the solubilities and all other physical properties of the members tend to approach those of the parent hydrocarbon.

Most organic compounds which lack a hydrogen-bonding hydrogen atom dissolve readily in ether, benzene, ligroin, and other typical nonassociated solvents, simply by a process of molecular mixing. Organic compounds, which themselves are associated in the liquid state, are likewise reasonably soluble in such solvents, unless (1) they have two or more hydrogen-bonding functional groups per molecule, approaching a ratio of one such group for each carbon atom, or (2) unless they are solids with high melting points. Thus, *n*-propyl alcohol ($CH_3CH_2CH_2OH$) and caproic acid ($CH_3-(CH_2)_4-COOH$) are soluble in ether, but glycerol ($HOCH_2-CHOH-CH_2OH$), with one hydroxyl group for each of the three carbon atoms, adipic acid ($HO-\overset{O}{\overset{\|}{C}}-(CH_2)_4-\overset{O}{\overset{\|}{C}}-OH$), with a melting point of 153°, and glucose ($HOCH_2(CHOH)_4CHO$), with five hydoxyl groups per six carbon atoms, are not.

Ether and benzene are quite similar in solvent action. Ether is, in general, a better solvent than benzene for associated compounds, and both are better than petroleum ether and ligroin. Petroleum ether is similar to ligroin, but has somewhat weaker solvent action.

The associated hydroxylic solvents, such as methyl alcohol, ethyl alcohol, and acetic acid (all three of which are completely miscible with water), are somewhat intermediate between water and ether (and benzene) in solvent properties. They are generally somewhat weaker solvents than ether and considerably stronger than water toward the hydrocarbons and their halogen derivatives. Toward organic compounds which are capable of association or co-association, they are powerful solvents. The solvent power of the three varies in the same order as their boiling points: acetic acid > ethyl alcohol > methyl alcohol. As a solvent, acetone is similar to ethyl alcohol, but more powerful.

The chlorinated hydrocarbons chloroform and carbon tetrachloride are excellent solvents for nonassociated substances. Because of their high chlorine content they are relatively expensive.

Often a substance is found to be too soluble in one solvent and too insoluble in another for satisfactory crystallization. Then solvent pairs, such as methyl alcohol–water, ethyl alcohol–water, ether–acetone, and benzene–ligroin, are frequently effective. The compound is dissolved (at or slightly below the boiling point) in the solvent in which it is very soluble and the hot solvent in which it is sparingly soluble is added dropwise until a slight turbidity is produced. Then just enough of the first solvent is added to clear the turbidity, and the solution is allowed to cool in the usual manner.

An ideal crystallization solvent should have a high temperature coefficient toward the substance to be purified; i.e., it should dissolve a large amount of the substance at its boiling point and only a small amount at room temperature or slightly below. It should have a low temperature coefficient toward the impurities. Furthermore, upon cooling it should readily yield well formed crystals of the purified compound, from which it should be easily removable. It should not react with the solute, and it should be perfectly safe to use (nonflammable). Of course, it should be inexpensive. If water meets all of the solubility and recrystallization requirements, it is usually the solvent of choice.

Preparation of the Solution. As a rule, the objective is to dissolve the solute in a minimum amount of solvent at the boiling point. The following procedure is recommended: place the finely divided material in an Erlen-

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[2] For the purposes of discussing solubility behavior, we may conveniently divide solutes into three classes: (1) those that are associated in the liquid state; (2) those that are not associated but can co-associate with water; and (3) those that are neither associated themselves nor capable of co-associating with water.

Aldehydes, ketones, esters, and tertiary amines (R_3N), and similar oxygen- and nitrogen-containing compounds, can co-associate with water, even though they, themselves, are nonassociated because of the lack of a hydrogen-bonding hydrogen. In the co-association of such nonassociated compounds with water, the hydrogen-bonding hydrogen must be supplied by the water molecules. With aldehydes, for example, the bonding would be represented as $R-\overset{H}{\overset{|}{C}}=O\cdots H\overset{O}{\diagup\ \diagdown}H$.

On the other hand, compounds such as alcohols, carboxylic acids, amides, and primary and secondary amines (RNH_2 and R_2NH), whose molecules possess hydrogen-bonding hydrogen atoms, are themselves associated in the liquid state, and can also co-associate with water. Theoretically, at least, such co-association can proceed through the hydrogen of water or through the hydrogen attached to oxygen or nitrogen in the organic molecule.

Finally, hydrocarbons and their simple halogen derivatives are neither associated nor can they co-associate with water.

meyer[3] flask of suitable size. Add a boiling chip and cover the solid with what is judged to be an insufficient volume of the selected solvent.

Warm to boiling on a steam bath (or, for high-boiling solvents, on a hot plate, covered with a layer of asbestos paper), constantly stirring the mixture by swirling the flask. To the boiling solution, add more solvent in small portions with stirring. Allow sufficient time between additions to give the solute a chance to dissolve. Continue the addition of solvent, until all the solute has dissolved[4] at the boiling temperature.

Decolorizing. Frequently the solution is colored by high-molecular weight organic impurities, which may occur in nature along with a desired natural product or may be formed as decomposition products or byproducts in a synthetic process. Boiling for 5 or 10 minutes with a few grams per liter of a highly adsorbent (activated) charcoal such as Norit, Darco, or Nuchar will usually remove the color.

The amount of charcoal should be kept to a minimum, for some of the desired product is invariably adsorbed, also. It has frequently been observed that charcoal is considerably more effective in solvents which are associated (particularly water) than in nonassociated solvents. Less charcoal is required if it is added in portions.

Filtration of the Hot Solution.[5] The hot solution should be filtered in such a way that none of the solute crystallizes on the filter paper or in the funnel. This usually requires rapid filtration with a minimum of evaporation through a previously warmed[6] short-stem funnel fitted with a doubly folded filter paper (folded in half, and that half again folded in half). (See Figure 11a for the complete assembly.)

Sometimes, however, special techniques are required. A fluted filter paper (Figure 11b) may be used to increase the rate of filtration. If slight cooling of the solution causes heavy crystallization, either a deliberate excess of solvent or a special hot water funnel heater (Figure 11c) may be employed. The funnel should not, however, be heated above the boiling point of the solvent. If excess solvent is added, it may be removed by concentration of the filtrate to the volume originally required to dissolve the material.

If the filtration is slowed by the clogging of the pores of the filter paper by a colloidal or gelatinous impurity, a filter aid should be added directly to the liquid or placed on the filter paper in a Büchner or Hirsch funnel in the form of a 2- to 3-mm. pad. Common filter aids such as Hyflo and Filter-cel are forms of diatomaceous earth which adsorb the undesirable colloidal material. They are also effective in preventing decolorizing charcoal from passing through the filter paper into the filtrate.

Cooling. The aim of the cooling process is to bring about the crystallization of the maximum amount of desired material with a minimum amount of impurity. The process should be carried out in an Erlenmeyer flask, covered with a watch glass in order to avoid evaporation. Usually medium-sized crystals are preferred, because large crystals are likely to include considerable amounts of solvent, which carries impurities with it and complicates the drying process; small crystals, with their large surface area, on the other hand, often adsorb significant amounts of impurities.

The size of the crystals is controlled by the rate of crystallization; rapid growth favors small crystals, and slow growth gives large crystals. Since most organic compounds do not tend to form large crystals, a slow to moderate rate of cooling is usually best. Supersaturation of the solution causes a high initial rate of crystallization. This may be avoided by occasional scratching of the inner surface of the glass (in order to provide tiny fragments of glass as nuclei for crystallization) or, better, by periodic addition of a tiny seed crystal.

The mixture should be allowed to stand with occasional shaking until crystallization is complete. As a precautionary measure, the filtrate obtained may be set aside for later observation.

Collecting the Crystals. The major aim here is the removal of a maximum amount of mother liquor from the crystals with a minimum amount of evaporation. This is usually accomplished with a Büchner funnel fitted by means of a rubber stopper into a clean filter flask connected through a safety bottle (or trap) to a water pump (see Figure 11d for a drawing of the complete apparatus).

All connections should be made with heavy-walled (pressure) tubing. Filter flasks of 500-ml. capacity or less should be clamped to a ring stand for support. The smallest funnel which will accommodate all of the crystals comfortably with no danger of overflow should be used. For very small samples, a Hirsch funnel (Figure 11e) is recommended.

The safety bottle serves to trap any tap water which may flow back into the system when there is a sudden

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[3] An Erlenmeyer flask is much preferred over a beaker. It is more convenient to handle, and loss of solvent by evaporation or boiling, with its attendant fire hazard, is minimized. With a highly volatile solvent (especially one that is flammable) it is frequently advisable to use a reflux condenser—very difficult with a beaker. Finally, an Erlenmeyer flask is ideally shaped for removal, by means of a suitable spatula, of solid material adhering to the walls.

[4] Occasionally a sizable amount of insoluble impurity may accumulate. If you suspect this to be the case, decant the solution from the solid material, and test its solubility in fresh solvent.

[5] The purpose of this step is to remove insoluble impurities; if the solution is perfectly clear, it may be omitted.

[6] The funnel and filter paper may be warmed in either of two ways: (1) a small amount of boiling solvent may be poured through the filter paper just in advance of the filtration, or (2) a small amount of the solvent may be boiled in the receiving flask until the funnel and filter paper are bathed with the hot vapor.

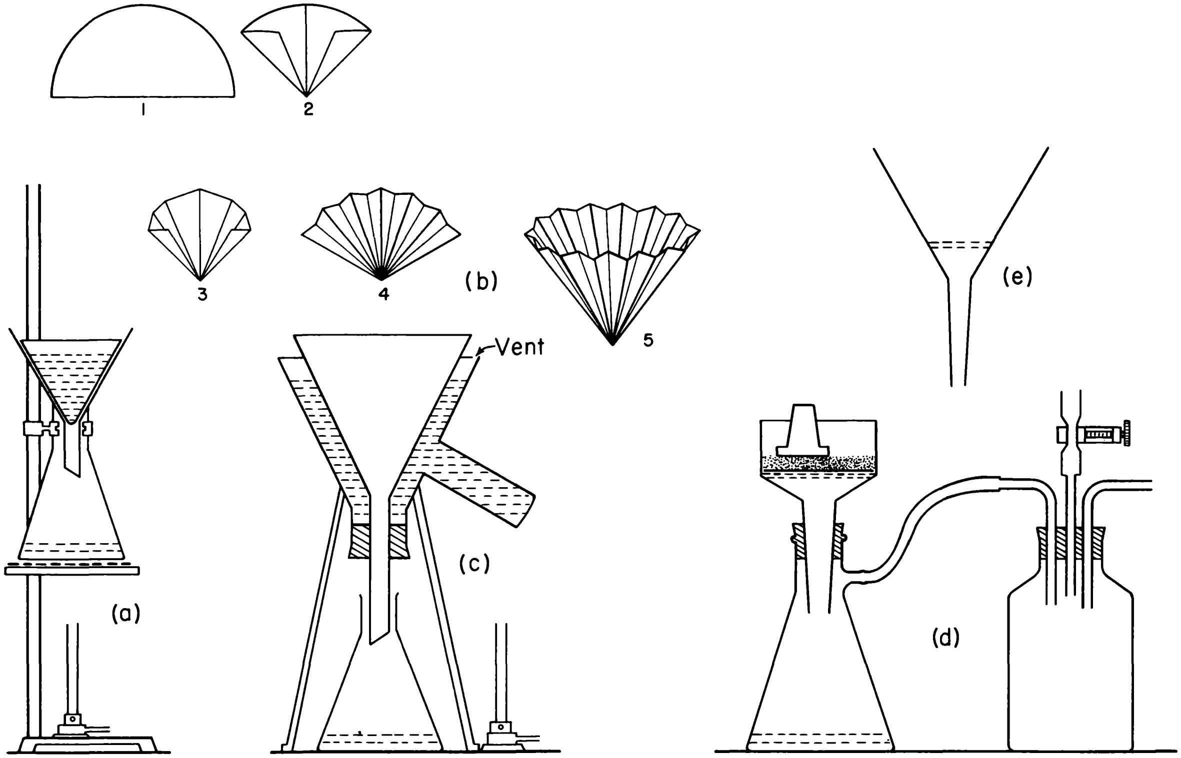


FIG. 11. (a) Assembly for filtering a hot solution. (b) Folding a fluted filter paper. (c) Special hot water funnel heater. (d) Büchner funnel assembly for filtration under reduced pressure. (e) Hirsch funnel. For a fluted filter paper, first fold the paper in half (1). Next, fold in half again. Then open out the last crease so as to have a half-circle; then fold each edge toward the center, making two additional creases in the same direction. This divides the paper into 4 equal sections (2). Then divide each section by a crease still in the same direction. This gives 8 equal sections (3). Divide each section in two by a crease in the opposite direction, thus making 16 sections (4), and 32 sections when the filter paper is opened (5).

drop in water pressure. You will notice that the trap is fitted so that any water present will be removed when suction is applied. The screw clamp on the safety bottle provides a convenient means of controlling the vacuum when low boiling solvents are filtered and of releasing the vacuum quickly.

The filter paper should cover the entire perforated plate but its diameter should be slightly less than that of the plate. It should be flat so that no solid material can pass under its edge. This is accomplished by wetting the paper with solvent and applying suction. Then, with no suction, or at best only slight suction, to avoid needless evaporation, the mixture (or first portion of it) is poured into the funnel. Then the full (or maximum desired) vacuum is applied. Use of a glass rod or spatula will make possible the rapid transfer of the bulk of the crystals to the funnel. Any remaining crystals are washed into the funnel by means of small aliquots of cold filtrate.

Just as soon as the filter cake is rigid enough, it is pressed down carefully but firmly by means of a cork or an inverted bottle stopper. When the flow of liquid stops, the suction is discontinued. If the filtrate is of value, it should be transferred to another vessel at this point.

The crystals are then washed to remove all adhering solution (which, of course, contains soluble impurities). With the suction released (screw clamp open), the crystals are covered with a small portion of fresh, cold solvent.

It may be advisable to stir the mixture carefully with a spatula or flattened stirring rod to insure uniform wetting of the crystals. Then suction is applied and the crystals tamped down as before. This process may be repeated several times, after the screw clamp has been reopened, but always with small portions of cold solvent.

Finally, if the solvent is high boiling, an ultimate washing with a small amount of a low-boiling solvent in which the crystals are insoluble or only sparingly soluble may be recommended.

Frequently the original mother liquor (filtrate) may be concentrated and further crystals obtained. These are, however, almost always somewhat less pure than the crystals which first separate.

Drying of the Crystals. As the final step of the crystallization procedure, the crystals must be freed of adhering solvent by drying. The Büchner funnel is inverted over three or four layers of coarse-grained smooth-surfaced filter paper and the crystals transferred with the aid of a clean spatula. Several additional sheets of the paper are placed on top of the crystals and most of the solvent squeezed out by firm pressing.

The crystals are then transferred to a clean watch glass or crystallizing dish and covered with a sheet of filter paper to keep out dust particles. They may be air dried at room temperature or in a vacuum desiccator (Figure 12a) over a desiccant which is effective in the removal of the solvent used.[7] Small samples are often dried on pieces of unglazed porcelain plates; such porous plates cannot be cleaned, however, and the same piece cannot be used for different substances.

Drying at higher temperatures may be accomplished in an oven, by means of a stream of hot air from a heater, such as an ordinary hair dryer, or, for small samples, in an Abderhalden drying pistol (Figure 12b). The sample is placed in a small boat (A) in the drying chamber (B) which is continuously heated by refluxing vapors from the liquid in the flask (C). The drying chamber is connected by means of a ground glass joint to the desiccant chamber (D) and both may be evacuated through stopcock E. The desiccant usually consists of phosphoric anhydride (mixed with charcoal or distributed on glass wool) when water is to be removed, and of silica gel or thin slivers of paraffin for organic solvents.

In drying solids above room temperature one must take into account that samples that are still moist with solvent melt considerably below the melting point of the pure material.

Experimental

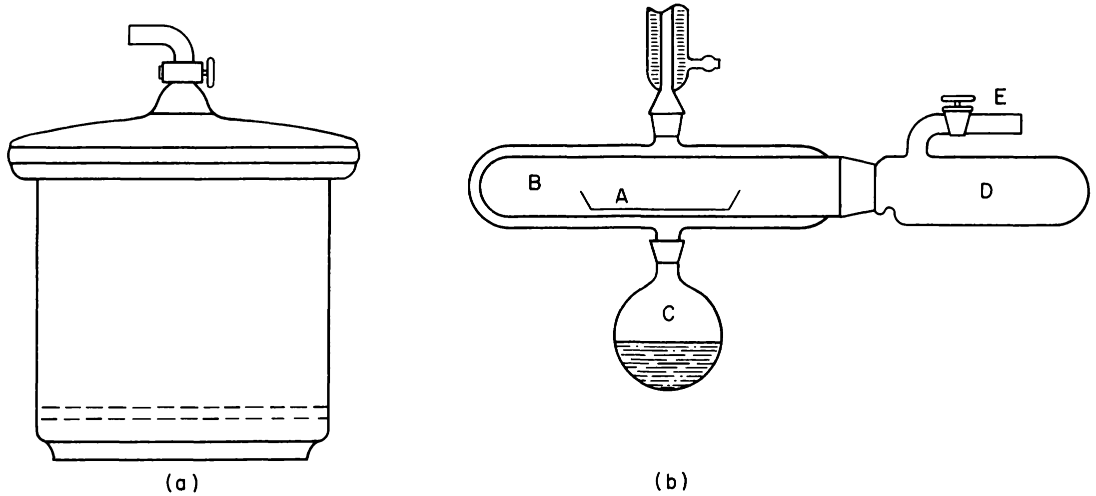
A. Selection of a Crystallizing Solvent

Make solubility tests in each of the following sol- **0-110**
vents on each of the compounds listed in Table 4: water, benzene, and ligroin.

TABLE 4. SOLIDS FOR CRYSTALLIZATION TESTS

Substance	*Formula*	*Chemical Type*
Benzoic acid	$C_6H_5COOH\cdot$	Carboxylic acid. Molecules can associate
Anthracene	$C_{14}H_{10}$	A hydrocarbon
Resorcinol	$C_6H_4(OH)_2$	A dihydroxyl compound
Sodium benzoate	$C_6H_5COO^-,Na^+$	An ionic compound (salt)
Stearic acid	$C_{17}H_{35}COOH$	A high molecular weight carboxylic acid

Observe and record the degree of solubility in each solvent, hot and cold. Select the best solvent or solvent pair for each of the substances. Record the general crystal form—needles, prisms, or platelets.



(a) (b)

FIG. 12. Drying apparatus. (a) Vacuum desiccator. (b) Abderhalden drying pistol.

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[7] For water, calcium chloride, concentrated sulfuric acid, silica gel, and sodium hydroxide are widely used. Sulfuric acid is effective also for ether, and silica gel or freshly cut shavings of paraffin, for benzene, toluene, ether, carbon tetrachloride, and chloroform.

Carry out the solubility tests as follows: with a small spatula transfer an amount roughly estimated to be 0.1 g. of the finely divided solid to a small (10 x 75 mm.) test tube and add the solvent drop by drop with continuous shaking. Stir with a fire polished 4-mm. stirring rod. After 1 ml. of solvent has been added, observe the mixture carefully.

If all the solid has dissolved in the cold solvent, the solvent is unsuitable. If not all of the solid has dissolved, warm the mixture gently to the boiling point with stirring. If all of the solid dissolves, you can declare it readily soluble in the hot solvent. If not all dissolves, add more solvent in 0.5-ml. portions until all of the solid dissolves at the boiling point or until a total of 3 ml. of solvent is present. If some of the solid still remains undissolved at the boiling point, you can judge it sparingly soluble in that solvent and you should try another crystallizing solvent. If all of the solid does dissolve in a total of less than 3 ml. of the hot solvent, you can declare the material at least moderately soluble in that solvent.

In every case, when a solution of solid in a hot solvent is obtained, slowly cool the solution, scratching the sides of the test tube with a small stirring rod. Observe the ease and amount of crystal formation. Note and record the approximate proportions of solute and solvent which give the best results. On this basis, select the most suitable crystallization solvent for each substance.

If no single solvent appears to be particularly suitable, try mixed solvents as described in the Introduction (p. 19) using the relative amounts of solid and solvent specified above.

110-170 B. Recrystallization of Acetanilide

Place 2 g. of crude acetanilide (Note 1) in a 125-ml. Erlenmeyer flask. Dissolve the acetanilide in a minimum amount of boiling water (the material contains impurities which will appear as insoluble solids, but the dark oil which forms is indicative of undissolved acetanilide). Add an additional 5 ml. of water at the boiling point and filter the hot solution through a short-stem funnel, which has been previously heated in a jet of steam, into a 125-ml. Erlenmeyer flask. Allow the solution to cool undisturbed in a bath of cold water for 30 minutes.

[Proceed to Part C]

When the solution is cool, collect the crystals by suction filtration and wash with two separate 5-ml. portions of cold water, each time pressing the crystals firmly with an inverted glass stopper or a cork. Transfer the crystals to a layer of three or four sheets of coarse-grained filter paper. Place a layer of two or three additional sheets of filter paper above the crystals and press them firmly to remove water. Transfer the crystals to a watch glass or crystallizing dish, and allow them to stand, covered with a sheet of filter paper, until the next period. During the next period, weigh the purified acetanilide and determine its melting point. Record your results.

C. Decolorization of Brown Sugar 130-150

Dissolve 10 g. of *dark* brown sugar in 75 ml. of water. Save a small portion of the solution for comparison purposes; add to the remainder 1 g. of decolorizing charcoal (Note 2), and boil for 5 minutes. Add 0.5 g. of Hyflo or Filter-cel as a filter aid. Then filter the hot solution and compare the color of the filtrate with that of the untreated material. Record your results.

D. Crystallization of an Unknown (For Specially Interested Students)

Obtain a weighed sample of an unknown impure solid from your instructor. Determine its melting point. Select a suitable crystallization solvent, and purify the material. Dry and weigh the purified material and determine its melting point. Record and report to your instructor the percentage recovery and the melting points of the impure and purified samples.

NOTES

1. If crude acetanilide is not available, a synthetic mixture of 9 parts of acetanilide, 1 part of oxalic acid, and 0.1 part of carbon may be used.
2. A very active grade of decolorizing charcoal is necessary for good results. You may find it advisable to heat your charcoal in an evaporating dish over a Bunsen burner prior to use.

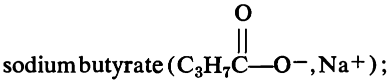
QUESTIONS

1. A solid (x) is soluble in water to the extent of 1 g. per 100 g. of water at room temperature and 10 g. per 100 g. of water at the boiling point. How would you purify x from a mixture of 10 g. of x with 0.1 g. of impurity y, completely insoluble in water, and 1 g. of impurity z, having the same solubility characteristics in water as x? How much absolutely pure x could be obtained after one recrystallization from water?

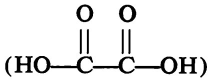
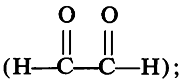
How much pure x could be obtained after one recrystallization from a mixture of 10 g. of x with 9 of z? What does this suggest in a general way about the use of crystallization as a purification technique?

2. Why is it important to minimize evaporation during the filtration of the hot solution?
3. When you are collecting a solid by suction filtration, why do you always break the suction before turning off the water pump?
4. Ethyl iodide, CH_3CH_2I is polar, but, unlike such

polar liquids as ethyl alcohol and acetic acid, is insoluble in water. Explain.

5. Suggest a good solvent for each of the following: naphthalene ($C_{10}H_8$); sodium butyrate  $(C_3H_7\overset{O}{\overset{\|}{C}}—O^-,Na^+)$; propyl amine ($C_3H_7NH_2$); arabinose ($HOCH_2CHOHCHOHCHOHCHO$); cetyl alcohol ($C_{16}H_{33}OH$).

6. What properties of activated charcoal make it a good adsorbing agent?

7. Predict which compound is more soluble in ether and benzene, oxalic acid  $(HO—\overset{O}{\overset{\|}{C}}—\overset{O}{\overset{\|}{C}}—OH)$ or glyoxal  $(H—\overset{O}{\overset{\|}{C}}—\overset{O}{\overset{\|}{C}}—H)$; ethylene diamine ($H_2N—CH_2—CH_2—NH_2$) or tetramethyl ethylene diamine [$(CH_3)_2N—CH_2—CH_2—N(CH_3)_2$].

EXPERIMENT 5

I. Extraction

II. Drying Agents

I. EXTRACTION

A. Theory

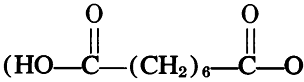
1. Definitions. No technique is more widely used for the separation of an organic product from its reaction mixture or for the isolation of naturally occurring organic substances than **extraction.** We may define extraction as the separation of a component from a mixture by means of a solvent.

In practice, extraction is usually employed to separate an organic compound from an aqueous solution or suspension. The process then consists of shaking the water solution or suspension with a water-immiscible organic solvent and allowing the layers to separate. The various solutes present then distribute themselves between the aqueous and organic layers according to their relative solubilities.

Thus inorganic salts, which are almost entirely insoluble in the common organic extraction solvents, will appear exclusively in the water layer, and nonhydrogen-bonding organic compounds, such as hydrocarbons and their halogen derivatives, which are essentially insoluble in water, in the organic solvent layer. A single extraction will usually suffice to effect a clean separation between compounds of these two types.

2. Distribution Coefficient. For organic compounds, such as alcohols, aldehydes, ketones, acids, esters, amines, etc., which form hydrogen bonds with water and therefore are usually at least partially soluble in water, as well as in organic solvents, repeated extractions may be required to remove essentially all of the compound from the water layer. When a water solution of any substance is shaken with an organic solvent O, in which that substance is at least somewhat soluble, it dissolves partially in each solvent. It will, in fact, distribute itself between the water and solvent O so that concentrations[1] (C_O and C_W) in the two solvent layers are roughly proportional to its solubilities (S_O and S_W) in the two solvents at the given temperature. The ratio of the concentrations of solute in the two solvents at equilibrium is called the **distribution coefficient,** K_D.[2]

$$K_D = \frac{C_O}{C_W} = \frac{S_O}{S_W}$$

For example, at 15° the solubility of solid suberic acid  $(\mathrm{HO{-}\overset{\overset{\large O}{\|}}{C}{-}(CH_2)_6{-}\overset{\overset{\large O}{\|}}{C}{-}OH})$ is 0.56 g. per 100 ml. of ethyl ether and 0.14 g. per 100 ml. of water. This means that when suberic acid is distributed between the solvents ether and water at 15°, its concentration in the ether layer will be 0.56/0.14 or 4.0 times that in the water layer, and the $K_D = 4.0$. If a solution of 40.0 mg. of suberic acid in 50 ml. of water is extracted with 50 ml. of ether, the weight (x) of suberic acid removed by the ether can be calculated as follows:

$$\frac{\dfrac{x}{50\text{ ml.}}}{\dfrac{40\text{ mg.} - x}{50\text{ ml.}}} = 4$$

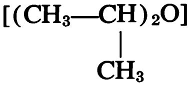
$$5x = 160\text{ mg.}$$

$$x = 32\text{ mg.}$$

In other words, the single extraction with 50 ml. of ether would remove 32 mg. of the suberic acid, leaving 8 mg. in the water layer. It is apparent that suberic acid can be separated readily from any ether insoluble contaminant by repeated extraction of a water solution with ether.

You can prove for yourself by straightforward calculations using the distribution coefficient equation that a double extraction with 25-ml. aliquots of ether would be considerably more effective than the single extraction with 50 ml. In general, for a given total volume of extracting solvent, the efficiency increases with the number of separate extractions used. In practice, however, this factor must always be weighed against the time and labor involved in repeated extractions and the inconveniences introduced when the aliquot of extracting solvent used becomes too small for easy handling.

As a rule of thumb, when the solute is considerably more soluble in the extracting solvent than in water, a volume of solvent approximately one third that of the solution is used for each extraction.

Other important organic extracting solvents are benzene (C_6H_6), petroleum ether (low molecular weight alkanes), methylene chloride (CH_2Cl_2), chloroform ($CHCl_3$), carbon tetrachloride (CCl_4), and di-isopropyl ether  $[(\mathrm{CH_3{-}\underset{\underset{\large CH_3}{|}}{C}H})_2\mathrm{O}]$. The choice of solvent depends upon the solubility of the substance to be extracted in that solvent and upon the ease with which the solvent can later be removed from the solute.

Ethyl ether, because of its powerful solvent action

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[1] Expressed here as weight of solute per unit volume of solvent.

[2] If the solute is completely miscible with one or both of the solvents, the distribution coefficient cannot, of course, be calculated from solubility data. It can still be determined experimentally, at least in dilute solution. In concentrated solutions, the two solvent phases may become miscible with each other.

toward most organic compounds and its low boiling point (35°), is the most widely used extraction solvent. Its high volatility and extreme flammability, however, constitute a dangerous fire hazard which must always be considered in its use.

B. Practice

1. Equipment and Procedure. The apparatus used for carrying out extractions is a separatory funnel, shown in Figure 13. You will use your separatory funnels so frequently in the weeks to come that you will save time by checking at once to see that they are in good working condition. The stopper and stopcock should fit tightly and should be absolutely leakproof. Both should be lubricated with a thin film of stopcock grease before each use.

FIG. 13a. Proper method for holding a separatory funnel.

When carrying out an extraction, always hold the funnel securely with both hands, one hand at the top so that the stopper rests at the base of your index finger, the other hand in position for ready opening and closing of the stopcock (Figure 13a). Invert the funnel, and immediately open the stopcock to relieve excess pressure. Shake gently for 1-2 seconds and open the stopcock again. When further pressure is no longer built up in the funnel, close the stopcock securely, and then shake vigorously for a minute or two. Vent the funnel again by means of the stopcock and then place the funnel upright, with stopcock securely closed, in an iron ring fitted with several strips of slit rubber tubing for protecting the funnel against breaking (Figure 13b).

Remove the stopper and allow the mixture to separate into two well defined layers. Always keep a large beaker under the separatory funnel so that all the contents of the funnel will be saved in case of an accident.

In separating layers, drain off the bottom layer through the stopcock and pour the upper layer from the top of the funnel to avoid contamination. The exact number of extractions required in any given case will depend upon the distribution coefficient and the relative volumes of solvent and water. You can determine the completeness of any extraction by evaporating a small portion of the last extract and noting the amount of residue.

The relative positions of the water and organic layers will, of course, depend upon their relative densities. You can determine whether a given layer is aqueous or organic by testing the solubility of a few drops in water. When carrying out a new reaction, you will find it a wise policy to save all layers until you have isolated the final product in the expected yield. *Then clean up.*

2. Emulsions. Frequently, especially when working with alkaline solutions, you will be plagued by the formation of emulsions during extraction. You can often break up an emulsion by (1) gently swirling the funnel while holding it in an upright position, (2) stirring the emulsified layer vigorously with a glass rod, (3) saturating the aqueous layer with salt, or (4) centrifuging.

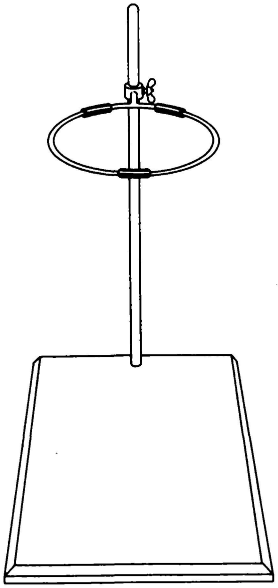
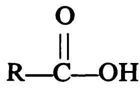
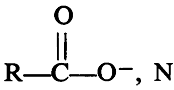


FIG. 13b. Ring support for separatory funnel.

Method 3, saturating the aqueous layer with salt, has a double advantage; it decreases the solubility of most organic solutes and of extraction solvents such as ether in the water layer. This is called the **salting-out** effect.

3. Extraction with Acids and Alkalies. Frequently the cleanest separations of organic compounds can be effected by use of acid or alkaline solutions which convert the compound to be extracted to a water-soluble, ether-insoluble salt. A 5 or 10 per cent solution of sodium hydroxide, for example, converts carboxylic acids,

 $R-\overset{\overset{\displaystyle O}{\|}}{C}-OH$, to their sodium salts,  $R-\overset{\overset{\displaystyle O}{\|}}{C}-O^-$, Na^+. Phenolic compounds undergo similar salt formation with sodium hydroxide solution. Hence, a sodium hydroxide solution can be used to extract a carboxylic acid or phenolic compound from its solution in an organic solvent, or, conversely, an organic solvent can be used to remove organic impurities from a carboxylic acid or phenol dissolved in aqueous sodium hydroxide.

Aqueous solutions of sodium bicarbonate likewise convert carboxylic acids to their sodium salts, but are not sufficiently alkaline to form salts of phenolic compounds. This provides an elegant method for the separation of a carboxylic acid and a phenolic compound. First the acid may be extracted from solution in an organic solvent by means of extraction with sodium bicarbonate solution, and then the phenol, with sodium hydroxide solution.

Inorganic acids are regularly removed from organic solvents by extraction with sodium hydroxide, sodium carbonate, or sodium bicarbonate solutions.

Dilute hydrochloric acid is often used in the extraction of basic substances from mixtures or in the removal of basic impurities. The dilute acid converts the base such as ammonia or an organic amine (R_3N)[3] into the water-soluble chloride salt (R_3NH^+, Cl^-). Conversely, organic impurities may be removed from amines by extraction from a dilute acid solution with organic solvents.

Sodium salts of carboxylic acids and phenolic compounds are readily reconverted to the parent compounds by treatment with sulfuric acid. The chlorides of amines revert to the original amine upon addition of sodium hydroxide solution.

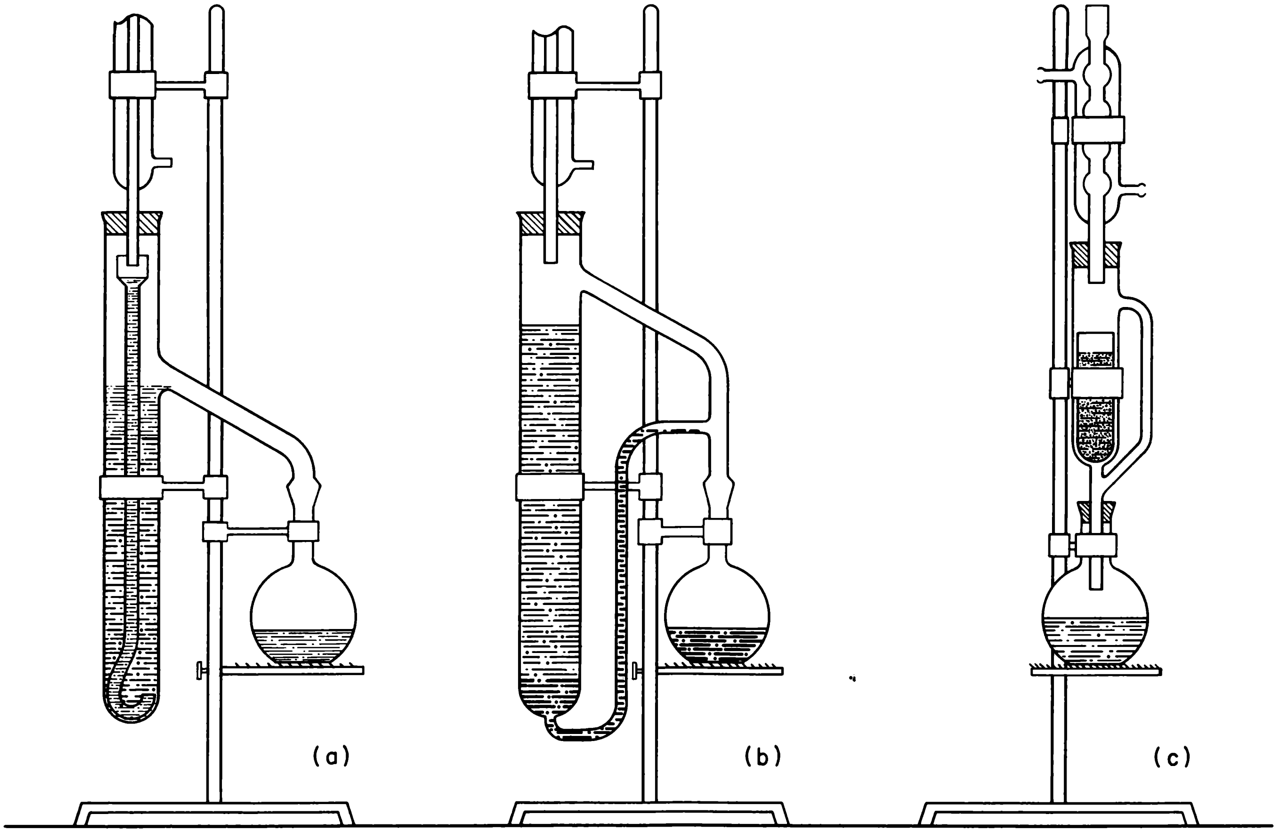


FIG. 14. Continuous extraction apparatus. (a) For solvents lighter than water. (b) For solvents heavier than water. (c) Soxhlet extraction apparatus for solids.

4. Continuous Extraction. Often, when the system being extracted forms intractable emulsions, or when the organic solute being extracted is more soluble in water than in the organic solvent, it is advisable to switch to a method of continuous extraction.

Two types of apparatus have been devised which, in effect, make possible the automatic treatment of water solutions with an almost infinite number of separate extractions with minute aliquots of extracting solvent. One type (Figure 14a) is used for solvents lighter

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[3] R may be a hydrogen atom or an alkyl group.

than water and the second (Figure 14b) for solvents heavier than water. In each case, the solvent is distilled continuously from the flask on the left. The drops of condensate trickle up (Figure 14a) or down (Figure 14b) through the solution and are finally returned, along with extracted solute, to the distilling flask, where the solute collects.

For the repeated and exhaustive extraction of a solid by hot liquid, the solid mixture is placed in the thimble (A) of a **Soxhlet Extraction Apparatus** (Figure 14c). The extracting solvent is boiled gently, the vapor passes through the side tube (B), and the condensate drops onto the solid and slowly leaches out soluble material.

Other Soxhlet extractors are constructed so that the solvent first fills the extraction chamber, and the solution which is formed is then siphoned into the distilling flask, this process being repeated automatically until the extraction is completed. Soxhlet extraction is particularly useful for the isolation of naturally occurring products from animal and plant tissues that have high water content and for leaching organic compounds from inorganic salts.

Experimental

0-40

A. Extraction of Crystal Violet

1. Simple Extraction. Dissolve a small crystal of crystal violet about the size of a pin-head in 60 ml. of water. Divide the solution into two equal parts. Place a clean, dry, and properly lubricated 125-ml. separatory funnel on a ring support and add to it (stopcock closed) the first portion of the crystal violet solution and 30 ml. of chloroform. Insert the stopper securely in the funnel, invert the funnel, and open the stopcock to relieve excess pressure. Close the stopcock, shake the funnel gently for a moment, and again open the stopcock to relieve excess pressure.

Repeat this process until no pressure builds up within the funnel during the shaking period. Then close the stopcock, shake vigorously for 1 minute, and finally place the funnel upright in the ring support. Remove the stopper from the top of the funnel and allow the mixture to separate into two sharply defined layers. (This will require several minutes. Use this time, in every case, to prepare the solution and to set up the melting point apparatus for Part B of this experiment.)

Drain off the chloroform (lower) layer into a test tube and pour the aqueous layer through the top of the funnel into a second test tube. Cork each test tube and set them aside for future reference.

40-100 *2. Multiple Extraction.* Extract the second portion of the crystal violet solution with three separate 10-ml. portions of chloroform. Combine the three chloroform extracts in a third test tube and pour the extracted water solution through the top of the funnel into a fourth test tube. Compare the intensity of color in the two chloroform solutions and then in the two aqueous solutions. Record your results.

B. Extraction with Sodium Hydroxide Solution 100-135

Dissolve in 35 ml. of ether (be certain that there are no flames in the laboratory) 0.7 g. of benzoic acid (C_6H_5COOH) and 0.7 g. of *p*-dichlorobenzene ($C_6H_4Cl_2$). Extract this solution with a single 15-ml. portion of fresh 10 per cent sodium hydroxide solution. Drain off the aqueous (lower) layer and pour the ether solution through the top of the funnel into a small Erlenmeyer flask.

Add to the ether solution three or four granules of calcium chloride (see the discussion on drying agents following this experiment) and shake the mixture occasionally until no turbidity remains. Then decant the ether solution in a tared (previously weighed) watch glass and set it aside (preferably in the hood) to allow the ether to evaporate while you begin Part C of this experiment. As soon as all the ether has evaporated, weigh the residue. Then determine its melting point. Pure *p*-dichlorobenzene melts at 53°. Record your results.

If you have time you may wish to devise your own method for isolating the benzoic acid quantitatively from the aqueous layer.

C. The Salting-Out Effect 135-170

Prepare a solution of 8 g. of *t*-butyl alcohol [$(CH_3)_3COH$] in 40 ml. of water and divide the solution into two equal portions. Extract the first with 25 g. of chloroform. Weigh the chloroform solution and calculate the weight of *t*-butyl alcohol extracted.

To the second portion of *t*-butyl alcohol solution, add 25 g. of chloroform. Then dissolve in the water solution 10 g. of potassium carbonate. Finally, extract the aqueous layer with the 25 g. of chloroform as before, and compare the weights of *t*-butyl alcohol extracted in the two cases.

D. Bonus Experiment for Specially Interested Students

Obtain from your instructor a 3-g. sample of a mixture[4] of benzoic acid, β-naphthol ($C_{10}H_7OH$) and *p*-dichlorobenzene. Devise a method for separating the mixture into the three pure components by extraction. After your instructor has approved your method, try it and record your results. Some of the pertinent properties of the three compounds are as follows:

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[4] Prepared by melting a mixture containing equal weights of the three components on a steam bath and then cooling, breaking up the solid with a spatula as it crystallizes.

	M.P.	K_{ion}	*Solubility in Water at 20°*
Benzoic acid, C_6H_5COOH	123°	6.3×10^{-5}	0.25 g./100 g.
β-Naphthol, $C_{10}H_7OH$	123°	7×10^{-9}	0.10 g./100 g.
p-Dichlorobenzene, $C_6H_4Cl_2$	53°	—	Insol.

QUESTIONS

1. On the basis of the extraction of crystal violet by the two methods, compare the efficiency of extraction with a single 30-ml. portion of solvent to that with three 10-ml. portions.

2. Aniline, $C_6H_5NH_2$, is very slightly soluble in water; the solution turns red litmus blue. Outline a method for the separation of a mixture of aniline, β-naphthol, and *p*-dichlorobenzene into the pure components.

3. What is the effect of the addition of potassium carbonate on the solubility of *t*-butyl alcohol and of ether in water? What effect does this have on the experimentally determined distribution coefficient, C_E, for *t*-butyl alcohol?

4. What advantages does di-isopropyl ether have over ethyl ether as an extraction solvent?

5. Explain why the pressure in a stoppered funnel containing a water solution–ether mixture increases when it is first shaken. Why does the pressure no longer increase after several extractions have been performed?

6. Chloroform is an excellent solvent for extracting caffeine from water. The distribution coefficient, K_D $\left(\frac{C_{\text{chloroform}}}{C_{\text{water}}}\right)$, for caffeine in chloroform–water at 25° is 10. What relative volumes of chloroform–water should be used for the extraction of 90 per cent of the caffeine from a water solution in a single extraction?

7. When a solution containing 4.0 g. of *n*-butyric acid in 100 ml. of water is extracted with 50 ml. of benzene at 15°, 2.4 g. of the acid is transferred to the benzene layer. What is the distribution coefficient for *n*-butyric acid in benzene–water at 15°?

8. The distribution coefficient, K_D $\left(\frac{C_{\text{ether}}}{C_{\text{water}}}\right)$, between ether and water for aspirin (acetylsalicylic acid) at room temperature is 3.5. What weight of aspirin would be extracted by a single extraction with 60 ml. of water of a solution of 5 g. of aspirin in 100 ml. of ether? Calculate the weight of aspirin which would be removed by three extractions with 20-ml. portions of ether.

9. What volume of ether would be required to extract 0.95 g. of aspirin from a solution of 1 g. of aspirin in 100 ml. of water in a single extraction?

10. Would carbon tetrachloride be a good solvent for extracting ethyl alcohol from water? (Consult a handbook.) Explain.

11. What effect does partial miscibility of the two solvents used have on the efficiency of extraction? Explain.

12. What practical advantage does an extraction solvent that is heavier than water have over one that is lighter than water?

13. Why should the stopper always be removed from a separatory funnel whenever a liquid is being drained through the stopcock?

14. (For Specially Interested Students) For efficiency in continuous extractions with solvents lighter than water, it is important that the extraction chamber should not be much larger than required to accommodate the solution to be extracted. Can you explain why this is true?

II. Drying Agents

1. Importance of Drying

Small amounts of moisture sharply inhibit the crystallization of many solids. In addition, many liquids, when distilled in the presence of water, react chemically (are hydrolyzed) with water or distill (or steam distill) with the water at temperatures far removed from their true boiling points. For these reasons, the usual final step just before the crystallization of a solid, or the distillation of a liquid, is the removal of water through some drying process.[5] As a rule, this is best accomplished while the organic compound is in solution (often in an extraction solvent).

2. Drying by Mechanical Means

Drying may be accomplished by mechanical or chemical means. Suspended water in an emulsion can often be removed mechanically by distillation, freezing, filtration, or centrifugation, and water dissolved in a liquid, by distillation or freezing. Sometimes a moist solid or high-boiling liquid which is only slightly soluble in water is dried by addition of a low-boiling solvent immiscible with water (usually benzene) and distillation of the resulting mixture.

When benzene is used, its steam distills with the water at 69.3°. After all of the water has been removed, dry benzene distills at 80°. The dried material is then usually distilled, if it is a liquid, or isolated directly, if it is a solid.

3. Chemical Drying Agents

Chemical drying is even more widely used than mechanical drying. A good chemical drying agent or desiccant should (1) be compatible with the substance to be dried; (2) have a high intensity, i.e., remove water completely or nearly completely; (3) have a high capacity, i.e., remove a large amount of water per unit weight of desiccant; (4) dry rapidly; and (5) be removed easily from the dried substance.

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[5] The removal of water from a reaction mixture is, of course, effective in driving to completion a reversible reaction in which water is one of the products. This is often accomplished by distillation, with water as one compound of a constant-boiling mixture. Effective use of this device is illustrated in Experiment 37.

Chemical drying agents may be divided broadly into two classes: (1) those which react chemically with water by a nonreversible process giving rise to a new water-free compound and (2) those that combine reversibly with water, either by hydrate formation or by adsorption. In some cases, the dividing line between these two classes is not sharp.

4. Nonreversible Drying Reactions

Phosphoric anhydride (P_4O_{10}), sodium, calcium hydride, and calcium oxide (quicklime) belong to the former class. The capacity of such drying agents depends upon the stoichiometry of their reaction with water, and their intensity, upon the equilibrium point in the system,

$$\text{Drying Agent} + \text{Water} \rightleftarrows \text{New Compound}$$

For desiccants of this type, the reaction products with water are quite stable at higher temperatures, and the dried material is frequently distilled directly from the desiccant.

Phosphoric anhydride reacts with water to form one of a variety of phosphoric acids, depending upon the ratio of anhydride to water. It removes water extremely efficiently and rapidly. It is, however, difficult to handle and expensive; it channels badly and tends to form a syrupy coating on the surface. It is employed only when extreme desiccation is required and only after preliminary drying with a less expensive desiccant of high capacity. Phosphoric anhydride is used for hydrocarbons and their simple halogenated derivatives, ethers, and nitriles, but never for alcohols, ketones, amines, and acids.

Metallic sodium reacts with water to form sodium hydroxide and hydrogen. It is highly effective, especially when drawn out in the form of a fine wire, but can be used only for ethers, alkanes, and aromatic hydrocarbons. Its use should always be preceded by a preliminary drying with calcium chloride, magnesium sulfate, or phosphoric anhydride. Sodium must be used with great caution. It should never be allowed to come into contact with water because a violent explosion may result. Scrap sodium may be destroyed by addition in small portions to a large quantity of ethyl or methyl alcohol.

Calcium hydride is a powerful, high-capacity desiccant which reacts with water irreversibly to form calcium hydroxide and hydrogen:

$$CaH_2 + 2H_2O \rightarrow Ca(OH)_2 + 2H_2\uparrow$$

From the equation, it can be seen that 42 g. of calcium hydride reacts quantitatively with 36 g. of water. Its effectiveness increases markedly with increase in temperature. Calcium hydride is recommended for the removal of traces of moisture from gases and from ethers and tertiary amines (R_3N).

Calcium oxide is commonly used for the drying of low molecular weight alcohols. The alcohol is refluxed with calcium oxide and finally removed by distillation from the calcium oxide–calcium hydroxide mixture.

5. Drying by Hydrate Formation

Most chemical drying agents function by combining reversibly with water to form hydrates. Their capacity depends upon the stoichiometry of the hydrate-forming reactions, and their intensity, upon the equilibrium vapor pressure of the system

$$\text{Desiccant} + \text{Water} \rightleftarrows \text{Hydrate}$$

at the drying temperature.

Calcium sulfate (Drierite), for example, as ordinarily used forms a hydrate containing only a half mole of water per mole of sulfate:

$$CaSO_4 + \tfrac{1}{2}H_2O \rightleftarrows CaSO_4 \cdot 0.5H_2O$$

On this basis, it has very low capacity, 1 g. of the desiccant removing only about 0.066 g. of water. However, the vapor pressure of the system calcium sulfate –calcium sulfate hemihydrate is only 0.004 mm. at 25°; this means that water is removed from any liquid phase in equilibrium with the calcium sulfate system until the partial pressure of water in the liquid phase is only 0.004 mm. Thus calcium sulfate has remarkably high intensity as a desiccant.

Most of the common hydrate-forming desiccants give a series of hydrates, depending upon the ratio of water to desiccant present. Thus anhydrous magnesium sulfate can add water to form hydrates containing 1, 2, 4, 5, 6, and 7 moles of water per mole of sulfate. The equilibrium vapor pressure of the various hydrate systems involved, of course, increases with the degree of hydration, from 1 mm. (25°) for the system

$$MgSO_4\ (\text{anhyd.}) + H_2O \rightleftarrows MgSO_4 \cdot H_2O$$

to 11.5 mm. for the system

$$MgSO_4 \cdot 6H_2O + H_2O \rightleftarrows MgSO_4 \cdot 7H_2O$$

Hence, with magnesium sulfate, different capacities and intensities of drying can be realized, depending upon the ratio of drying agent to water. If at least 1 mole of the sulfate per mole of water is added, the demonstrated capacity will be low but the intensity will be relatively high. If 1 mole of magnesium sulfate per 6-7 moles of water is present, the capacity will be high but the observed intensity low. The equilibrium vapor pressure of hydrate systems also increases rapidly with increasing temperature; hence desiccants which form hydrates are most effective at low temperatures.

The facts constitute the principles which underly the common practices in the use of hydrate-forming desiccants. In the first place, such a desiccant is almost always removed, either by filtration or decantation, prior to distillation, or a large part of the water of hydration will be driven off with the distilling product. Similarly, at times drying is carried out at very low temperatures in order to exploit the maximum intensity of the drying agent. Frequent agitation helps to hasten attainment of equilibrium, thereby speeding the removal of water.

When a large amount of water is to be removed by a desiccant which forms several hydrates, it is not advisable to attempt intense drying in a single step by the addition of a large amount of desiccant. Preferably, drying should be conducted in stages, with one portion of desiccant being removed before the next is added. In this way, the bulk of the water is removed through the formation of a higher hydrate, and the final traces of water yield to the full drying power of the lowest hydrate. Similarly, it is often advantageous to remove the bulk of the water with an inexpensive primary desiccant of large capacity, such as sodium sulfate, and then to complete the process with an agent of high intensity, such as calcium sulfate.

6. Common Hydrate-forming Drying Agents

A list of some of the common hydrate-forming drying agents with their important characteristics, application, and limitations follows:

Anhydrous calcium chloride is widely used because it has high capacity and is relatively cheap. It is rather slow, however, and not unusually efficient. It is particularly useful for preliminary drying, but is recommended only for hydrocarbons and their halogen derivatives and for ethers. It is usually unsuitable for acidic compounds, such as carboxylic acids and phenols, because it often contains some lime, and for alcohols, phenols, ketones, amines, amino acids, amides, and some aldehydes and esters, because of the formation of complexes.

Neutral anhydrous salts, such as anhydrous sodium sulfate, magnesium sulfate, and calcium sulfate, are inert and insoluble in organic liquids and can be used for all types of compounds. **Sodium sulfate** is cheap and has a high capacity, since at temperatures below 33° it forms hydrates up to a decahydrate, $Na_2SO_4 \cdot 10\,H_2O$. It is slow, however, and because of its low intensity is almost useless for solvents such as benzene, toluene, and chloroform in which water solubility is low. It is recommended as a preliminary drying agent for the removal of large amounts of water, especially from ether solutions.

Anhydrous magnesium sulfate is an excellent all-purpose desiccant with good capacity and good intensity. It is cheap and fairly rapid.

Anhydrous calcium sulfate (Drierite) is extremely rapid and efficient, but has low capacity (at maximum intensity it absorbs only 6.6 per cent of its weight of water). It is often used after a primary desiccant such as sodium sulfate.

Anhydrous sodium hydroxide and particularly **anhydrous potassium hydroxide** are the reagents of choice for the drying of amines. Because of their strong basicity, they find little other use as desiccants, except in desiccators where they do not come into contact with the material being dried.

Anhydrous potassium carbonate has moderate intensity and capacity. It is used to some extent for ketones, esters, alcohols, and amines (when a strongly alkaline reagent is to be avoided), especially as a preliminary drying agent. It is the reagent of choice for salting out (see p. 26) water-soluble alcohols, amines, and ketones.

7. Adsorbing Agents

Two of the most common desiccants which function by adsorption of water at the surface are a specially treated form of silica called **silica gel**[6] and a series of highly porous crystalline sodium and calcium aluminosilicates that have been heated to remove water of hydration called **molecular sieves.**[7] These agents are extremely effective in removing water vapor from gases.

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[6] Available from the Davison Chemical Company, Baltimore, Maryland.

[7] Supplied by the Linde Division of Union Carbide Corporation.

EXPERIMENT 6

Steam Distillation

Introduction

A. Principle of Steam Distillation

Steam distillation is an ingenious technique for the separation of slightly volatile water-insoluble substances from nonvolatile materials. It makes possible the convenient purification of many high-boiling substances by low-temperature distillation. Steam distillation is particularly valuable when the desired substance boils above 100° at atmospheric pressure and decomposes at or below its boiling point. In such cases, it takes the place of vacuum distillation and is much more convenient.

In order to appreciate how this is possible, we must consider the distillation behavior of two-phase systems consisting of two immiscible liquids. In Experiment 3, we discussed the distillation of solutions. The behavior of two-phase systems is quite different, but equally important.

In a mixture of two completely immiscible liquids, x and y, each liquid exerts its own characteristic vapor pressure independently of the other. Thus the total vapor pressure, P_T, may be calculated as follows:

$$P_T = P_x + P_y \text{ (at } T\text{)}$$

where P_x = the vapor pressure at x at temperature T
and P_y = the vapor pressure of y at temperature T.

The vapor pressures are totally independent of the relative amounts of x and y present in the mixtures.

The boiling point of the mixture will be the temperature at which the total pressure, P_T, is equal to 760 mm. Unless either P_x or $P_y = 0$, this temperature will be lower than the boiling point of both x and y.

Now, since gases exert pressures (at a given temperature) in proportion to the concentration of the molecules, it follows that the ratio of vapor pressures of x and y at the boiling point of the mixture is the numerical ratio in which the molecules of x and y distill from the mixture. In other words, the composition of the vapor may be calculated as follows:

$$\frac{N_x}{N_y} = \frac{P_x}{P_y}$$

where N_x/N_y is the molar ratio of x to y in the vapor. The ratio of *weights* of x and y in the vapor will depend not only upon the ratio of *moles* but also upon the *molecular weights* of x and y, and this weight ratio, w_x/w_y, is as follows:

$$\frac{w_x}{w_y} = \frac{M_xN_x}{M_yN_y} = \frac{M_xP_x}{M_yP_y}$$

where M_x and M_y are the molecular weights of x and y, respectively.

Stated in words, this important equation tells us that in the distillation of a mixture of two immiscible liquids, the relative weights of the two liquids which are collected in the receiver are directly proportional both (1) to the vapor pressures of the liquids at the distillation temperature and (2) to their molecular weights. Furthermore, the mixture will distill at a constant temperature as long as at least some of each component is present.

These facts constitute the basis for the purification and separation of substances by **steam distillation.** There are many relatively high-boiling organic compounds which with water will distill in a favorable weight concentration below 100°. This is true because of their relatively high molecular weight compared to water.

B. Steam Distillation of Bromobenzene

To illustrate this in a practical way, let us consider the distillation of a mixture of water and bromobenzene, C_6H_5Br, which is almost completely immiscible with water. At 95.3° the vapor pressure of water is 641 mm. and that of bromobenzene is 119 mm. The vapor pressure of the mixture is therefore 760 mm. (641 mm. + 119 mm.). Hence, a mixture of water and bromobenzene will distill at 95.3° and the molar ratio of bromobenzene to water in the distillate will be only 119/641. But the molecular weight of bromobenzene is 157 compared to 18 for water. Therefore the theoretical[1] ratio of bromobenzene to water in the distillate will be as follows:

$$\frac{\text{Wt. of bromobenzene}}{\text{Wt. of water}} = \frac{119 \times 157}{641 \times 18} = 1.6$$

Despite the much lower vapor pressure of bromobenzene, on a weight basis it will distill 1.6 times as fast as water—all because of its much greater molecular weight.

C. Applications of Steam Distillation

This process—the distillation of a somewhat volatile, insoluble substance with water—is called steam distillation. For successful steam distillation, the insoluble substance to be distilled should have a vapor pressure of at least 5-10 mm. at 100°. Besides serving as a convenient substitute for vacuum distillation, steam distillation is particularly useful when a relatively small amount of material is to be separated from a large bulk of solid or tarry material, which makes ordinary distillation, filtration, and extraction difficult or impractical (see the preparation of aniline in Experiment 49).

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[1] The actual value will be less than the theoretical, because the two liquids are not completely immiscible in each other.

Thus steam distillation is often used in the isolation of natural products and of reaction products which are contaminated with large amounts of tarry by-products. It is also useful in the separation of desired slightly volatile organic compounds from (1) aqueous mixtures containing inorganic salts; (2) from other organic compounds which are not appreciably volatile with steam (see the separation of *o*-nitrophenol from *p*-nitrophenol in Experiment 63); and (3) when the distilled material is a solid and would clog the condenser were it not washed down with water.

If the water-insoluble phase in a steam distillation contains two components, the two different phases (water and organic) distill according to the principles of steam distillation. In other words, the molar ratio of the two phases in the distillate is the same as that of the vapor pressures of the two phases. The components of the organic phase, however, distill relative to each other according to the principles of ordinary distillation (see Experiment 3); i.e., the distillate is richer than the residue in the more volatile component.

Most organic compounds which are distilled with steam are not completely insoluble in water, especially at the distillation temperature. This decreases somewhat the calculated efficiency of the process. The addition of sodium chloride to saturate the aqueous phase has the double advantage of decreasing the solubility of the organic compound in the aqueous phase and of decreasing the vapor pressure of the water relative to that of the organic phase.

D. Apparatus and Procedure

A typical apparatus for steam distillation is shown in Figure 15. Steam is admitted from the flask A equipped with a safety tube B into the steam distillation flask E, through delivery tube D, which is bent so that it extends to the bottom of the tilted flask. The distillate passes through the bent tube F into the condenser G, where it is channeled by means of a curved adapter H, into the receiving flask I.

All connections are made as short as possible to keep condensation to a minimum. All glass tubing should be at least 7 mm. in diameter to permit the distillation to be carried out as rapidly as the capacity of the condenser permits. The rubber stoppers should fit snugly and should be inserted tightly. The distillation flask should be clamped to a ring stand and also supported by a wire gauze supported on a ring. It should not be more than half filled with liquid and may be heated with a small flame to prevent excessive condensation during the distillation.

As an alternative method of generating steam a metal can or flask, A′, provided with a 2-ft. safety tube, B′, may be used. A pinch of zinc dust, which slowly reacts with the water to liberate hydrogen, prevents bumping in the generator. Use of a Fischer burner or two Bunsen burners may be necessary to keep the flow of steam up to capacity. The moment generation of steam is stopped or interrupted, pinch-cock C must be opened (CAUTION! Steam is released.) to prevent the contents of flask E from sucking back into the generator.

If live steam is available at the laboratory table, the steam line should be connected to the distillation flask E through a trap J or K; K is easily constructed from an adapter. The screw clamp is adjusted carefully so that a small liquid seal is maintained to prevent the escape of steam.

An improved type of steam-distillation head is pictured in Figure 15L. It is compact and convenient and greatly reduces the likelihood that liquid from the flask will splash over into the steam distillate.

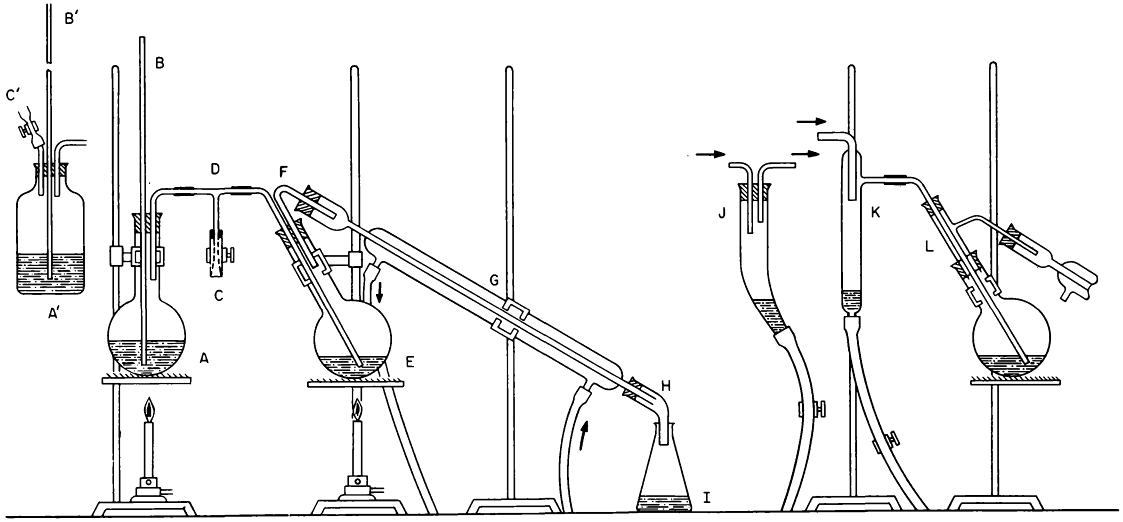

FIG. 15. Steam distillation apparatus.

Experimental

A. Steam Distillation of Bromobenzene

Assemble a steam distillation apparatus as shown in Figure 15. If live steam is available, connect the steam outlet to the steam inlet tube through a trap. If not, assemble a steam generator (Figure 15).

0-70 Place a mixture of 25 ml. of water and 30 ml. of bromobenzene in the distillation flask. Insert all the stoppers tightly. Place a lighted burner (small flame) under the flask. Then pass a steady stream of steam into the flask, steam distilling as rapidly as the condenser capacity will allow. Collect exactly 25 ml. of distillate as measured by means of a graduated cylinder. Then change receivers and collect a second 25-ml. fraction of distillate. Compare the volumes of bromobenzene in each of the two fractions. Record your data.

B. Steam Distillation of a Mixture of Benzene and Xylene

70-110 Add to the distillation flask 20 ml. of water, 15 ml. of benzene (C_6H_6, b.p. 80.0°), and 15 ml. of xylene (mixture of $C_6H_4(CH_3)_2$ isomers, b.p. 135°). Steam distill the mixture, collecting two separate 25-ml. fractions of distillate. Measure and record the volume of the upper (hydrocarbon) layer in each fraction. Note how they compare.

C. Steam Distillation of a Mixture of *p*-Dichlorobenzene and Salicylic Acid

110-170 By means of a mortar and pestle or by rubbing the materials on a filter paper with a spatula, prepare an intimate mixture of 3.5 g. of salicylic acid ($HO—C_6H_4—COOH$) and 1.5 g. of *p*-dichlorobenzene ($C_6H_4Cl_2$). Take a melting point on a small sample of the mixture. Then transfer the remainder of the mixture, along with 25 ml. of water, to the distillation flask and steam distill.

Run water through the condenser only occasionally, if necessary to condense the steam. Any sudden rise of the water level in the safety tube is a danger signal indicating that the condenser may be plugged. If this occurs, drain all of the water from the condenser until the plug is removed. Continue the distillation until the distillate is clear.

Filter the distillate and press the solid between several sheets of filter paper to remove the water. Weigh the dried sample. Wrap the solid in a piece of filter paper and set it aside until the next period. At that time, determine its melting point. Record your data.

Transfer the residue from the steam distillation to a small Erlenmeyer flask, cool it in ice, and add 5 ml. of concentrated hydrochloric acid. Filter the ice-cold mixture by suction filtration, and press the solid between several sheets of filter paper for drying. Weigh the dried material and then set it aside until the next period. At that time, determine its melting point. Submit both the recovered *p*-dichlorobenzene and salicylic acid to your instructor, properly bottled and labeled.

QUESTIONS

1. Compare the volumes of the organic layers in the first two fractions from the bromobenzene distillation. Do the same for the two fractions in the benzene-xylene distillation. How do you account for the difference?

2. How cleanly does steam distillation separate *p*-dichlorobenzene and salicylic acid? Cite experimental evidence to support your statement.

3. What is the purpose of adding hydrochloric acid to the residue from the steam distillation before filtration? Why is it important to have the mixture ice-cold when it is filtered?

4. Judging from the results with salicylic acid, can you describe in general terms the nature of functional groups which tend to decrease the volatility of compounds in steam?

5. At 90.3° the vapor pressure of chlorobenzene, C_6H_5Cl, is 230 mm. and of water, 530 mm. Calculate the weight percentage of chlorobenzene in the distillate when it is steam distilled at atmospheric pressure.

6. What advantages would co-distillation with mercury have over steam distillation? What disadvantages?

7. (For Specially Interested Students) The International Critical Tables give the following values for the vapor pressure of nitrobenzene ($C_6H_5NO_2$): 80°, 7.5 mm.; 90°, 12.9 mm.; 100°, 20.8 mm.; 110°, 32.5 mm. From these data, draw a vapor pressure–temperature curve that will show the vapor pressure of nitrobenzene at intermediate temperatures. From this curve and the vapor pressure values for water, calculate both the boiling point of a mixture of nitrobenzene and water (at the pressure in your laboratory) and the ratio by weight in which they should distill. Devise the best experimental conditions for checking these results in the laboratory. After you have your instructor's approval, carry out the experiment. Record your results.

EXPERIMENT 7

Adsorption Chromatography

Introduction. The technique of adsorption chromatography may be illustrated by a description of how two dyes, methyl orange and methylene blue, are separated when a solution of the dyes is passed through a column of powdered alumina contained in a vertical glass tube. At first the two dyes are adsorbed at the top of the column, giving this region a nearly uniform purple color. However, when the flow of solution is discontinued and pure solvent is allowed to flow (**percolate**) through the column, a process known as **development** occurs.

The methyl orange is held tenaciously at the top of the column while the methylene blue begins to separate and move down the column. As development continues, the separation becomes more pronounced until there results a pure orange zone in the upper part of the column and a pure blue zone in the lower part of the column. This pattern is called a **chromatogram.**

At this point the passage of solvent through the alumina could be discontinued, the moist adsorbent pushed out of the glass tube, the colored zones separated mechanically, and the individual dyes washed (**eluted**) from the respective portions of adsorbent by use of a suitable solvent. However, it is usually more convenient to continue the passage of fresh solvent through the intact column until the blue and orange zones have been successively eluted from the adsorbent. Evaporation of the respective fractions of filtrate afford pure methylene blue and pure methyl orange.

This simple experiment illustrates all of the essential steps of a process which is in constant use in laboratories throughout the world to effect separation of mixtures of compounds, both organic and inorganic, which in many instances can be separated in other ways only with extreme difficulty. It should not be inferred from the experiment just described that only mixtures of colored substances can be separated by the technique of adsorption chromatography. Even mixtures of completely colorless compounds may be separated in this manner, but, as might be expected, the details of the operation need to be modified, depending on the nature of the substances being handled. Some of these details can best be treated under the headings of adsorbents, solvents, and apparatus.

Adsorbents. There are several considerations which govern the choice of adsorbent for a given chromatographic separation. It should be insoluble in the solvents to be used for the separation, and it must neither react with the substances to be separated nor act as a catalyst for their decomposition, rearrangement, or isomerization. It should have a uniform composition, regardless of the source, and it should be colorless when zones containing colored compounds are to be located visually.

Theoretically, the smaller the particle size the greater will be the degree of separation of the mixture being treated. However, there is a practical point which also needs to be considered; the smaller the particle size, the slower will be the rate of flow of solution or solvent through the column. Therefore a compromise is required. The adsorbent should be neither too coarse nor too fine; the average particle size should be about 8-12 microns in diameter. Where a required adsorbent is available only as a fine powder, the rate of flow of solution or solvent may be increased by mixing the adsorbent with filter-aid, such as Hyflo Super-cel (Johns-Manville Company). Application of gentle suction (about 680 mm. pressure) or of pressure also accelerates the rate of flow of solvent through the column.

The most widely used of all adsorbents is alumina (Al_2O_3). The most powerfully adsorbing variety is prepared by heating commercial activated alumina at red heat for a period of about 4 hours and then cooling it in an evacuated desiccator. However, alumina activated in this manner is usually too strong an adsorbent; it is difficult to remove adsorbed material from the column. Material more suitable for general use can be obtained by heating commercial alumina for a shorter period of time at a lower temperature or by deliberately adding water to the dehydrated powder prepared at the higher temperature.

The adsorbent power of a given material depends not only on the material itself but also on the solvent used in the preparation of the chromatogram. Therefore, it is not possible to provide a rigorous classification of relative adsorbent powers of different substances. However, a rough classification is as follows: strong adsorbents—alumina of low water content, activated carbon and fuller's earth; intermediate adsorbents—calcium carbonate, calcium phosphate, magnesia and slaked lime; weak adsorbents—sucrose, inulin, starch and talc.

Solvents. As already mentioned, adsorption depends upon both the nature of the solvent and the adsorbent. In any given separation of a mixture of compounds by the chromatographic procedure, it is likely that different solvents will be used for placing the solute on the column, developing the chromatogram, and eluting the adsorbed materials. Although only one adsorbent is ordinarily used for a given separation, there are cases where the simultaneous use of two or more adsorbents is advantageous. In fact, in one of the experiments which may be carried out today, the use of three different adsorbents—sucrose, calcium carbonate, and alumina—is required.

It is common practice to use a relatively nonpolar solvent to place the mixture of compounds to be sepaated on the column, then to use a somewhat polar solvent to develop the chromatogram and an even more polar solvent to elute the adsorbed materials. Of course, this is subject to wide variation, depending on the nature of the mixture to be separated. An approximate order of increasing polarity of common solvents is as follows: petroleum ether, carbon tetrachloride, cyclohexane, carbon disulfide, ether, acetone, benzene, esters of organic acids, chloroform, alcohols, water, pyridine, organic acids, and mixtures of acids or bases with water, alcohol, or pyridine.[1] In a representative chromatographic separation process, the mixture may be placed on the column as a solution in petroleum ether, the chromatogram developed with benzene and the different bands eluted with ethanol. Of course, finer shadings of development and elution are attained by using appropriate mixed solvents, such as petroleum ether-benzene, benzene-ethanol, etc.

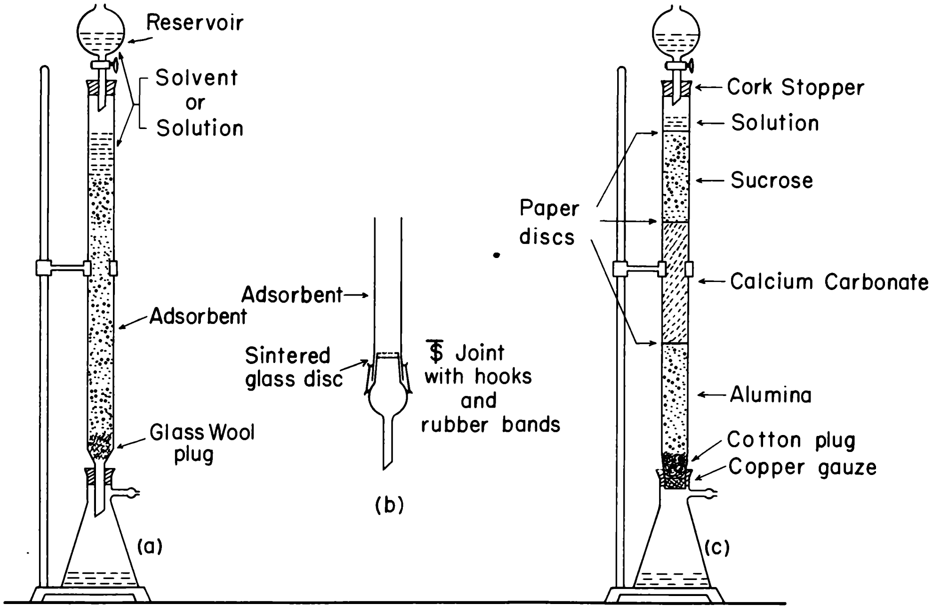

FIG. 16. Chromatographic adsorption apparatus. (a) Apparatus for adsorption chromatography with removal of products by elution. (b) Two-piece chromatographic column which permits ready extrusion of the adsorbent. (c) Adsorption apparatus with open-ended column for extrusion of adsorbent.

Apparatus. In its simplest form, the only two pieces of apparatus needed for chromatography are: (1) a length of glass tubing drawn out at the lower end, with a plug of glass wool placed at the top of the constricted portion to retain the adsorbent in the tube; and (2) a filter flask. The tube may be connected to the filter flask by means of a bored cork or a one-holed rubber stopper, as shown in Figure 16a. A tube that is distinctly longer than its column of adsorbent may function as its own reservoir, or an extra reservoir may be fitted to the top of the tube.

Refinements in the apparatus might include a perforated porcelain or sintered glass disc sealed into the tube just above the constriction, the presence of a stopcock in the drawn out portion of the tube just above the segment that fits into the filter flask through the stopper, and the use of ground glass joints throughout. If the column of adsorbent is to be pushed out of the tube and cut into segments following the development of the chromatogram, it is desirable to use a tube having no constriction; the glass wool plug and column of adsorbent may be held in place by a copper gauze folded over the bottom of the tube (Figure 16c) or by the use of a two-piece column, equipped with ground glass joints, in which there is a constriction and disc in the lower portion and all of the adsorbent is held in the upper portion (Figure 16b).

The sizes of chromatographic columns range from those which are designed to contain about 20 micrograms of adsorbent to those which can hold 20 pounds of adsorbent. The proportions of columns may vary

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[1] Although the given order of increasing solvent polarities does not correspond exactly to an order of either increasing dielectric constants or dipole moments, common criteria of the "polarity" of a solvent, it does give a good measure of the increasing abilities of these solvents to elute adsorbed compounds from a variety of adsorbents.

considerably, but a length:breadth ratio of 5:1 is generally satisfactory. The ratio of adsorbent to material being adsorbed is always generous; it is not at all uncommon to use about 50 g. of adsorbent per gram of material being adsorbed. One of the most important aspects of column chromatography is the packing of the column. In order to give satisfactory results, the adsorbent must be packed uniformly in the column, air bubbles and channels being rigorously excluded.

There are several satisfactory methods for filling chromatographic columns. One wet method consists of filling the column with solvent and sprinkling in the adsorbent, which is then allowed to settle until the proper height has been built up. The glass wool (or cotton) plug should be thoroughly wetted with solvent before this procedure is initiated; otherwise air bubbles form in the column. Another wet method consists of preparing a slurry of solvent and adsorbent and pouring this into the column and allowing it to settle. If the column contains a stopcock at the bottom, this can be opened slightly during the settling process. The slow flow of solvent through the column tends to increase the uniformity of the packing process. Another useful device is to place a rubber stopper over the end of a glass rod, and then tap the stopper gently along the walls of the chromatographic tube as the adsorbent is settling.

A satisfactory dry method for packing a column involves the addition of sufficient adsorbent to fill 1-2 cm. of the column and then tamping this down gently before adding another like portion of adsorbent. A cork having a diameter slightly less than the inner diameter of the tube serves as a convenient ramrod. The cork is attached to a glass rod which is slightly longer than the column. An even more simple way to attain uniform packing is to add small quantities of adsorbent to the tube and then to tap the bottom of the tube gently on the laboratory bench. It is important that the top portion of the adsorbent be level and remain so during the development of the chromatogram. It is a good idea to protect the surface by placing a disc of filter paper or a ½-cm. layer of filter-aid at the top of the column. Once the column has been wetted, it should not be permitted to become dry again, for this causes the adsorbent to shrink away from the glass walls and to form channels.

Adsorbability of Organic Compounds

The adsorbability of organic compounds is primarily influenced by the nature and number of the polar groups present in their molecules. It is not possible to provide a list of relative adsorbabilities of the various classes of organic compounds that is applicable to all types of adsorbents and solvents, but the following series is arranged roughly in the order of decreasing adsorbabilities; i.e., the more strongly adsorbed compounds are listed at the top.

1. Carboxylic acids
2. Alcohols, amines, and thiols
3. Aldehydes, ketones and esters
4. Organic halides
5. Unsaturated hydrocarbons; the greater the degree of unsaturation, the greater the adsorbability
6. Saturated hydrocarbons.

Chromatography of Colorless Substances

Although colorless compounds can form well defined bands on a chromatographic adsorption column, special methods must be employed in order to locate these bands and to effect a clean separation of the components of a mixture. The use of an ultraviolet lamp has proved to be the most generally useful method for locating bands of adsorbed material. Its use depends upon the fact that many substances which are colorless in ordinary light show strong fluorescence in ultraviolet light. When such compounds are adsorbed on a column, the bands stand out strongly if the column is irradiated with ultraviolet light in a partially darkened room. The use of ultraviolet light is also advantageous when dark adsorbents, such as activated carbon or fuller's earth, are used. The zones of fluorescent materials in the chromatogram are readily apparent under the ultraviolet radiation. Relatively inexpensive ultraviolet lamps may be purchased from a variety of chemical supply companies.

Colorless substances which are not fluorescent may be detected in other ways. For example, a reagent with which the adsorbed compounds form a color may be painted as a streak up the side of an extruded column. As an illustration of this technique, a dilute solution of potassium permanganate may be painted up the side of an extruded column on which two or more alkenes have been adsorbed. Where the oxidant comes in contact with an alkene, the purple color disappears and the brown color of manganese dioxide becomes apparent. The column can then be cut into appropriate sections, the surface layer of oxidized alkene and manganese dioxide scraped off, and the alkene eluted from the adsorbent.

Purely empirical methods can also be used to locate the different fractions of an adsorbed mixture. For example, the column can be eluted with a series of solvents of gradually increasing polarity and the filtrate (**percolate**) collected in small batches. Evaporation of the solvent from each of these fractions will give the organic compound which has been eluted. After the compound has been identified by means of its melting point or some other property, it can be combined with identical material obtained from the neighboring fractions.

Uses of Column Adsorption Chromatography

The use of adsorption chromatography which has been emphasized in the previous discussion has been the separation of mixtures into the pure individual components. However, there are other valuable applications of column chromatography. These include: (1) the purification of compounds by removal of small amounts of contaminants; (2) the determination of the homogeneity of chemical substances; (3) the comparison of compounds thought to be identical; and (4) the concentration of materials from dilute solutions such as those obtained when natural products are extracted from the roots, bark, or leaves of a plant or tree by extraction with a large volume of organic solvent.

Other Types of Column Chromatography

Column chromatography is not limited to adsorption chromatography. Other methods in common use are partition chromatography and ion exchange chromatography. In partition chromatography, separation of the components of a mixture depends upon the fact that, as a rule, different compounds distribute themselves in different ratios (have different partition coefficients) between two different solvents. The practice of column chromatography is much the same whether separations are based on differential adsorption or on partition. In the latter procedure adsorbent powders are replaced by materials, such as silica gel or cellulose, which contain significant amounts of bound water. The solvent used in partition chromatography is usually one in which water has a limited solubility and which itself is partially soluble in water; *n*-butyl alcohol is frequently used as the solvent.

When a mixture of compounds, such as the amino acids obtained on hydrolysis of a protein, is dissolved in the solvent and passed through the column, the components of the solute distribute themselves between the water in the stationary phase and the solvent, which is the moving phase. The more hydrophilic components of the solute are held more strongly on the column, and the more lipophilic solutes come through the column first. Paper chromatography represents a special case of partition chromatography and is discussed further in Experiment 39, page 113.

As the name implies, ion exchange chromatography makes use of special resins which, under appropriate circumstances, have the power of replacing ions present in a solution in contact with them by ions originally a part of their own structures. The technique of column ion exchange chromatography is very similar to that used in differential adsorption or partition chromatography.

Background Material for Today's Experiments

Two separate experiments are presented as the assignment for today. It is recommended that half the class perform one separation and half the other separation, provided that all of the required materials are available. Alternatively, one experiment may be assigned to all of the students, and the second reserved as a bonus experiment for the more advanced students.

In the first experiment any one of three pairs of dyes are to be separated by chromatography. Activated alumina is used as the adsorbent and 95 per cent ethanol as the solvent for developing the chromatogram. By this procedure, water-soluble fluorescein may be separated from methylene blue, methyl orange from methylene blue, or methyl orange from Victoria Blue B.

In the second experiment, the naturally occurring pigments of fresh green leaves (for example, spinach leaves) or of grass are to be extracted by a mixture of petroleum ether, benzene, and methanol, and then a petroleum ether-benzene concentrate of the pigments is to be chromatographed on a column containing three different adsorbents—sucrose, calcium carbonate, and alumina (Figure 16c). After development of the chromatogram with petroleum ether-benzene, the following bands appear on the column:

Top: olive-green (chlorophyll-b)
Upper middle: blue-green (chlorophyll-a)
Lower middle: yellow (xanthophylls)
Bottom: pink-orange (carotenes).

Experimental

I. SEPARATION OF DYESTUFFS

Procedure. Set up a column of the general type
shown in Figure 16a. The dimensions of the column
should be about 1.8 x 30 cm. Tamp a plug of glass 0-45
wool firmly into the constricted portion of the glass
tube and cover it with a layer of sand not more than
5 mm. thick. Tap the tube gently to level off the sand,
and slowly add, with continual tapping of the tube, an
intimate mixture of 28 g. of activated adsorption
alumina (Aluminum Company of America) and 2 g.
of Hyflo Super-cel (Johns-Manville).

Cut a piece of filter paper so that it has the same diameter as the inner part of the glass tube and place it on top of the adsorbent. Now wash the column with 95 per cent ethanol, and apply sufficient suction by means of the water aspirator for the rate of flow of solvent through the column to be about 15 drops per minute. The 95 per cent ethanol is continually added so that the top of the column never runs dry.

After the proper flow rate has been attained, allow the solvent to come within about 1 mm. of the top of the adsorbent, then add the dye solution all at once. When the dye solution, in turn, gets within 1 mm. of the top of the column of adsorbent, rinse the top part of the tube with about 2 ml. of 95 per cent ethanol. Carry out one of the following separations.

Separation of Water-Soluble Fluorescein and Methyl-
ene Blue. Pour a solution containing 5 mg. of water- 45-160
soluble fluorescein and 5 mg. of methylene blue in 4 ml.
of 95 per cent ethanol into the column, and, after the

tube has been rinsed with 95 per cent ethanol, continue to add the same solvent until the band of methylene blue has separated from the tightly held band of fluorescein. Add sufficient 95 per cent ethanol to elute all of the methylene blue from the column. When the eluate dropping into the filter flask is colorless, empty the flask and begin to use water as the eluent. The water-soluble fluorescein immediately migrates down the column.

Separation of Methyl Orange from Methylene Blue. **45-160** Use a solution containing 1 mg. of methyl orange and 5 mg. of methylene blue in 2.2 ml. of 95 per cent ethanol. Develop the chromatogram with 95 per cent ethanol, and elute the methylene blue with the same solvent. Use water to elute the methyl orange after all of the methylene blue has passed into the filter flask.

Separation of Methyl Orange from Victoria Blue B. **45-160** Use 2.2 ml. of a 95 per cent ethanol solution containing 1 mg. of methyl orange and 5 mg. of Victoria Blue B. Develop the chromatogram with 95 per cent ethanol, and elute the Victoria Blue B with the same solvent. Methyl orange again exhibits the stronger adsorption affinity and remains near the top of the column of adsorbent. Elute the methyl orange with water after all of the Victoria Blue B has passed through the column.

II. Separation of Leaf Pigments

Procedure. Chop four spinach leaves or a handful of grass into a fine mash, and soak the mash for 3 hours in a mixed solvent consisting of 90 ml. of petroleum ether (boiling point 60°-80°), 10 ml. of benzene, and 30 ml. of methanol.

While the mash is being extracted, assemble the apparatus shown in Figure 16c. Wire on the lower end of the clean 20 x 1.7 cm. column a piece of clean copper gauze, and push a small cotton plug to the bottom of the column. Prepare a slurry of 8 g. of adsorption alumina in 15 ml. of petroleum ether (boiling point 60°-80°) and pour this into the column (Note 1). Allow the alumina to settle while you tap the tube continuously. Rinse down the inside of the tube carefully with the same solvent, and, after the alumina has settled, drop a fitted disc of filter paper on top of the adsorbent. The presence of liquid above the adsorbent allows the disc to settle properly without trapping air.

When the solvent level has fallen to within about 2 cm. of the top of the alumina, pour a slurry of 5.3 g. of calcium carbonate in 30 ml. of petroleum ether into the column. Tap the column, wash it down with fresh solvent, and add a paper disc as before. Finally pour into the column a slurry of 7 g. of powdered sucrose in 20 ml. of petroleum ether. Once again, tap the tube, wash it down with solvent, and add a disc of filter paper. Fit the reservoir into the top of the column, and allow petroleum ether to flow through the column as the solution of leaf pigments is being treated so that it can be added to the column. Do not allow the top of the column of adsorbent to become dry.

Filter with suction the mixture of leaves or grass and the ternary solvent, and wash the extract with four 50-ml. portions of water to remove the methanol. Dry the solution over anhydrous sodium sulfate for about 15 minutes, filter the mixture, and concentrate the filtrate to about 1 ml. in a partial vacuum. This can best be accomplished by placing the filtrate in a large filter flask, setting a solid rubber stopper in the mouth of the flask, and attaching the side outlet of the flask to the aspirator with heavy-walled rubber tubing. Then heat the flask on the steam bath and shake it constantly to prevent the solution from bumping.

Pour the concentrated solution of pigment onto the chromatographic column and develop the chromatogram with petroleum ether (boiling point 40°-60°) (Note 2). Note the eventual appearance of four distinct adsorption bands. The olive-green band of chlorophyll-b will be found on the sucrose, the blue-green band of chlorophyll-a either on the sucrose or the calcium carbonate, the yellow band of xanthophylls on the calcium carbonate, and the pink-orange band of carotenes on the alumina.

After the chromatogram has been developed fully, apply suction to the receiver and drain the column nearly dry. Carefully push the column of adsorbents out of the glass tube onto a sheet of paper with the aid of a glass rod flattened at one end. Cut the colored bands from the extruded column of adsorbents and elute each with 10 ml. of a 2 per cent solution of methanol in ether.

It is obvious that all of the operations described in this section cannot be completed within 3 hours. However, if you can at least carry the operation to the stage of development of the chromatogram, which you can do in the allotted time only by preparing the solution of leaf pigments and drying the adsorbents in advance of the regularly scheduled laboratory period, you will have learned the essential details of the chromatographic method.

NOTES

1. Some students report that they obtain better results in this experiment when the column is packed with dry absorbents rather than with slurries. When the dry adsorbents are employed, paper discs are not used to separate the three different adsorbents. Instead, the tube is tapped on the desk as each adsorbent is added, and, after all of one variety has been put into the column, the material is tamped lightly with a cork stopper attached to a rod before the next adsorbent is added. All 3 adsorbents should be heated at 100° for several hours before being used.

2. At this point, the rate of flow of solvent out of the column should be decreased to about 10 drops per minute.

QUESTIONS

1. If a mixture of naphthacene, anthracene, and naphthalene was chromatographed on alumina, then eluted, which material would come through the column first? Which last?

2. An unknown dyestuff is thought to be methylene blue. How might its identity be verified by a procedure making use of the chromatographic technique?

3. Suppose that an initial attempt to separate a particular mixture of organic compounds by chromatography on calcium carbonate, with chloroform as the solvent, failed. What steps might be taken to achieve satisfactory results in subsequent runs; i.e., what changes in solvent and/or adsorbent might prove helpful?

4. Define or describe each of the following terms: (a) development; (b) elution; (c) percolation; (d) adsorption; (e) adsorbent; (f) micron; (g) filter-aid; (h) fluorescence; (i) resin.

5. What are some of the considerations that govern the choice of adsorbent for a given chromatographic separation?

6. Describe two wet methods and one dry method for filling a chromatographic column.

7. What are some of the methods used for the location of adsorption bands when colorless compounds are subjected to chromatographic adsorption?

8. What are some of the applications of column adsorption chromatography?

9. What is an anion exchange resin? A cation exchange resin?

10. What do the words "hydrophilic" and "lipophilic" mean? Why are the more hydrophilic components of a mixture held more tightly on a column of silica gel or cellulose than are the more lipophilic components when butanol is used as the solvent?

EXPERIMENT 8

Qualitative Tests for the Elements

Introduction

Principles of Organic Chemistry Analysis. In the characterization of any unknown organic compound, a knowledge of the elementary constituents is essential. Before the usual qualitative tests can be applied, however, the elements must be converted from the covalent form in which they usually occur in organic compounds into ions or simple compounds for which routine tests are available. The elements which commonly occur in organic compounds along with carbon, hydrogen, and oxygen, and with which we are primarily concerned, are nitrogen, sulfur, and the halogens.

A preliminary ignition over a free flame of a 0.1-g. sample of the unknown in a crucible cover or on the tip of a spatula is revealing. If the sample burns with a luminous flame leaving little,[1] if any, residue, the unknown is almost certainly organic (contains carbon). Evidence of water (usually in the form of condensed vapor) confirms the presence of hydrogen. No test is ordinarily made for oxygen.

A somewhat more refined adaptation of the oxidative decomposition consists of heating a 0.1-g. sample of the unknown with 1-2 g. of fine copper oxide powder in a small test tube. Carbon is converted to carbon dioxide, which can be detected by precipitation of barium carbonate with a solution of barium hydroxide, and hydrogen, to water, which condenses in the cool portion of the tube.

The method for the detection of sulfur, nitrogen, and halogens depends upon the fact that fusion of an organic compound containing these elements converts them to easily identifiable ions.

$$\mathrm{C, H, O, S, N, X} \xrightarrow{\text{Na fusion}} \left\{\begin{array}{l} \mathrm{Na_2S} \\ \mathrm{NaCN} \\ \mathrm{NaX} \end{array}\right.$$

Detection of Sulfur, Nitrogen, and Halogens. Sulfur is converted to sulfide ion, which forms a black precipitate of lead sulfide with lead acetate in a solution acidified with acetic acid:

$$\mathrm{Pb^{++} + S^{=} \rightarrow PbS\ (Black)}$$

Nitrogen appears in the fusion product as cyanide ion. Upon addition first of ferrous sulfate and then of ferric chloride, both under controlled pH, the characteristic bright color of Prussian blue appears:

$$\mathrm{Fe^{++} + 2CN^{-} \rightarrow Fe(CN)_2}$$

$$\mathrm{Na^{+} + Fe^{+++} + Fe(CN)_2 + 4CN^{-} \rightarrow NaFe^{III}[Fe^{II}(CN)_6]}$$

("Soluble" Prussian blue)

Halogens are converted in every case to the corresponding halide, which, upon addition of silver nitrate solution, forms a precipitate of silver halide, insoluble in nitric acid. Distinctions among chloride, bromide, and iodide ions are made by the usual methods of inorganic qualitative analysis.

The Beilstein Test. A preliminary test for the possible presence of halogen, called the Beilstein[2] test, can be made directly on the original unknown. In this test, a small sample of the unknown is burned on a previously ignited copper spiral in the oxidizing portion of a hot flame. Any halogen present is converted to the corresponding copper$^{\mathrm{II}}$ halide, which imparts a bluish-green color to the mantle of the flame as it volatilizes. The appearance of this color cannot be interpreted as positive evidence of halogen, for the test is extremely sensitive and minute traces of halogen-containing impurities will suffice to give the test.

In addition, some organic acids and some nitrogen-containing compounds, such as pyridine and quinoline, produce the colored flame. However, unless the unknown is so volatile that it evaporates completely before the wire can be heated sufficiently to effect decomposition, a negative test indicates the absence of any halogen except fluorine ($\mathrm{CuF_2}$ is not volatile).

Experimental

Described below are the best simple procedures for the ignition test, the sodium fusion, and the detection of sulfur, nitrogen, and halogens. Perform each test on a known sample (Note 1) containing all three, until you obtain an excellent test for each. Then obtain two unknowns from your instructor and ignite each and test for sulfur, nitrogen, and halogens. Report for each unknown the elements present and as much additional information about the chemical nature of the unknown as you can, on the basis of the tests. After your report has been accepted, use the remainder of the period to answer the questions at the end of this experiment.

Ignition Test. Place about 0.1 g. of the material on a small crucible cover or on the tip of a spatula and heat (use tongs for crucible cover) in the oxidizing portion of a small flame. Observe the following phenomena: (1) melting, (2) character of the flame, (3)

---

[1] Metallic salts of organic acids leave a small amount of ash, but are not confused with inorganic salts which, almost without exception, do not burn. Since the number of metallic elements commonly found in organic compounds is small, a few simple tests, beginning with a flame test, on the residue will usually reveal the nature of the metal present.

[2] Named after the discoverer Friedrich Konrad Beilstein (1838-1906), who also compiled the first editions of the famous Beilstein *Handbuch der Organischen Chemie.*

evidence of water vapor, (4) residue left after heating to red heat, and (5) reaction of residue with red litmus and with hydrochloric acid.

The melting behavior indicates the possibility of making a melting-point determination on the sample. A flame indicates that the compound is volatile or forms volatile decomposition products, and a very sooty flame suggests unsaturation (probably aromatic). Condensation of water vapor on a cool glass tube held above the burning sample confirms the presence of hydrogen. Finally, a residue indicates the presence of a metal, an alkaline metal if the residue is basic to litmus and a heavy metal if it is insoluble in hydrochloric acid.

The Sodium Fusion. (CAUTION! Sodium is dangerous and should be treated with respect. It should always be handled with forceps, never directly with the fingers. It should be dried with filter paper and cut with a sharp knife or scissors. Sodium scrap or residues should be destroyed by treatment with a large volume of ethyl alcohol. Never allow sodium to come into contact with water. The sodium fusion is sometimes accompanied by a sharp report or explosion. Wear goggles or safety glasses. Be certain that the fusion tube is not pointed toward anyone.)

Place a piece of clean sodium the size of a *small* pea (about 4 mm. in diameter) in a 150 x 12 mm. (5-inch) Pyrex test tube that is held in a vertical position by means of a clamp lined with asbestos sleeves. Heat the lower part of the tube with a hot flame until the sodium melts and sodium vapors rise about 3 cm. in the tube. Then remove the flame and *quickly* but *carefully* allow 4 drops of the unknown (or about 0.2 g. if it is a solid) to fall directly into the sodium vapor without touching the sides of the tube. Then heat the tube to redness for at least 1 minute and finally allow it to cool to room temperature.

Add 3 ml. of ethyl alcohol dropwise, and break up the charred solid with a stirring rod to be sure that all unreacted sodium is destroyed. Then half-fill the test tube with *distilled* water, boil gently for several minutes, and, finally, filter the hot mixture and retain the alkaline filtrate as a stock solution for subsequent tests (Note 2).

The Sulfur Test. Acidify 2 ml. of the stock solution with dilute acetic acid and add 5 drops of lead acetate solution. A black precipitate of lead sulfide indicates the presence of sulfur. The brown color of the liquid may obscure the black of the precipitate, so, if you are in doubt, filter.

The Nitrogen Test. To 3 ml. of the filtrate, add 5 drops of a fresh 5 per cent solution of ferrous sulfate and 5 drops of a 10 per cent solution of potassium fluoride (Note 3). Boil the resulting mixture gently for 5 seconds, allow the suspension of iron hydroxides to cool, and then add 2 drops of a 5 per cent solution of ferric chloride. Finally add sufficient dilute (25 per cent) sulfuric acid to dissolve the insoluble iron hydroxides and to make the solution distinctly acid to litmus.

If nitrogen (as cyanide ion from the fusion) is present, a brilliant blue solution or suspension of Prussian blue will appear. Formation of a greenish-blue color suggests that nitrogen is present but that the fusion was incomplete.

The Test for Halogens. Acidify 3 ml. of the stock solution with dilute nitric acid. If sulfur or nitrogen, or both, are present, boil in a small test tube for 3-4 minutes to expel all hydrogen sulfide and hydrogen cyanide. Add 4 or 5 drops of silver nitrate.

A white or yellow precipitate which darkens rapidly upon exposure to light indicates the presence of halogen. If the precipitate is colorless and is soluble in fresh concentrated ammonium hydroxide, it is silver chloride. If it is pale yellow and difficultly soluble, it is probably silver bromide. If it is bright yellow and completely insoluble, it is silver iodide. When two or three different halogens are present, standard methods of inorganic qualitative analysis are used for their detection.

Carry out a preliminary test for halogen on a sample of the original unknown as follows: make a small loop, 2 to 3 mm. in diameter, at one end of a piece of short copper wire and insert the other end into a cork to serve as a holder. Heat the coil in the hot portion of a Bunsen flame until it imparts no color to the flame. Allow the wire to cool, dip it into a small portion of the original unknown, and heat in the edge of a Bunsen flame. A green color indicates the probability of the presence of halogen. If no green color is formed, no chlorine, bromine, or iodine-containing compound other than an extremely volatile liquid can be present.

NOTES

1. A 1:1 mixture of thiocarbanilide and *p*-chloroaniline or *p*-dichlorobenzene makes a convenient "known" for sulfur, nitrogen, and halogen tests.

2. With this procedure, the same test tube can be used for many sodium fusions. It should be retained and used only for this purpose, as it will soon become etched and discolored.

3. Potassium fluoride increases the sensitivity of the Prussian blue test. It forms an unusually stable complex with ferric ion, thereby preventing the ferric ion concentration from reaching a level at which insoluble ferric ferrocyanide, rather than the desired soluble Prussian blue, would be formed, and also minimizing the formation of ferricyanide ion.

QUESTIONS

1. In inorganic chemistry, detection of the elements (usually in the form of ions) present in an unknown is

almost always sufficient to provide complete characterization of an unknown. With organic compounds, this is not the case. For example, how completely is a compound characterized if it is shown to contain only carbon and hydrogen? Or if, by quantitative analysis, it is shown to contain 85.7 per cent carbon and 14.3 per cent hydrogen by weight?

Of what value, then, is a qualitative and quantitative elementary analysis in the characterization of an organic compound?

2. Why must hydrogen cyanide and hydrogen sulfide be expelled before a test is made for halide ion?

3. An unknown leaves a residue upon ignition. Predict the solubility in ether and benzene of the original unknown.

An aqueous solution of the residue turns red litmus blue. Predict the solubility in water of the original unknown.

4. An unknown is found to contain carbon, hydrogen, and oxygen only. Can the unknown be an amine or a mercaptan? Name several additional homologous series which are eliminated as possibilities.

5. What elements are found in organic compounds isolated from natural sources? What additional elements may occur in synthetic compounds?

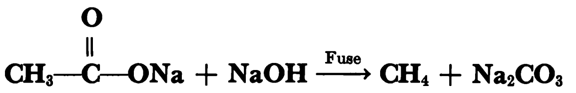
6. How can the presence of oxygen in an organic compound be proved?

7. Write a balanced equation for the oxidation of *D*-glucose, $C_6H_{12}O_6$, with copper oxide.

8. Write equations for the reactions which can occur between carbon dioxide and a solution of barium hydroxide.

EXPERIMENT 9

Preparation and Properties of Methane

(A) 

$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-ONa + NaOH \xrightarrow{\text{Fuse}} CH_4 + Na_2CO_3$$

(B) $$CHCl_3 + 3\,Zn + 3HOH \rightarrow CH_4 + 3\,Zn(OH)Cl$$

(C) $$Al_4C_3 + 12HCl \rightarrow 3CH_4 + 4AlCl_3$$

Introduction. Methane is the simplest of all organic compounds. It is the first member of the family of hydrocarbons called the **methane, paraffin,** or **alkane** series. In fact, all the other members of this series may be considered as derivatives of methane in which one or more of the methane hydrogen atoms have been replaced by alkyl groups.

Methane constitutes 50 to 97 per cent of natural gas and is formed in nature by bacterial decomposition of cellulose in the absence of oxygen.

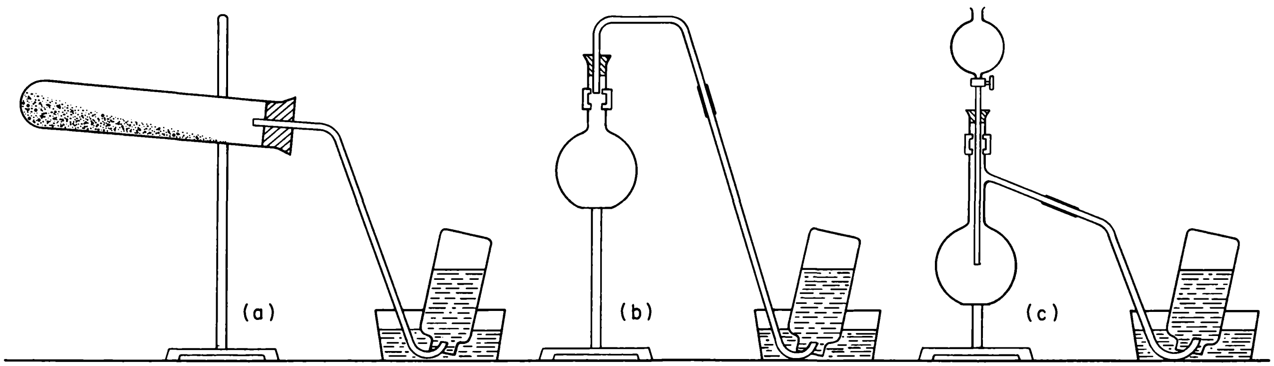
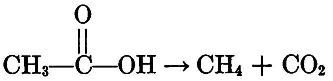


FIG. 17. Apparatus for the synthesis of methane. (a) By pyrolysis of sodium acetate. (b) By reduction of chloroform. (c) By hydrolysis of aluminum carbide.

In this experiment, you will prepare methane by three simple laboratory methods: (a) the decarboxylation of acetic acid, (b) the reduction of a halogenated methane (chloroform), and (c) the reaction of certain metallic carbides, such as aluminum carbide, with an acid. In nature, acetic acid is decarboxylated at room temperature through the action of certain microorganisms.



$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-OH \rightarrow CH_4 + CO_2$$

In the laboratory, drastic conditions, such as the pyrolysis of a salt of acetic acid, are required to bring about the reaction.

The chemical properties observed for methane in this experiment are characteristic of the alkanes as a group.

A. Preparation of Methane by Pyrolysis of Sodium Acetate

0-60 Mix thoroughly in a mortar 8.2 g. (0.1 mole) of anhydrous (fused) sodium acetate (Note 1) and 10 g. of soda lime (Note 2). Introduce the mixture rapidly into a large (8-inch) test tube fitted with a rubber stopper and glass delivery tube as shown in Figure 17a. Be sure to tilt the test tube downward so that adsorbed water driven from the mixture upon heating will not run back into the heated portion of the tube and break it.

Heat the test tube on all sides with a free flame, cautiously at first, and then more strongly, in order to maintain a steady evolution of methane. (Hold the burner in your hand and play the flame over the tube.) After the air in the test tube has been displaced, collect (over water) 5 gas bottles of methane and store the gas for later use by keeping the bottles inverted over water. *Always remove the delivery tube from the water trough before discontinuing the heating.*

Now test the methane as follows: 60-80

(a) Apply a flame to the mouth of one of the bottles of methane. Observe the character of the reaction and of the flame. Note any indication of the nature of the products of the reaction. Record your observations.

(b) Allow a second bottle of methane to stand upright and uncovered for about 15 seconds. Again, apply a flame to the mouth of the bottle. Note the character of the reaction and of the flame.

(c) Shake about 2 ml. of a 0.3 per cent solution of potassium permanganate in a third bottle of methane. Observe whether or not the permanganate color is discharged.

(d) To each of the remaining bottles of methane, add 4 or 5 drops of a 5 per cent solution of bromine in carbon tetrachloride. Stopper one of the bottles and place it in your desk and leave the other in a bright light (preferably sunlight). After a few minutes, observe the results. Blow your breath across the mouth of each of the bottles. Note and record any differences in the two cases.

B. Preparation of Methane by Reduction of Chloroform

80-120 Introduce 10 g. of zinc dust into a small round-bottomed flask mounted on a ring stand and add 10 ml. of ethyl alcohol and 10 ml. of water. Fit the flask with a rubber stopper and delivery tube for collection of the gas over water (Figure 17b). Add to the mixture 5 ml. of chloroform and 1 ml. of a 10 per cent copper sulfate solution (Note 3). The reaction may require several minutes to start. If it becomes too rapid, cool the flask in a pan of cold water. Collect two bottles of the gas by upward displacement of air and two by downward displacement. Test for methane in each bottle by methods suggested in A. Note and record the results.

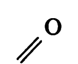
C. Preparation of Methane by Hydrolysis of Aluminum Carbide

120-150 Place 8 g. of aluminum carbide in a 250-ml. distilling flask fitted with a dropping funnel and glass delivery tube (Figure 17c). Drop a total of 20 ml. of dilute hydrochloric acid (Note 4) upon the aluminum carbide to generate the gas. Collect several bottles of the gas as before. Run tests designed to show that the collected gas has all the properties observed for methane in A.

D. Preparation of Absolute Ether

If each student is to prepare his own absolute ether for Experiment 10 (see p. 46), use the remainder of the period for this purpose.

NOTES

1. If the sodium acetate is hydrated  $(CH_3\text{—}\overset{O}{\overset{/\!/}{C}}\text{—}ONa\cdot 3H_2O)$, it must first be dehydrated. To do this, place about 15 g. of the hydrated crystals in an iron dish or porcelain evaporating dish on a ring stand and heat directly with the flame of a Bunsen or Fisher burner. (Goggles!) The salt will melt almost at once. Continue to heat, stirring constantly with a glass rod; it is advisable to steady the dish by holding it with tongs. As the water of crystallization is driven off, the salt will resolidify. Heat further until the anhydrous sodium acetate begins to melt, being careful not to overheat, as indicated by darkening of the material. The anhydrous salt should be gray in color and flaky. Finally, weigh 8 g. of the fused salt for use.

2. Soda lime is a granular mixture of sodium hydroxide and calcium oxide. It is much more easily stored and handled in finely divided form than is sodium hydroxide alone.

3. The zinc and copper sulfate react to form a zinc-copper couple which is much more effective in the reduction than zinc alone.

4. This synthesis can be carried out as a simple hydrolysis, with water functioning as the acid in place of hydrochloric acid, but the reaction is then much slower and the reacting mixture must be heated.

QUESTIONS

1. In the preparation of methane by pyrolysis of sodium acetate, why must the delivery tube be removed from the water trough before the heating is discontinued?

2. Calculate the relative densities of methane and air. If you were to collect methane by displacement of air, would you use upward or downward displacement of air?

3. Write balanced equations for the combustion of methane; the reaction of methane with bromine in the light; the combustion of pentane; the reaction of pentane with bromine in the light.

4. How can you magnify the effect observed when you blow your breath across the mouth of a tube containing methane and bromine?

5. Derive a generalized equation for the complete combustion of any alkane, C_nH_{2n+2}.

6. If you were trying to make a highly explosive mixture of oxygen and methane, approximately in what ratio would you mix the gases?

What volume of oxygen would be required for the complete combustion of 5 liters of methane? Of pentane?

7. What general name is applied to the reaction of alkanes with halogens? What is the function of the light?

8. Can you explain why hydrochloric acid reacts more rapidly with aluminum carbide than does water?

9. What volume of methane at standard conditions could be obtained theoretically from 8.2 g. of sodium acetate? This is called the **theoretical yield** for the reaction.

An actual yield of 1.12 l. of methane (standard conditions) would represent what percentage of the theoretical yield? This value is called the **percentage yield.**

Construct an equation which shows how the percentage yield for any reaction may be calculated.

10. Write a balanced equation for the synthesis of ethane by each of the general methods illustrated in today's experiment that is applicable.

EXPERIMENT 10

Preparation of Ethane by Means of the Grignard Reaction

$$C_2H_5Br + Mg \rightarrow C_2H_5MgBr$$

$$C_2H_5MgBr + H_2O \rightarrow CH_3{-}CH_3 + MgBr(OH)$$

Introduction. Perhaps the most versatile synthetic reagents in all of organic chemistry are the alkyl magnesium halides, RMgX. This class of compounds has been named the Grignard reagent, after the renowned French chemist, Victor Grignard, who was awarded the Nobel Prize in chemistry (1912) for his pioneer work in this field. Grignard reagents have been used for the synthesis of compounds of almost every homologous series, and their use in research is widespread.

The synthesis of an alkane *via* the Grignard reagent actually constitutes a two-step reduction of an alkyl halide to an alkane. In the first step, the Grignard reagent is prepared by the reaction of an alkyl halide with metallic magnesium in anhydrous ether. In the second step, the Grignard reagent is hydrolyzed to yield the alkane and the basic magnesium halide.

In this experiment, the Grignard reagent you will prepare and hydrolyze is ethylmagnesium bromide. Preparation of a Grignard reagent is a critical test of your experimental technique. If conditions are proper, the reaction proceeds readily in good yield; if not, the reaction may proceed sluggishly or not at all.

Grignard reagents react with compounds containing even weakly acidic hydrogen to form the corresponding alkane. Ethylmagnesium bromide is frequently used in a quantitative test to determine the amount of so-called "active" (weakly acidic) hydrogen present in a compound (Zerewitinoff determination). The volume of ethane liberated in reaction of ethylmagnesium bromide affords a convenient measure of the amount of active hydrogen present in the compound. Such weakly acidic hydrogen as that present in water and alcohols may be determined quantitatively in this fashion.

Absolute Ether

[To have been prepared during previous period.]

The ether that is used in the preparation of the Grignard reagent (ethylmagnesium bromide) must be made **absolute,** i.e., free from both water and alcohol (Note 1). In order to accomplish this (Note 2), shake 150 ml. of commercial ether with a cold solution of 20 g. of calcium chloride in 20 g. of water. Separate the ether (top) layer from the water layer and dry the ether for several hours (overnight) over 20 g. of calcium chloride.

Decant the ether from the calcium chloride into a 250-ml. Erlenmeyer flask. Add 10 g. of phosphoric anhydride. (*Weigh the phosphoric anhydride rapidly, as it readily absorbs moisture from the air, and handle it only in glass apparatus, as it may cause filter paper to ignite in air.*) Cork the flask and allow it to stand for 1 hour with occasional shaking. Then distill on a steam bath (*or if an open flame is used, see Figure 21 for precautions against fire*) through a clean, dry condenser, transfer to a clean dry bottle, and store for at least 24 hours over a few thin shavings of sodium or a few lengths of sodium wire from a sodium press. It is advisable to test the ether for gas evolution with fresh sodium before use.

Preparation of Ethylmagnesium Bromide

Fit a clean, dry 250-ml. round-bottomed flask with 0-90
a dry condenser for reflux, using a clean, well-fitting cork. Attach a drying tube with soda lime to the top of the condenser (Figure 18a). Be certain that a brisk stream of cold water is circulating through the condenser.

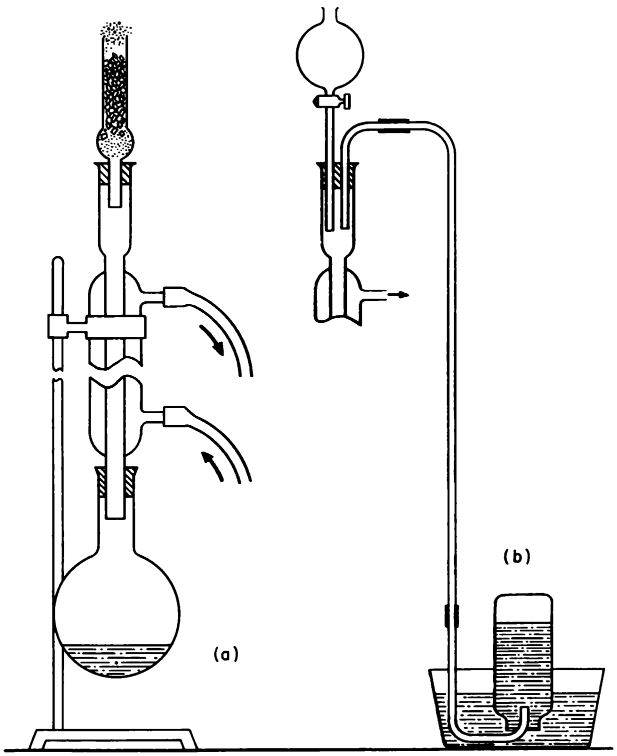


FIG. 18. Apparatus for the preparation of ethane. (a) For the synthesis of the Grignard reagent. (b) For the hydrolysis of the Grignard reagent.

At this point, complete the bending of all tubing required for the hydrolysis of the ethylmagnesium bromide as described in the next section (see Figure

18b) and extinguish all flames before proceeding. Then prepare an ice bath for use in case control of the reaction becomes necessary. Next place 1.9 g. (0.08 mole) of magnesium turnings, a crystal of iodine, 15 ml. of *absolute* ether, and 6.5 ml. (9.5 g., 0.087 mole) of ethyl bromide directly into the flask and quickly replace the condenser. Force a brisk stream of cold water from the tap through the condenser. More ether will be added as the reaction begins, but at the outset the concentration of the ethyl bromide is kept high to promote easy starting.

Watch the mixture carefully. Sudden appearance of cloudiness in the liquid and ebullition at the surface of the magnesium are signs that the reaction has begun. At this point, add an additional 15 ml. of absolute ether through the top of the condenser. (If you have difficulty in initiating the reaction, warm the outside of the flask with your hand and swirl the flask gently. If necessary, scratch one of the magnesium turnings against the side of the flask with a glass stirring rod and add an extra crystal of iodine.)

Once the reaction has begun, allow it to proceed under as lively reflux as can be accommodated by the condenser. If reflux is too vigorous, it may be necessary to cool the flask for a moment by means of the ice bath. When spontaneous reflux ceases, reflux on a steam or water bath for about 25 minutes. The reaction is complete when only a few small remnants of magnesium or magnesium contaminants remain.

90-140

Preparation of Ethane by Hydrolysis of the Ethylmagnesium Bromide

Insert in the top of the condenser a well fitting, two-holed rubber stopper fitted with a 125-ml. dropping funnel and a delivery tube leading to a deep pneumatic trough (Figure 18b). Prepare in the pneumatic trough an inverted, water-filled, 2000-ml. wide-mouth bottle for collection of a gas by displacement of water.

Place the reaction flask in the ice bath and wait until temperature equilibrium is established. Be certain that there is a brisk flow of cold water through the condenser. Then by means of the dropping funnel add (DROPWISE!) a total of 20 ml. of water (or until ethane evolution ceases), collecting the evolved ethane in the 2000-ml. bottle. Read the temperature of the water and the barometric pressure. Then adjust the height of the collecting bottle so that the water level inside the bottle is equal to that outside, place a watch glass firmly at the mouth, and invert the bottle.

Fill the bottle with water by means of a graduated cylinder, carefully measuring the total volume of water required. This is, of course, the volume of ethane evolved as measured at the observed temperature and pressure. Convert this volume to standard conditions. Now calculate the percentage yield. Record all of your data and calculations. **140-150**

NOTES

1. The reaction is difficult to start in the presence of water or alcohol, and the yield is reduced materially.

2. The nearly anhydrous ether supplied by the Carbide and Carbon Chemical Corporation is sufficiently anhydrous to be subjected to the treatment with metallic sodium directly without prior processing.

QUESTIONS

1. What effect would the following have on the calculated percentage yield:

(a) Failure to correct the ethane volume for the effect of water vapor?

(b) Entrainment in the ethane of ether vapor which is carried over to the collecting bottle?

(c) Loss of ethane because of loose fittings?

(d) Weighing of 1.4 instead of 2.4 g. of magnesium?

2. Assuming that a drop of water weighs 0.05 g., what volume of ethane measured at standard conditions should be evolved for each drop of water added as long as excess Grignard reagent remains? What volume as measured in your experiment?

3. Write balanced equations for the reaction of ethylmagnesium bromide with ammonia; methyl alcohol (CH_3OH); acetic acid (CH_3COOH); hydrogen sulfide. On the basis of electronic structure, account for the reaction of the Grignard reagent, RMgX, with compounds containing even very weakly acidic hydrogen.

4. Can you propose a possible mechanism for the catalytic action of iodine in the preparation of the Grignard reagent?

5. A compound has the molecular formula $C_4H_{10}O_2$. Reaction of 0.45 g. of the compound with excess ethylmagnesium bromide affords 253 ml. of ethane as measured over water at 20° and a pressure of 740 mm. of mercury.

What statements can you make about the hydrogen atoms in the compound?

6. How does the over-all transformation effected in the preparation of an alkane from an akyl halide *via* the Grignard reagent compare with that accomplished in the reduction of an alkyl halide by means of zinc dust and water?

EXPERIMENT 11

I. Properties of Kerosene

II. Assemble Apparatus for Experiment 12

Introduction. Most petroleum products are not pure compounds but are mixtures obtained as a certain fraction collected over a particular temperature range in the fractional distillation of petroleum. This is the case for kerosene, which consists largely of a mixture of alkanes in the C_{12} to C_{16} range. Kerosene is used as a fuel for oil stoves and in Diesel engines and tractors. As homologs of methane, the hydrocarbons which make up kerosene exhibit the same general chemical properties as does methane; some of these are more easily studied for the liquid kerosene than they are for the gas methane. Several of those investigated in today's experiment will explain how the name paraffin ("little affinity") came to be applied to members of this series.

[The study of kerosene will require only about half of the period. The other half is to be spent in assembling the apparatus to be used in the synthesis of ethylene bromide (Experiment 12).]

I. PROPERTIES OF KEROSENE

0-30 A. Distillation of Kerosene

Place 15 ml. of kerosene and 2 boiling chips in a small distilling flask clamped to a ring stand and supported by a wire gauze on a ring. Attach to it a condenser fitted with a curved adapter leading into a small receiving flask. Heat the distilling flask gently with a free flame so that the kerosene distills at the rate of 1-2 drops per second. Record the distillation range. All the tests described below should be run on the distillate.

30-60 B. Solubility of Kerosene

Test the solubility of the distilled kerosene in water, ether, ethyl alcohol, ligroin, concentrated sulfuric acid, and concentrated nitric acid. In each case, place 5 drops of kerosene in a small, dry test tube and add the specified solvent dropwise until complete solution occurs or until a total of 3 ml. has been added. Observe and record the solubilities as very soluble, slightly soluble, or insoluble.

C. Reactivity of Kerosene toward Sodium Hydroxide and Potassium Permanganate 60-75

Add 5 drops of kerosene first to 3 ml. of dilute sodium hydroxide solution and then to 5 drops of aqueous potassium permanganate in separate test tubes. Shake vigorously and inspect each mixture carefully for evidence of reaction.

D. Substitution Reaction on Kerosene 75-90

Add 3 ml. of kerosene to each of two test tubes. Then pour into each enough bromine in carbon tetrachloride solution to give the mixture a pronounced bromine color. Insert a cork into each test tube. Place one in a dark cupboard or drawer at once, the other in direct sunlight or in the light of a 200-watt bulb. After 3 minutes, compare the two mixtures as to color and effect on moist litmus paper.

II. ASSEMBLE APPARATUS FOR EXPERIMENT 12

QUESTIONS

1. What distillation range did you observe for the kerosene sample?

What is the distillation range for a typical sample of gasoline? When your grandfather was a boy, almost every state in the United States had a law in the books imposing severe penalties for the adulteration of kerosene with gasoline. Can you explain why?

Is the exact method used for distillation of the kerosene suitable for the distillation of gasoline? Of petroleum ether? Explain.

2. What is the behavior of alkane hydrocarbons toward each of the following at room temperature: (a) concentrated sulfuric acid; (b) concentrated nitric acid; (c) aqueous potassium permanganate; (d) dilute sodium hydroxide solution?

3. Do the alkane hydrocarbons have any significant acid or basic character in a broad sense? Explain.

4. Write a balanced equation for the reaction of a typical constituent of kerosene with bromine in the light.

EXPERIMENT 12

Ethylene and Ethylene Bromide

$$CH_3—CH_2OH \xrightarrow[160°]{H_2SO_4} CH_2═CH_2 + H_2O$$

$$CH_2═CH_2 + Br_2 \longrightarrow BrCH_2—CH_2Br$$

Introduction. Complete dehydration of alcohols (elimination of one molecule of water from one molecule of alcohol) constitutes a simple laboratory method for the preparation of alkenes. The dehydration may be effected by heating of the alcohol in the presence of an acid catalyst. For a single batch operation, it is most convenient to heat the alcohol in a flask with a nonvolatile protonic acid, such as sulfuric or phosphoric acid.

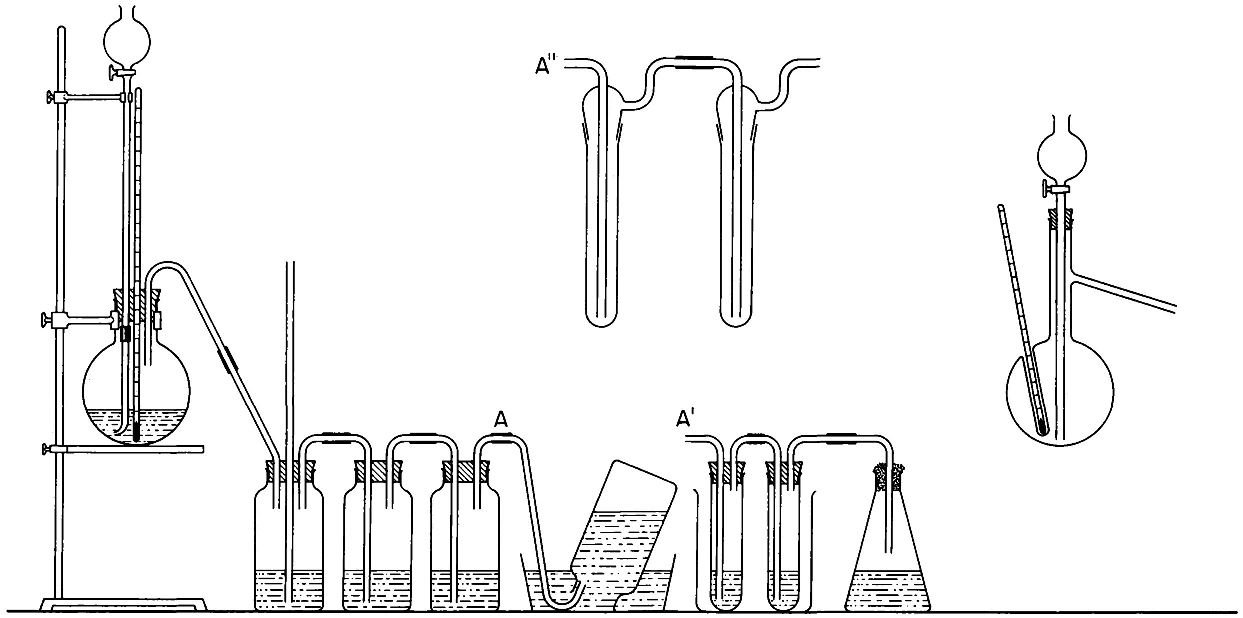


FIG. 19. Apparatus for the synthesis of ethylene and of ethylene bromide.

The relative ease of dehydration of alcohols is tertiary > secondary > primary. Primary alcohols, such as ethyl alcohol, are dehydrated only at elevated temperatures. Many tertiary alcohols, on the other hand, are dehydrated by acids even at room temperature. This fact must be borne in mind whenever an attempt is made to carry out other reactions on tertiary alcohols in the presence of strong acids.

For continuous or repeated batch operation, it is timesaving in the long run to use a column packed with coarse granules of the Lewis acid catalyst activated alumina[1] and heated so that the vaporized alcohol can be passed through it at 350°-400°. The alkene product, together with water, is collected in suitable condensers connected to the column. The yield of alkene is, in general, considerably higher in this process than for the protonic acid catalytic reaction, where partial dehydration of the alcohol (elimination of one molecule of water between two molecules of alcohol) to form an ether is an inevitable and troublesome side reaction.

When sulfuric acid is used as the catalyst, the hot concentrated acid also oxidizes some of the organic material. The acid is reduced to sulfur dioxide, which can often be recognized by its odor as a contaminant of the olefin product.

As a by-product of the cracking still, ethylene is an inexpensive and tremendously important raw material. Its usefulness depends largely upon the ease with which it undergoes addition reactions to form products of great commercial importance. The addition of bromine to ethylene is selected as a typical addition reaction of the olefin.

A. Ethylene Bromide

Assemble the apparatus as shown in Figure 19. The **0-120**
generator should be a 2000-ml. round-bottomed flask,

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[1] Activated alumina is aluminum oxide which has been treated so that it has an optimum porosity and an optimum amount of water for maximum activity as a dehydration catalyst.

the wash bottles and the Erlenmeyer flask at the end of the train 250 ml. in size, and the safety tube about 2 ft. long. Use rubber stoppers throughout the entire assembly and be sure that all connections are tight.

Fit the generator flask, by means of a three-holed rubber stopper, with a thermometer, delivery tube, and dropping funnel. Be certain that the end of the thermometer bulb extends to within 2 inches of the bottom of the flask. If necessary, extend the dropping funnel by attaching a glass tube, preferably one that is constricted slightly at the tip, to it by means of a rubber sleeve. Be certain that the two sections of glass from the dropping funnel and extension tube meet within the sleeve. Adjust the height of the dropping funnel so that the rubber sleeve is located in the neck of the generator flask when the rubber stopper is inserted.

Make smooth, strong bends in the glass tubing and fire polish the ends of each piece of glass by heating in the hot portion of a Bunsen flame. When inserting glass tubing into rubber stoppers, always use glycerol liberally as a lubricant and protect each hand by means of a towel. Note carefully how far each tube extends into the wash bottles, test tube, and Erlenmeyer flask.

Fill each wash bottle about one-third full and the safety bottle to a height of 2 cm. with 10 per cent sodium hydroxide solution. Extend the safety tube into the solution at least 1 cm. Add about 150 ml. of 10 per cent sodium hydroxide to the Erlenmeyer flask following the test tubes in the train. Mount the generator flask securely over a wire gauze on a ring stand with the neck of the flask carefully clamped to the stand.

After the entire apparatus has been assembled, remove the rubber stopper from the generator flask and cautiously charge the flask directly with 40 ml. of ethyl alcohol, 80 ml. of concentrated sulfuric acid, and 3 g. of diatomaceous earth or other finely divided siliceous earth (Note 1). Then replace the stopper, making sure that it fits tightly. From the bromine bottle in the hood, measure 13 ml. (40 g., 0.25 mole) of bromine and divide it approximately equally between two 8-inch test tubes. *Do not allow the bromine vapor to escape into the laboratory* (Note 2). Cover the bromine in each tube with 5 ml. of water, place the tubes in a large beaker containing water with a small amount of ice, and insert the rubber stoppers bearing the bent glass tubes as shown in Figure 19.

Now transfer the bromine tubes to the laboratory desk and connect the second tube as shown in Figure 19 with a 250-ml. Erlenmeyer flask which contains 10 per cent sodium hydroxide solution for the absorption of any escaping bromine vapors. The tube leading into the flask should be inserted through a cotton plug and should terminate about 1 cm. above the surface of the solution. In the bromine tubes, it is critical that the inlet tubes extend *below* the surface of the bromine itself.

Arrange the trough for the collection of 4 bottles of ethylene. Heat the generating flask strongly on the wire gauze until the evolution of gas begins. This occurs at about 160°, but a smooth evolution of gas is more important than the exact temperature, which will vary somewhat with the mesh of the siliceous earth. Avoid, however, heating above 200°.

When the air has been expelled from the apparatus, collect 4 bottles of ethylene by displacement of water for use in Section B. Store the ethylene by placing the filled bottles mouth down in the trough. When all the bottles are full, quickly disconnect the apparatus at A, set the trough and bottles aside, and connect the bromine tubes of either type shown into the train. Allow the ethylene to bubble through the bromine, with occasional shaking of the bromine tubes, until the bromine color is discharged. This operation will require about 40 minutes.

> [While it is in progress, you may make the short tests in Section B.]

During this period, be sure that a steady and continuous flow of ethylene is maintained and shake the bromine tubes occasionally. It may be necessary to replenish the generator flask by adding through the dropping funnel a cooled solution of ethyl alcohol—sulfuric acid (prepared by adding 20 ml. of concentrated sulfuric acid to 20 ml. of ethyl alcohol with stirring and cooling by means of an ice bath).

When the decolorization of the bromine is complete, disconnect the tubes containing the ethylene bromide from the rest of the train and allow the generator flask, still connected to the wash bottles, to cool. Then wash the cooled contents of the flask down the sink with liberal quantities of water.

Transfer the contents of the test tubes (ethylene bromide and water) to a small separatory funnel. Wash the ethylene bromide once with 50 ml. of water. To accomplish this, add the water to the funnel, stopper the funnel, invert carefully, and open the stopcock momentarily to relieve any pressure which may develop. Shake, gently at first, stopping to open the stopcock at frequent intervals. Finally shake vigorously, then mount the separatory funnel on a ring stand, and carefully tap off the ethylene bromide into a small Erlenmeyer flask, separating it cleanly from the water layer. Discard the water layer by pouring it out of the top of the funnel, thus keeping the aqueous layer from the stem of the funnel where it could contaminate the ethylene bromide. **120-150**

Repeat the washing process with 50 ml. of cold 10 per cent sodium hydroxide solution, and finally with a second 50-ml. portion of water, separating the layers carefully in each case. Drain off the ethylene bromide layer from the final washing into a small Erlenmeyer flask, and add 1-2 g. of granular anhydrous calcium chloride.

Stopper the flask and set it aside, except for occasional shaking, while you clear away the apparatus on the desk and fit a small distilling flask with a *dry* thermometer and a *dry* water-jacketed condenser for final distillation of the product. Use tightfitting rubber stoppers. Be certain that the top of the thermometer bulb extends just to the lower end of the side arm of the distilling flask and that the end of the side arm extends into the condenser at least a centimeter beyond the end of the rubber stopper.

When the ethylene bromide is dry, as indicated by absence of turbidity, decant it from the calcium chloride (Note 3) into the distilling flask, and clamp the distilling flask to a ring stand over a wire gauze mounted on a ring.

Distill the ethylene bromide slowly, with a slow stream of water passing through the condenser, collecting the portion boiling at 127°-135° separately in a tared flask. If any lower boiling material is obtained, you may dry it over fresh calcium chloride and redistill it, adding the fraction boiling at 127°-135° to the main portion, in order to improve your yield. Weigh your ethylene bromide and calculate the percentage yield. Record your results and submit your product in a properly labeled bottle to your instructor.

100-120 B. Properties of Ethylene

a. Flammability. Test the flammability of ethylene by bringing a flame to the mouth of one of the bottles. You can keep the ethylene burning steadily at the mouth of the bottle by pouring water into the bottle while the gas is burning. Note whether or not the flame is luminous. Record all observations and results.

b. Explosive Properties. Remove one of the bottles of ethylene from the trough, hold its mouth down for 15 seconds, and then bring a flame to the mouth. Note the results.

c. Baeyer's Test for Unsaturation. To the third bottle of ethylene add 2 ml. of 0.3 per cent potassium permanganate solution and shake. Observe the results.

d. Reaction with Iodine. To the final bottle of ethylene, add 2 drops of alcoholic iodine solution and shake vigorously. Note the results.

150-170 C. Regeneration of Ethylene from Ethylene Bromide

Place 3 g. of granular zinc in a hard glass test tube fitted with a delivery tube for collection of a gas over water. Add a mixture of 3 ml. of ethylene bromide and 3 ml. of *n*-amyl alcohol. Heat the tube gently to start the reaction and, after the air has been driven from the apparatus, collect several small bottles of the gas. Devise and conduct tests designed to reveal the identity of the gas. Record the results.

NOTES

1. The acid-catalyzed dehydration of olefins is promoted by many finely divided insoluble siliceous materials, such as kieselguhr, fuller's earth, diatomaceous earth, and powdered pumice.

2. Procedures for safe handling of bromine vary somewhat among different laboratories. Ask your instructor for the procedure to be followed. If bromine should accidentally be spilled on the hands, wash at once with water and then with alcohol. Apply moistened sodium bicarbonate and glycerol to the area. Minor burns may not require further treatment, but report the accident to the instructor in any case.

3. If considerable ethylene bromide is occluded by the calcium chloride, shake the calcium chloride with a few ml. of chloroform, allow it to settle, and decant the chloroform solution into the distilling flask.

QUESTIONS

1. What could be used in place of sulfuric acid in the generating flask?

2. What is the purpose of the wash bottles?

3. What is the function of the safety tube?

4. What size distilling flask did you use for the distillation of the ethylene bromide? Why?

5. Did you observe any by-product in the preparation of ethylene? How do you account for its formation?

6. If you could not complete the entire experiment on the preparation of ethylene bromide in one period, at what stage would you interrupt it?

7. What effect would each of the following have on the observed yield of ethylene bromide?

(a) Allowing the bromine to become too warm.

(b) Use throughout the experiment of equipment which is much larger than necessary.

(c) The use, by mistake, of only 20 g. of bromine.

(d) Distillation of the ethyl bromide directly from the calcium chloride.

(e) Extremely rapid bubbling of the ethylene through the bromine.

(f) Loss of ethylene through a leak in the system.

8. Why is chloroform preferred to ether as a solvent for removing occluded product from a desiccant?

9. Explain exactly how the various steps in the purification and isolation of the ethylene bromide are designed to eliminate all possible contaminants.

10. Write balanced equations for the complete and the partial combustion of ethylene.

11. Compare ethylene with methane in the following respects: (a) nature of the flame when the gas is burned; (b) reaction with bromine; (c) reaction toward aqueous potassium permanganate. Write balanced equations for the reactions involved in (b) and (c).

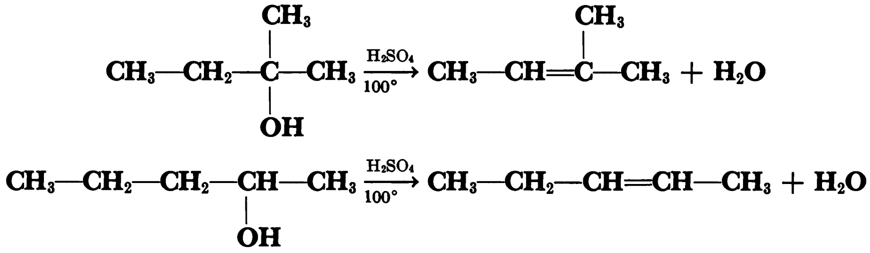
12. Write balanced equations to show exactly how the addition of halogens to alkenes differs from the substitution of halogens in alkanes.

13. Assume that you had two bottles, each containing a colorless gas, one methane and one ethene, from which the labels were lost. How could you determine which bottle contained methane and which contained ethene? Write balanced equations for all reactions involved.

14. (For Specially Interested Students) Calculate the percentage increase in volume which occurs in the quantitative conversion of bromine to ethylene bromide. If you used 100 g. of bromine in the synthesis, what would be the preferred size of the separatory funnel to be used in washing the product?

EXPERIMENT 13

The Amylenes: 2-Methyl-2-Butene and 2-Pentene



$$CH_3-CH_2-\underset{\underset{OH}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_3 \xrightarrow[100^\circ]{H_2SO_4} CH_3-CH=\overset{\overset{CH_3}{|}}{C}-CH_3 + H_2O$$

$$CH_3-CH_2-CH_2-\underset{\underset{OH}{|}}{CH}-CH_3 \xrightarrow[100^\circ]{H_2SO_4} CH_3-CH_2-CH=CH-CH_3 + H_2O$$

Introduction. Amylene is a generic term applied to the alkenes of formula C_5H_{10}. All of the amylenes are well known, readily available compounds. In this experiment, you will prepare two of the amylenes from common amyl alcohols, *t*-amyl alcohol (2-methyl-2-butanol) and *s*-amyl alcohol (2-pentanol).

Each of the two dehydration reactions theoretically could proceed in two ways to give two products, but the major product obtained in each case is that represented by the equation. This is in keeping with the general rule that in the acid-catalyzed dehydration of alcohols which can give rise to two isomeric olefins, the hydrogen atom will be removed from the adjacent (to the —OH bearing carbon) carbon atom which bears the fewer hydrogen atoms to give the more highly branched olefin. The greater ease of dehydration of tertiary vs. secondary alcohols is here illustrated by the fact that less concentrated sulfuric acid is required to dehydrate *t*-amyl alcohol than *s*-amyl alcohol.

The amylenes add bromine vigorously and with the evolution of considerable heat. You should consider this fact in planning an experimental procedure for the addition of bromine to either 2-methyl-2-butene or 2-pentene. The acid-catalyzed addition of water to each of these olefins follows the direction predicted for normal addition of unsymmetrical reagents to unsymmetrical alkenes.

0-100 A. 2-Methyl-2-butene

Prepare a 2:1 sulfuric acid mixture by adding cautiously, in small portions, 27 ml. of concentrated sulfuric acid to 54 ml. of cold water in a 200-ml. round-bottomed flask. Cool the flask by swirling it gently in an ice bath or a stream of cold water between each addition. Then add 54 ml. (44 g., 0.50 mole) of *t*-amyl alcohol with cooling and shaking. Mount the flask over a steam bath (Note 1) on a ring stand and attach it to an efficient condenser arranged for distillation. Fit the condenser with a curved adapter which leads through a cotton plug into a 250-ml. Erlenmeyer receiving flask packed in ice (Note 2).

Heat the flask strongly with steam until alkene is no longer obtained in the distillate (Note 3).

[Prepare reagents and apparatus for C and D.]

Transfer the cooled product to a small separatory funnel and add 15 ml. of cold 10 per cent sodium hydroxide solution. Invert the funnel, open the stopcock to release the pressure, then close the stopcock and shake vigorously, stopping occasionally to release the pressure. Tap off and discard the lower aqueous layer and pour the alkene through the mouth of the separatory funnel into a small, *dry*, Erlenmeyer flask. Add about 2 g. of anhydrous calcium chloride and allow the flask to stand with cooling and occasional shaking. When the hydrocarbon is dry, as indicated by absence of turbidity, transfer it into a small distilling flask fitted with a thermometer, and a *dry* condenser attached as before to a curved adapter. Distill over a water bath collecting the fraction boiling at 37°-43° in a small tared collecting bottle packed in ice. Pure 2-methyl-2-butene is reported to boil at 38.5° at 760 mm. Record the data and calculate the percentage yield.

NOTES

1. For efficient heating it is advisable to wrap a towel around the flask and extend the towel over the top of the steam bath. Escaping steam is then used effectively to heat the flask.
2. The amylenes are all low boiling and highly flammable, so efficient condensation is critical.
3. This requires about 25 minutes if heating is efficient.

B. (Alternative Procedure) 2-Pentene 0-100

Follow the procedure described in A exactly except to substitute 54 ml. of *s*-amyl alcohol for the *t*-amyl alcohol and to use 1:1 sulfuric acid prepared by adding 54 ml. of water to 54 ml. of concentrated sulfuric acid. Collect the fraction boiling at 34°-41°. Pure 2-butene boils at 36.5° at 760 mm.

C. Hydration of the Amylene 100-120

Add 2 ml. of concentrated sulfuric acid to 2 ml. of water in a test tube and cool in ice. Then add 4 ml. of your amylene and shake vigorously with cooling. If a layer of the alcohol does not appear, saturate the solution with sodium chloride to salt out the alcohol. Observe the properties of the alcohol and compare it with the alcohol from which you prepared the amylene.

120-170 D. Amylene Bromide

Now weigh the remaining amylene and from it prepare the corresponding bromide by the addition of bromine. Devise your own experimental procedure in detail, keeping in mind the obnoxious odor and hazards of bromine and the fact that the reaction is a vigorous one. Obtain approval of your procedure from your instructor before you begin. Report the yield and physical constants of the dibromide exactly as you observe them.

QUESTIONS

1. Write structural formulas for all of the possible amylenes. Indicate for each the alcohol from which that isomer could best be prepared.
2. Write equations for the hydration of 2-methyl-2-butene and 2-pentene. What is the function of the sulfuric acid?
3. List the various isomeric amyl alcohols, as completely as you can, in order of decreasing ease of dehydration.
4. The cycle alkene → dibromide → alkene is frequently carried out in research for very good reasons. Can you suggest two?
5. List your reasons for carrying out the addition of bromine to your amylene and isolating the dibromide by the exact procedure which you used.

EXPERIMENT 14

Preparation and Properties of Acetylene

$$CaC_2 + 2H_2O \rightarrow HC{\equiv}CH + Ca(OH)_2$$

Introduction. Acetylene is the first and only commercially important member of the alkyne series of hydrocarbons. In general, alkynes may be prepared conveniently by any of three general methods:

1. Alkylation of acetylene or of a monoalkylated acetylene by reaction of an alkylating agent (alkyl halide or sulfate) with the sodium salt.

$$RX + NaC{\equiv}CH \rightarrow RC{\equiv}CH$$

$$R'X + RC{\equiv}CNa \rightarrow RC{\equiv}CR'$$

2. Elimination of 2 moles of hydrogen halide from a suitable dihalide with potassium hydroxide or sodamide.

$$\begin{array}{l} \text{RCHX—CHXR}' \\ \text{or}\ \ \text{RCH}_2\text{—CX}_2\text{R}' \\ \text{or}\ \ \text{RCX}_2\text{—CH}_2\text{R}' \end{array} \begin{array}{l} + 2KOH \rightarrow \\ \qquad R{—}C{\equiv}C{—}R' + 2KBr + 2H_2O \end{array}$$

3. Elimination of 4 halogen atoms, two from each of two adjacent carbon atoms, from a tetrahalide, by means of zinc.

$$RCX_2{—}CX_2R' + Zn \xrightarrow{\text{(in alcohol)}} RC{\equiv}CR' + 2ZnX_2$$

These methods are applicable to the preparation of acetylene, but, as one of the most important intermediates in the chemical industry, acetylene is produced much more cheaply by the hydrolysis of calcium carbide.[1] The hydrolysis may be viewed simply as a protolysis reaction in which a weak diprotic acid (acetylene) is formed from its conjugate base (acetylide ion) which accepts 2 protons from a stronger acid (water). In this sense, calcium carbide is a salt of the very weak acid acetylene and should properly be called calcium acetylide.

Acetylene is most conveniently prepared in the laboratory by the calcium carbide method. The product is contaminated with traces of hydrides of phosphorus, arsenic, and sulfur, which give it the characteristic odor; pure acetylene is practically odorless.

In this experiment, you will prepare acetylene by the carefully controlled hydrolysis of calcium carbide and study some of its properties. Today's assignment completes our laboratory study of alkanes, alkenes, and alkynes and therefore marks an especially appropriate time for a review drill on aliphatic hydrocarbons.

0-50 Preparation of Acetylene

Fit a dry 100-ml. distilling flask with a cork carrying a small dropping funnel and clamp the flask securely on a ring stand. Attach to the side arm a delivery tube arranged for collection of the acetylene over water. Add 10 g. of calcium carbide in the form of small lumps to the flask and 20 ml. of water to the dropping funnel. Insert the cork tightly into the distilling flask. Check to be certain that there is no flame within 8 ft. of your acetylene generator (Note 1). Then allow the water to flow slowly, drop by drop, onto the calcium carbide.

As soon as a sample of the gas collected over water in a test tube (Note 2) burns quietly when ignited, collect five full 100-ml. wide-mouth bottles of acetylene. In a sixth bottle displace approximately 1/20 its volume of water. Then bubble acetylene into 5 ml. of benzene in a test tube for 2 minutes. Stopper the solution for later study. Finally, allow a slow stream of acetylene to bubble into 5 ml. of concentrated sulfuric acid in a small test tube. Note whether or not it dissolves.

Properties of Acetylene 50-80

a. Flammability. Ignite a bottle of acetylene, under a hood if possible; in order to keep the gas burning smoothly, pour a stream of water into the bottle while the gas burns. Note the character of the flame. Record all of your observations.

b. Reaction with Bromine. In the hood, add 2 drops of bromine to a second bottle of acetylene and shake vigorously for a minute. Note the result. Examine the contents of the bottle for evidence of chemical change. Compare the behavior of acetylene with that of methane and ethylene.

c. Baeyer Test for Unsaturation. Test the action of potassium permanganate on acetylene by adding a few ml. of a 0.3 per cent solution to the third bottle of acetylene. Observe the result. Test the material in the bottle with litmus paper.

d. Acidity of Acetylene. To the benzene solution of acetylene, add a small piece of sodium about *half* the *size* of a *pea.* Observe the results. Transfer the material to a watch glass and allow the benzene to evaporate. Examine the residue. Add a few drops of water to it and observe the results. Test the solution with litmus paper.

e. Reaction with Ammoniacal Cuprous Chloride. Add 2 ml. of ammoniacal cuprous chloride solution to a fourth bottle of acetylene. Note the formation of red cuprous acetylide. Remove the precipitate rapidly by filtration and heat it *cautiously* (Note 3) on a spatula.

f. Reaction with Ammoniacal Silver Nitrate. Add 3 ml. of ammoniacal silver nitrate solution to a fourth bottle of acetylene. Note the formation of a white precipitate of silver acetylide. Remove the precipitate rapidly by filtration and heat it cautiously (Note 3) on a spatula.

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[1] Calcium carbide itself is manufactured by the reaction of calcium oxide with coke at temperatures of 2000° in an electric furnace.

g. Explosion with Air. Remove the sixth, partially filled bottle from the collecting trough, allowing air to displace the water. Then ignite the mixture. Note the character of the reaction and of the products.

NOTES

1. Acetylene–air mixtures are explosive over a wide range—from 2.5 to 80 per cent of acetylene in air. For methane the explosive range is from 5.3 to 14 per cent methane and for ethylene 3.0 to 34 per cent.

2. Do not allow the acetylene to escape freely into the air. Acetylene is a poisonous gas. If feasible, use a hood. When you have finished the experiment, take the generating flask to the hood and add water until the excess carbide is completely decomposed. Add dilute hydrochloric acid to dissolve the bulk of the residue and wash the material down the sink *in the hood* with a liberal supply of water.

3. Cuprous and silver acetylide are extremely explosive when dry.

QUESTIONS

1. Write balanced equations for the complete combustion of acetylene to carbon dioxide and water and for incomplete combustion in the presence of insufficient oxygen. Compare the character of the flame of burning acetylene with that of methane and of ethane. What causes a flame to be luminous? Does this test suggest an important use of acetylene in former days?

2. Compare the balanced equations for the complete combustion of ethane, ethylene, and acetylene. Can you suggest any reason, in addition to its high energy content, why acetylene is the best of the three gases for use in welding?

3. Which is more explosive, a mixture of ethylene and air or a mixture of acetylene and air? Why?

4. Write balanced equations for the possible reactions of acetylene with bromine. Predict some of the physical properties of acetylene tertabromide (1,1,2,2-tetrabromoethane). Check your predictions in a handbook.

5. Write balanced equations for possible reactions which occur when acetylene is treated with aqueous permanganate. How do you account for the effect of the reaction mixture on litmus?

6. Write a balanced equation for the reaction of acetylene with sodium. Name the product.

To what general class of compounds does it belong? Is the anion a weaker or stronger base than hydroxide ion? On what evidence do you base your answer? Is acetylene a stronger or weaker acid than water? Explain.

Would 1-hexyne give a positive test with sodium? 2-hexyne?

7. Write balanced equations for the reaction of acetylene with ammoniacal cuprous chloride and with ammoniacal silver nitrate.

Of the two general types of acetylene derivatives, $\mathrm{R{-}C{\equiv}C{-}H}$ and $\mathrm{R{-}C{\equiv}C{-}R'}$, which would be expected to give a positive test with these reagents? What structural feature is required for reaction?

8. In what sense is acetylene a protonic acid? Can you explain why its reactions with ammoniacal copper chloride and silver nitrate are considered as reactions of an acid?

9. What volume of acetylene measured at standard conditions could be obtained from 10 g. of pure calcium carbide? **80-160**

10. Describe by means of balanced equations how ethylene and acetylene differ from methane in their behavior toward (a) concentrated sulfuric acid; (b) bromine; (c) aqueous permanganate. What structural feature of ethylene and acetylene is responsible for their reactivity?

11. Describe by means of balanced equations how acetylene differs from methane and ethylene in its behavior toward (a) metallic sodium; (b) ammoniacal cuprous chloride; (c) ammoniacal silver nitrate. What structural feature of acetylene is responsible for its reactivity toward these reagents?

12. Assume that you had in the laboratory stock bottles of heptane, 1-heptene, and 1-heptyne, all of which had lost their labels. What series of reactions would you use to ascertain which of the three possible compounds each bottle contained? If you are ahead of schedule in your laboratory work, perhaps your instructor would like to assign you this, or a similar project, as a test of your reasoning and experimental ability.

How would the problem be complicated if there were four bottles, with 2-heptyne as an added possibility? Could you still solve the problem?

13. Now assume that you had a single bottle containing a mixture of equal amounts of each of the three compounds heptane, 1-heptene, and 1-hexyne. How would you proceed to separate the mixture into pure individual components, isolating each in its original form?

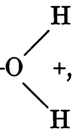
How would the separation be complicated if 2-heptyne were also present in the mixture? How could this difficulty be solved?

EXPERIMENT 15

Chemistry of the Alcohols

Introduction. Like water, which may be regarded as the first member of the alcohol series, alcohols are in a general sense both acids and bases. This dual character is revealed by the tendency of alcohol molecules to associate through hydrogen bonding; it is this tendency which accounts for the fact that alcohols in general boil at considerably higher temperatures than hydrocarbons of the same molecular weight.

With water molecules, alcohol molecules co-associate through hydrogen bonding, and, as a result, the lower molecular weight alcohols are completely miscible with water. As acids, the alcohols react with active metals such as sodium with evolution of hydrogen. The relative rates of reaction of alcohols in such reactions, in which only the hydrogen of the hydroxyl group is removed leaving behind both electrons of the pair through which it was originally bonded to the oxygen, are in the order primary > secondary > tertiary.

As bases, the alcohols accept a proton from strong mineral acids to form alkyl oxonium ions,  $\mathrm{R{-}O}\begin{smallmatrix}\diagup \mathrm{H}\\ \diagdown \mathrm{H}\end{smallmatrix}+$, comparable to the hydronium ion formed from water. Depending upon the conditions, especially the temperature, the protolysis may be followed by any of a number of other reactions: (1) complete dehydration to an alkene, (2) partial dehydration to an ether, or (3) displacement of the water molecule from the alkyl oxonium ion by an anion to form an alkyl halide, an alkyl nitrate, an alkyl hydrogen sulfate, or similar product. For all of these reactions, in which the hydroxyl group of the alcohol is ultimately removed, taking with it both electrons of the pair through which it was originally bonded to carbon, the relative rate of reactions are in the order tertiary > secondary > primary.

Primary and secondary alcohols are also moderately active reducing agents and are oxidized by many of the common chemical oxidizing agents. The structure of tertiary alcohols makes it impossible for them to undergo oxidation except under conditions sufficiently severe (strong oxidizing agents and high temperatures) to bring about oxidative cleavage of a carbon-carbon bond. In strong acid solution, a tertiary alcohol may sometimes give a positive test with oxidizing agents because of the reducing action of the alkene formed by dehydration of the tertiary alcohol.

In general, the rate of oxidation of alcohols varies, not only with the nature and concentration both of the alcohol and of the oxidizing agent, but also with the temperature and the acidity or alkalinity of the solutions. Potassium permanganate is a favorite oxidizing agent for test purposes, because the changes, especially in color, that accompany its reduction are so easily observed. It is effective in acid, alkaline, and neutral solutions, but its strength as an oxidizing agent can be controlled over broad limits by regulation of the pH.

Solubility Tests 0-35

Add 10 ml. of 95 per cent ethyl alcohol to 10 ml. of water in a test tube. Then saturate the solution with potassium carbonate. Observe the results. Determine approximately the weights of *n*-butyl alcohol, *s*-butyl alcohol, and *t*-butyl alcohol which can be dissolved in 5 ml. of water. Record all of your observations and results.

Acid Properties of Alcohols 35-60

Add a small piece of sodium about the size of a pea to 5 ml. of absolute ethyl alcohol (Note 1) in a small test tube. When the reaction is over, add an equal volume of absolute ether and observe the results. Now transfer the mixture to a watch glass and allow the ether and excess ethyl alcohol to evaporate. Note the character of the residue. Add to it about 3 ml. of water. Test the resulting solution with litmus and note its odor.

To each of three 8-inch test tubes, add 5 ml. of dry *n*-butyl, *s*-butyl, and *t*-butyl alcohol, respectively. To each add a small piece of sodium about the size of a pea, and compare the rates of reaction. Warm if necessary to complete the reaction.

Comparative Rates of Reaction with Hydrochloric Acid 60-100

Place 3 ml. of *n*-butyl, *s*-butyl, and *t*-butyl alcohol in each of three 8-inch test tubes, respectively. Add to each 10 ml. of concentrated hydrochloric acid. Watch carefully for evidence of reaction.

[Proceed to next experiment.]

Select those tubes in which the solutions are still clear and homogeneous after 10 minutes of standing at room temperature and place them in a beaker of boiling water for 15 minutes, and observe any changes which occur.

Oxidation of Alcohols

a. With Potassium Permanganate at Different pH's. 75-85
Prepare a solution for testing by adding 5 ml. of methyl alcohol to 45 ml. of water. Pour 5-ml. portions into each of three test tubes. Make one portion alkaline with 1 drop of 10 per cent sodium hydroxide solution, acidify the second with 1 drop of a 10 per cent sulfuric acid solution, and leave the third neutral. Now add to each solution 2 drops of a 0.3 per cent solution of potassium permanganate. Allow the mixtures to stand for 2 min-

utes. Then warm, if necessary, to effect reaction. Observe the order in which reduction of the permanganate occurs.

85-100 *b. Comparison of a Primary, Secondary, and Tertiary Alcohol.* Prepare the oxidizing solution by dissolving 5 g. of sodium dichromate in 50 ml. of water and adding 5 ml. of concentrated sulfuric acid. Pour 10 ml. of this solution into an 8-inch test tube and add 2 ml. of *n*-butyl alcohol. Shake the tube and note any rise in temperature or change in color. Repeat, using 2 ml. of *s*-butyl alcohol and finally with 2 ml. of *t*-butyl alcohol.

100-170 Tests for Water in Alcohol

a. With Anhydrous Copper Sulfate. Add about 0.5 g. of anhydrous copper sulfate (Note 2) to 5 ml. of 95 per cent alcohol in a dry test tube and shake vigorously. Repeat with 5 ml. of absolute alcohol.

b. With Calcium Carbide. Heat a piece of calcium carbide half the size of a pea gently in a Bunsen flame to drive off any occluded moisture. Immediately introduce the calcium carbide into about 5 ml. of absolute alcohol in a test tube. Repeat, using 5 ml. of 95 per cent alcohol. Note any differences.

[Proceed to c.]

If no difference is observed after 10 minutes, stopper the test tubes with cork stoppers and observe again after an hour.

c. With Paraffin Oil. Add one drop of paraffin (mineral oil) to 5-ml. samples of absolute alcohol and 95 per cent alcohol, respectively. Note the difference. Test similarly the relative solubilities of ammonium chloride, anhydrous sodium sulfate, acetanilide, naphthalene, and sucrose in absolute and in 95 per cent alcohol.

130-160 Distinguishing Tests for Ethyl and Methyl Alcohols (Note 3)

Acetate Test. Add 1 ml. of concentrated sulfuric acid (Note 4) to a mixture of 1 ml. of absolute ethyl alcohol and 1 ml. of glacial acetic acid in a test tube, and warm gently (*do not boil*). Cool below 20° and add to 5 ml. of a cold brine solution. Note the characteristic odor of the ester ethyl acetate.

Repeat with pure methyl alcohol, and note the odor of methyl acetate.

For interest, repeat this test with pure *n*-amyl alcohol.

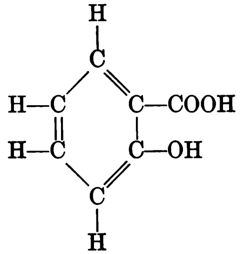
Salicylate Test. Add 1 ml. of concentrated sulfuric acid to a mixture of 1 ml. of pure methyl alcohol and about 0.25 g. of salicylic acid (Note 5). Warm gently for a few minutes, then cool, and pour into 10 ml. of cold water contained in a small beaker. Note the odor of methyl salicylate.

[Repeat with absolute ethyl alcohol.]

"Solid Alcohol." Mix 45 ml. of 96 per cent alcohol with 5 ml. of a saturated aqueous solution of calcium acetate by pouring the two solutions simultaneously into a small beaker. Allow the mixture to stand until it gels. Then inspect it. Place a small amount of the material in an iron dish and burn it. This is a form of **solid alcohol** or **canned heat.**

NOTES

1. If absolute ethyl alcohol is not available it may be prepared by refluxing 95 per cent alcohol (2.5 parts) with lumps of fresh quicklime (1 part) for at least 1 hour and then distilling the alcohol directly from the calcium oxide–calcium hydroxide mixture.
2. If it is not available, anhydrous copper sulfate can be prepared by heating the blue hydrate very gently in an evaporating dish until all of the water of crystallization is removed.
3. The iodoform test (p. 78) should be noted as an additional test to distinguish ethyl alcohol, which gives a positive iodoform test, from methyl alcohol, which does not.
4. The sulfuric acid acts as a catalyst for the esterification reaction and also, in the concentration used here, increases the yield of ester by reducing the effective concentration of the product water available for participation in the reverse reaction.
5. Salicylic acid is an aromatic carboxylic acid which has the formula:



($C_6H_4(OH)$—COOH)

QUESTIONS

1. Write a formula to indicate the probable structure of co-associated ethyl alcohol–water molecules in a solution of ethyl alcohol in water. How does potassium carbonate function in decreasing the solubility? Can you suggest any reason why a divalent anion should be particularly effective?
2. Of the three isomeric butyl alcohols tested—primary, secondary, tertiary—which is most soluble in water? Which is the least soluble? Does this order generally hold for a series of isomeric primary, secondary, and tertiary alcohols? Can you offer an explanation of this fact?
3. Write a balanced equation for the reaction of sodium with ethyl alcohol. Does this reaction occur more or less readily than that of sodium with water? What type of compound is sodium ethoxide?

Write a balanced equation for the reaction that occurs when sodium ethoxide is placed in water.

What do these reactions indicate concerning the relative strengths of water and ethyl alcohol as acids and of hydroxide and ethoxide ions as bases? Would it be possible for ethoxide ions to exist in appreciable concentration in water (in the form of a soluble salt)? Explain.

4. Compare the rate of reaction toward sodium of primary, secondary, and tertiary butyl alcohols. Can you account for the observed order of reactivity on the basis of structure? Which of the three alcohols is most acidic?

5. Write balanced equations for the reaction of tertiary and of secondary butyl alcohol with hydrochloric acid. How do you account for the fact that the butyl alcohols are much more soluble in water than the corresponding chlorides? Can you explain the observed order of reactivity of the alcohols toward hydrochloric acid on the basis of structure?

6. At what general pH range is potassium permanganate the strongest oxidizing agent toward methyl alcohol? Does this agree with what you know about the relative oxidation potentials of potassium permanganate in acid and basic solutions? Write balanced equations for the reactions involved.

7. Compare the relative ease of oxidation of primary, secondary, and tertiary butyl alcohols toward acid dichromate. Could this order be predicted in part?

8. In general, is absolute or 95 per cent ethyl alcohol a better solvent for ionic substances? For covalent nonpolar substances?

9. Write balanced equations for the esterification of acetic acid and of salicylic acid with methyl and ethyl alcohols.

Could *t*-butyl esters be made satisfactorily by this method?

Identify the odors of the esters you prepared which were familiar to you from previous experience.

10. Judging from its behavior with calcium acetate, would you predict that ethyl alcohol could be dried satisfactorily with calcium chloride as the desiccant? You might be interested in trying it.

EXPERIMENT 16

I. Ethyl Iodide

(1) $$2P + 3I_2 \rightarrow 2PI_3$$

(2) $$3C_2H_5OH + PI_3 \rightarrow 3C_2H_5I + H_3PO_3$$

II. Tertiary Butyl Chloride

$$(CH_3)_3COH + HCl \rightarrow (CH_3)_3CCl + H_2O$$

Introduction. Conversion of an alcohol to the corresponding alkyl halide by means of a phosphorus trihalide or a hydrohalic acid constitutes a convenient laboratory synthesis of alkyl halides.

Primary, secondary, and tertiary alcohols all react readily with phosphorus halides to yield the corresponding alkyl halides. For the synthesis of alkyl chlorides, phosphorus trichloride is customarily used directly, but for bromides and iodides, it is convenient to generate the phosphorus tribromide or triodide *in situ,* by treatment of phosphorus with bromine or iodine.

All three classes of alcohols react with hydrohalic acids to form alkyl halides, but, as you have already observed in Experiment 15, at markedly different rates. Tertiary alcohols react rapidly at room temperature, secondary alcohols more slowly, and primary alcohols require elevated temperatures. This difference in reaction rate is the basis for the Lucas[1] test for primary, secondary and tertiary alcohols, in which the alcohol to be tested is treated with concentrated hydrochloric acid (usually in the presence of the catalyst zinc chloride). Tertiary alcohols form an upper layer of the insoluble halide almost instantaneously at room temperature, secondary alcohols within 5-10 minutes, but primary alcohols react only at higher temperatures. This pronounced difference in reactivity is illustrated by a comparison of the severity of reaction conditions required to synthesize tertiary butyl chloride in this experiment and ethyl bromide in the next experiment.

For the hydrohalic acids, the rate of the reaction follows the order $HI > HBr > HCl > HF$. Thus, the strongest acid, hydriodic acid, reacts with a given alcohol to produce the corresponding alkyl halide most readily, and the weakest acid, hydrogen fluoride, least rapidly.

In general, the rate of reactivity of any group of corresponding halides follows the order $RI > RBr > RCl$. Thus, ethyl iodide is more reactive toward most reagents than is ethyl bromide, with ethyl chloride the least reactive of all three.

To make efficient use of your time, first assemble the apparatus for both Parts I and II of this assignment. While you are refluxing the ethyl iodide reaction mixture in Part I, proceed with the synthesis of tertiary butyl chloride in Part II.

I. Ethyl Iodide 0-150

Place 3.5 g. (0.11 mole) of red phosphorus (Note 1) and 25 ml. (0.43 mole) of ethanol (preferably absolute) in a 200-ml. flask and fit the flask with a water-cooled reflux condenser as shown in Figure 20a. Detach the flask from the condenser and gradually add 25 g. (0.1 mole) of iodine in portions of 2-3 g. each. After each addition of iodine, shake the flask and reattach it to the reflux condenser if necessary to prevent loss of alcohol by evaporation. If the reaction becomes too rapid, cool the flask in cold water.

After all the iodine has been added and the mixture no longer heats spontaneously, attach the flask to the reflux condenser and reflux the mixture for 30 minutes on a water bath to complete the reaction.

[Proceed to Part II.]

Remove the flask and cool it in cold water. By means of a bent glass tube connect the flask and condenser for distillation (Figure 20b) and distill to dryness. Transfer the crude iodide to a small separatory funnel and add enough 3 per cent sodium hydroxide solution so that all of the free iodine is removed by shaking, as evidenced by the discharge of the iodine color.

Separate the bottom ethyl iodide layer from the alkaline solution and wash it with 25 ml. of water by shaking a mixture of the two in the separatory funnel. Separate the ethyl iodide layer as carefully as possible and dry it in a small flask over 8-12 granules of anhydrous calcium chloride. During this time wash the condenser, rinse it with a little acetone, and clamp it in a vertical position to dry.

Decant the ethyl iodide from the calcium chloride into a small distilling flask and redistill it. Carefully note and record the distillation range. Collect the pure product in a tared (previously weighed) bottle. Determine its weight and calculate the percentage yield. Save at least a few ml. of the ethyl iodide for tests in Experiment 17.

Other Alkyl Iodides. (For Specially Interested Students) As optional experiments, other alkyl iodides may be made by this general method simply by substi-

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[1] Named for Howard Lucas, emeritus professor of chemistry at the California Institute of Technology.

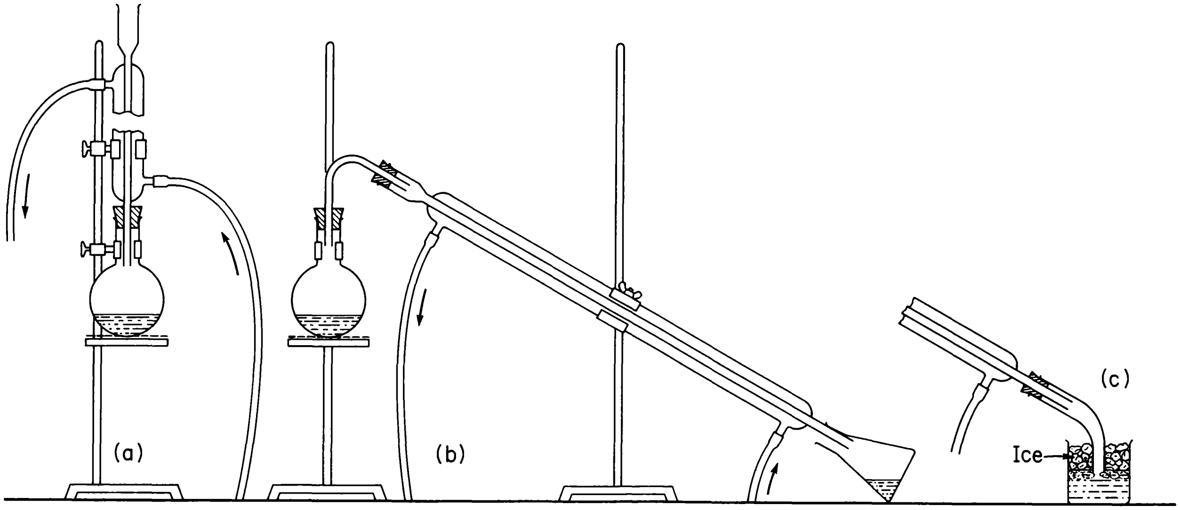


FIG. 20. Apparatus for the preparation of ethyl iodide. (a) For refluxing of reaction mixture. (b) For distillation of ethyl iodide. (c) For collection of product.

tuting 0.4 mole of the appropriate alcohol for the ethyl alcohol. The normal boiling points of some common alkyl iodides are as follows:

Methyl iodide	43°	*n*-Butyl iodide	130°
n-Propyl iodide	102°	*s*-Butyl iodide	119°
Isopropyl iodide	89°	*n*-Amyl iodide	155°

If methyl iodide is prepared, the receiving flask should be well cooled in ice during the distillation to prevent loss by evaporation. For storage, the methyl iodide should be sealed in a glass tube.

NOTE

1. For safety, red phosphorus is often kept in a moist condition while stored. In such a case, dry the phosphorus by pressing it between the two halves of a piece of folded filter paper before weighing out 3.5 g. for use in today's experiment.

Neither phosphorus nor iodine should be allowed to come into contact with the skin. Both stain the skin badly and may cause severe burns.

40-170 II. TERTIARY BUTYL CHLORIDE

Add to a 250-ml. separatory funnel, 37 g. (0.50 mole) of *t*-butyl alcohol and 125 ml. of C.p. (Note 1) concentrated hydrochloric acid. Gently swirl the unstoppered funnel for approximately 1 minute. Then stopper the funnel, invert it, and open the stopcock momentarily to release excess pressure. Shake the funnel for about 4 minutes, venting it at intervals. Then mount the funnel on a ring stand and allow it to stand until the two layers have separated and are completely clear.

Drain off the lower aqueous layer and discard it. Add 50 ml. of saturated sodium bicarbonate solution to the crude tertiary butyl chloride in the separatory funnel. Gently swirl the unstoppered funnel several times until vigorous effervescence ceases. Then stopper the funnel, invert carefully, and open the stopcock momentarily to relieve the pressure. Shake, gently at first, opening the stopcock at frequent intervals. Then shake vigorously, still opening the stopcock intermittently. Finally remove the lower bicarbonate layer, wash the *t*-butyl chloride remaining in the funnel with 40 ml. of water, and carefully draw off the lower water layer.

Transfer the crude *t*-butyl chloride into a small Erlenmeyer flask and dry over 8-12 granules of calcium chloride (Note 2) until it becomes clear. Decant the liquid into a small *dry* distilling flask and distill through a *dry* condenser. Collect the fraction boiling at 48°-52° as *t*-butyl chloride, refractionating any lower boiling distillate. Because of the low boiling point of *t*-butyl chloride, it is well to cool the receiving flask in ice water. Save at least a few ml. of the *t*-butyl chloride for tests in Experiment 17.

NOTES

1. For a good yield of *t*-butyl chloride, the concentration of hydrochloric acid is critical. The usual C.p. (36-38 per cent) acid is sufficiently concentrated to give good results, whereas the technical acid is not.

2. You can speed the drying process markedly by intermittent shaking of the flask.

QUESTIONS

1. How do you account on a theoretical basis for the relative rates of reactivity of primary, secondary, and tertiary alcohols toward hydrohalic acids? For the relative reactivity of HI, HBr, and HCl toward alcohols?

2. Which of the reactants constitutes the basis for your calculation of the theoretical yield of ethyl iodide? Why?

3. Calculate the percentage yield realized by a student who obtained 5.0 g. of ethyl iodide by reaction of 3.5 g. of red phosphorus and 25 g. of iodine with excess ethanol. What might you conclude about his experimental technique?

4. Would you expect *t*-butyl alcohol to be more or less expensive than isobutyl? Why?

5. Look up the melting point and the boiling point of *t*-butyl alcohol. What observation would you make about the size of the temperature range in which *t*-butyl alcohol exists as a liquid? Can you offer any explanation for this fact?

6. Explain how the various steps in the purification and isolation of ethyl iodide are designed to remove all possible contaminants.

EXPERIMENT 17

I. Ethyl Bromide

(1) $H_2SO_4 + NaBr \rightarrow HBr + NaHSO_4$

(2) $C_2H_5OH + HBr \rightarrow C_2H_5Br + H_2O$

II. Properties of Alkyl Halides

Introduction. Perhaps the most convenient way to prepare a primary alkyl bromide is to heat the corresponding alcohol with a mixture of sodium or potassium bromide and sulfuric acid. The bromide–sulfuric acid combination serves a double function: (1) it liberates the hydrogen bromide for the reaction, and (2) it forms with the alcohol a mixture which boils above the temperature required for fairly rapid reaction of hydrogen bromide with even a primary alcohol.

0-120

I. Preparation of Ethyl Bromide

Measure 60 ml. (47.3 g., 1.03 moles) of ethyl alcohol into a 1-liter round-bottomed flask. Add cautiously with stirring and cooling 50 ml. of concentrated sulfuric acid. With further shaking and cooling add 69.5 g. (0.500 mole) of crystalline sodium bromide ($NaBr \cdot 2H_2O$) which has been previously ground to a fine powder with a mortar and pestle. Mount the flask securely above a wire gauze on a ring stand. By means of a rubber stopper, curved tube, and second rubber stopper, fit the flask for distillation with a condenser carrying an adapter which dips *just below the surface* (Note 1) of some ice water in a 250-ml. beaker (Figure 20b, but with receiver c). Heat gently at first and then more strongly, finally distilling as rapidly as possible without undue frothing. You will be able to observe droplets of ethyl bromide forming in the water and settling to the bottom of the beaker. Continue heating until a water insoluble oil is no longer obtained. The reaction mixture will foam considerably throughout the distillation but settles to a quietly simmering liquid as the reaction comes to an end and no more volatile material is formed.

Pour the crude ethyl bromide and ice water into a separatory funnel, and tap off the lower ethyl bromide layer into a small Erlenmeyer flask. Immediately cool the flask in an ice bath. Slowly add 10 ml. of concentrated sulfuric acid and shake gently (Note 2). Transfer the mixture to a small separatory funnel and carefully add a single drop of water. Observe the behavior of the water in order to determine which is the sulfuric acid and which the ethyl bromide layer. Separate the layers (Note 3) and wash the ethyl bromide, first with 25 ml. of water, then with 15 ml. of dilute sodium hydroxide solution and again with 25 ml. of water.

Dry the ethyl bromide over about 10 granules of calcium chloride in a small Erlenmeyer flask with occasional shaking to hasten the process (Note 4). Decant the liquid into a small, dry distilling flask, add 2 or 3 boiling chips, fit the flask by means of rubber stoppers with a thermometer and *dry* condenser, and distill. Collect the distillate in a small Erlenmeyer flask packed in ice in a beaker. Collect separately the portion distilling at 37°-40° and redistill any higher or lower boiling fractions. Submit your product to your instructor at once for storage in a refrigerator.

Allow the residue in the reaction flask to cool until it can be handled conveniently, then dispose of it by pouring it directly into the sink and washing it down with a large excess of cold water.

NOTES

1. If the adapter dips too far below the surface of the water, it may be possible for water to rise into the condenser tube and into the reaction flask with disastrous results.
2. This treatment is designed to remove the ethyl ether which is formed as a by-product in the reaction. Usually there is sufficient ethyl ether to dilute the sulfuric acid to the extent that the sulfuric acid–ethyl ether mixture forms the less dense top layer. If the amount of ether is small, however, the ethyl bromide may appear as the top layer.
3. In order to distinguish the interface, you may find it necessary to view the funnel from several different angles.
4. Disappearance of turbidity indicates that the ethyl bromide is dry.

II. Properties of Alkyl Halides **120-170**

1. Shake a few drops of ethyl bromide with 2 ml. of distilled water and add 2 drops of silver nitrate solution. Repeat with a few drops of ethyl iodide, *t*-butyl chloride, and *n*-butyl chloride. Allow each mixture to stand for at least 15 minutes.

[Proceed to parts 2 and 3.]

Observe the rate at which a precipitate appears.

2. Expose a few drops of ethyl iodide to a bright light. Observe the results.
3. Dissolve approximately 1 g. of sodium iodide in 7 ml. of acetone. To 1 ml. of the solution in a small test tube, add 2 drops of ethyl bromide with vigorous shaking. Allow the mixture to stand for 3 minutes at room temperature. If no precipitate forms, place the test tube in a beaker of water at 50° for 6 minutes. Again observe whether or not a precipitate has formed. Repeat with isopropyl bromide and *t*-butyl chloride.

QUESTIONS

1. Would the method used in today's experiment be suitable for the synthesis of secondary and tertiary bromides? Explain.

2. Propose a function of the sulfuric acid in the preparation of ethyl bromide based on a preliminary reaction of the acid with ethyl alcohol. Write a series of equations to show all the steps involved in the over-all reaction for such a mechanism. Actually, the ethyl bromide may be formed in part through this route.

3. Write a balanced equation for the formation of ethyl ether as a by-product in this reaction. Assume that 8.0 g. of ethyl ether were formed. What would then be the maximum yield of ethyl bromide that could have been formed?

4. What is the relation of ethyl bromide to ethane? Write balanced equations for the synthesis of ethane from ethyl bromide and from ethyl chloride. Could isobutane be obtained from *t*-butyl chloride in good yield by this method?

5. Compare the rates of reaction of primary, secondary, and tertiary halides with silver nitrate solution. With sodium iodide in acetone. Can you propose any reason for the differences? Write general equations for the reactions involved.

EXPERIMENT 18

Ethyl Ether

$$2C_2H_5OH \xrightarrow[140\text{-}150°]{H_2SO_4} C_2H_5\text{—}O\text{—}C_2H_5 + H_2O$$

Introduction. Ethyl ether may be synthesized conveniently in good yield from ethyl alcohol by partial dehydration (removal of one molecule of water between two molecules of alcohol) in the presence of a nonvolatile acid such as sulfuric acid as catalyst. In practice, the ether is distilled directly from the reaction mixture and temperature control is critical. Some ethylene is inevitably formed as a by-product, and complete dehydration of the alcohol to an alkene is an unavoidable competitive reaction that limits the applicability of this method to alcohols which are not easily dehydrated to alkenes.

In general, low-boiling, diprimary ethers can be synthesized readily in good yield by catalytic partial dehydration of primary alcohols. If the ether formed boils above the temperature at which sulfuric acid effects complete dehydration of the alcohol to olefin, the ether may still be synthesized successfully if it is removed by distillation under reduced pressure.

In the preparation of disecondary ethers from secondary alcohols by this method, the yields are greatly reduced because of the ease with which sulfuric acid dehydrates secondary alcohols to alkenes. With tertiary alcohols, complete dehydration to alkenes is almost quantitative; hence ditertiary ethers cannot be prepared by this process.

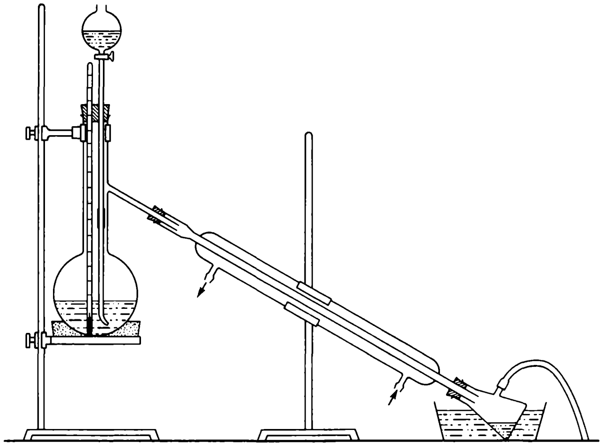


FIG. 21a. Assembly for the preparation of ethyl ether.

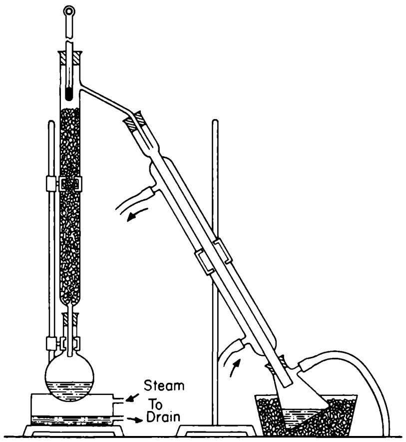


FIG. 21b. Assembly for fractional distillation of ethyl ether product mixture.

As a cheap, nonvolatile acid, sulfuric acid is a widely used catalyst for ether synthesis. It does, however, suffer from the fact that when hot and concentrated it is an oxidizing agent, and considerable oxidation of organic material occurs at the expense of the sulfuric acid. Commercially, ethyl ether is widely produced by partial dehydration of ethyl alcohol over the Lewis acid catalyst aluminum oxide at temperatures of 240°-260°.

Ethyl ether is highly volatile and extremely flammable; therefore it is dangerous if handled improperly. You will, however, encounter no difficulty if you perform this experiment carefully and thoughtfully.

Like most ethers, ethyl ether upon exposure to air reacts with oxygen to form peroxides of undetermined structure which explode violently when ether is distilled to dryness and the residue heated excessively. Ether which has been stored with access to air should be tested for peroxides before use. Peroxides should be removed by shaking with any one of a variety of reducing agents such as, for example, acidified ferrous sulfate solution. Iron wire is often added to containers of commercial ether to inhibit peroxide formation.

A. Preparation of Ether 0-110

Fit a 500-ml. distilling flask by means of a two-holed rubber stopper with a thermometer and dropping funnel as shown in Figure 21a (Note 1). Be certain that the end of the thermometer bulb extends to within one inch of the bottom of the flask.

If necessary, extend the dropping funnel by attaching a glass tube, preferably one that is constricted slightly at the tip, to it by means of a rubber sleeve. Be certain that the two sections of glass from the dropping funnel and tube meet within the sleeve. Adjust the height of the dropping funnel so that the rubber sleeve is located in the neck of the distilling flask when the rubber stopper is inserted. Attach a rubber stopper to the side arm of the distilling flask to connect the flask with a condenser provided with a suction flask receiver as shown in Figure 21a.

Remove the rubber stopper bearing the thermometer and dropping funnel and disengage the distilling flask from the condenser. Then pour 94 ml. (72 g., 1.50 moles) of 96 per cent ethyl alcohol into the flask. Add carefully, in 5-ml. portions, a total of 40 ml. of C.p. concentrated sulfuric acid, shaking the flask and cooling it in a stream of cold water after each addition. Then place the flask on a sand bath mounted on a ring stand, insert the stopper with the thermometer and dropping funnel, attach the condenser, and surround the receiver with a pan of crushed ice.

Attach to the side arm of the receiver a length of rubber tubing which extends almost to the floor. *Be certain that this receiver is not near your neighbor's burner and keep your own burner away from your neighbor's receiver.*

Heat the flask on the sand bath until the thermometer registers 140°-145°. Maintain this temperature as nearly as possible and admit slowly through the addition funnel 104 ml. (80 g., 1.65 moles) of 96 per cent ethyl alcohol. Heat for an additional 5 minutes after all of the alcohol has been added, in order to drive off the last of the ether. Extinguish the flame and arrange an apparatus for fractional distillation as shown in Figure 21b, using a 250-ml. round-bottomed flask. For the fractionation column, use a column or air condenser packed with copper sponge, as in Experiment 3.
110-170 Transfer the crude ether to the flask, add 2 or 3 boiling chips and also 2 g. of solid sodium hydroxide to convert the dissolved sulfur dioxide to sodium sulfite, and distill over a steam bath.

Collect fractions as follows: I, 34°-42° (ether); II, 42°-55°; III, 53°-75°; IV, 75°-82° (alcohol); V, 82°-95°; and VI, residue, largely water. Refractionate fractions II, III, and IV to separate them into the three principal components: (1) ether, 34°-42°; (2) alcohol, 75°-82°; and (3) water (residue). Measure the volume of the alcohol fraction, weigh it, and calculate its density.

From handbook tables, find the alcohol concentration in alcohol–water solutions of that density and calculate the weight of recovered alcohol. Calculate the percentage yield, both on the basis of the total alcohol used during the experiment and on the basis of that actually consumed during the reaction (not recovered).

NOTE

1. Insert the thermometer and dropping funnel into the rubber stopper with great care. Protect each hand by means of a towel. Lubricate the holes in the stopper liberally with glycerol. Hold the glass piece to be inserted near the stopper and push very gently while rotating the stopper. Never use brute force. Be sure that the end of the glass tube is fire polished.

B. Properties of Ether (Optional, for Specially Interested Students)

Ether as a Solvent and Solute—Salting Out Effect.

1. Test the solubility of each of the following by determining the volume or weight (Note 1) which can be dissolved in 3 ml. of ether: (1) kerosene, (2) benzene, (3) paraffin, (4) iodine, (5) carbon tetrachloride, (6) cottonseed oil, (7) alcohol, (8) water, (9) sodium chloride, and (10) ammonium chloride.

2. Determine what volume of ether can be dissolved in 10 ml. of water.

3. Add 5 ml. of cold sulfuric acid to 2 ml. of ice-cold ether in a small test tube. Stir vigorously, keeping the test tube in an ice bath. Finally pour the material onto about 15 g. of cracked ice. Note the results.

4. Introduce 5 ml. of ether into a graduated cylinder and add 5-ml. portions of water until the ether is dissolved, noting the total amount of water added. Then add 15 g. of sodium chloride and shake until the salt is dissolved. Note the results.

Test for Peroxides in Ether. Add 1 ml. of a 10 per cent solution of potassium iodide to 10 ml. of water in a small test tube and acidify the solution with a few drops of dilute sulfuric acid. Add 2 ml. of commercial ether from the side shelf and shake the tube for a moment. Add a few drops of starch paste indicator or a strip of starch-iodide paper and shake. Appearance of a blue color (Note 2) indicates the presence of peroxides in the ether.

NOTES

1. You can do this conveniently by starting with a known volume or weight of solute, adding it in small portions, and subtracting the amount which remains unused after the ether has been saturated.

2. The typical blue color is characteristic of the product formed when the so-called amylose fraction of starch absorbs iodine.

QUESTIONS

1. Write balanced equations for the various reactions which ethyl alcohol may undergo with sulfuric acid. What factors determine which reaction predominates under a given set of conditions?

If the desired product is ethyl ether, what is indicated about the reaction conditions used if (a) a large amount of ethylene is formed, or (b) a large amount of ethyl alcohol is recovered?

2. Write a balanced equation for a likely side reaction in the ether synthesis of which sulfur dioxide is one of the products. What does the production of much sulfur dioxide indicate about the yield that may be expected in the reaction?

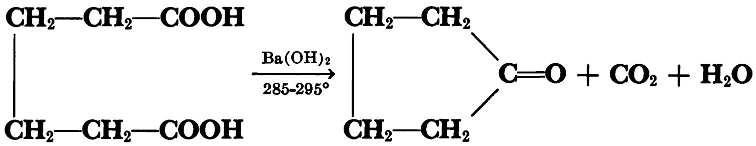
3. What properties of ethyl ether make it a good extrac-

tion solvent? Which of the properties are undesirable for this purpose?

4. What simple method for distinguishing between ethers and alkanes is suggested by the behavior of ethyl ether toward cold, concentrated sulfuric acid? Write a balanced equation for the reaction. What property of ethers is involved in this reaction? What is the effect of the addition of water?

EXPERIMENT 19

Preparation of Cyclopentanone



Introduction. As you observed in Experiment 9, pyrolysis of the carboxylate salt of a monovalent metal (RCOOM) effects complete decarboxylation (loss of 1 mole of CO_2 for each mole of acid) to the corresponding alkane, RH. Decarboxylation of the carboxylate salts $[(R{-}\overset{O}{\overset{\|}{C}}{-}O)_2M]$ of divalent metals (*such as calcium, barium, manganese, thorium, and cerium*), on the other hand, gives partial decarboxylation (loss of 1 mole of CO_2 from 2 moles of acid) to the corresponding ketone.

In fact, symmetrical ketones, $R{-}\overset{O}{\overset{\|}{C}}{-}R$, may be prepared conveniently by the pyrolysis of the calcium, barium, or manganese salt of the appropriate acid, $R{-}\overset{O}{\overset{\|}{C}}{-}OH$. In practice, the ketone formed is allowed to distill directly from the reaction mixture. For many years, calcium acetate, formed by addition of lime to pyroligneous acid, constituted the principal source of acetone.

It is possible to prepare an unsymmetrical ketone, $R{-}\overset{O}{\overset{\|}{C}}{-}R'$ by heating a mixture of the salts of two acids, $(R{-}\overset{O}{\overset{\|}{C}}{-}OH$ and $R'{-}\overset{O}{\overset{\|}{C}}{-}OH)$, or even an aldehyde, $R{-}\overset{O}{\overset{\|}{C}}{-}H$, if one of the acids is formic acid $\left(H{-}\overset{O}{\overset{\|}{C}}{-}OH\right)$. In such cases, however, the decarboxylation may occur in three ways to give a mixture of three different carbonyl compounds, and the yield of the desired unsymmetrical ketone or aldehyde is low. Thus, in the synthesis of the unsymmetrical ketone, $R{-}\overset{O}{\overset{\|}{C}}{-}R'$, the two symmetrical ketones, $R{-}\overset{O}{\overset{\|}{C}}{-}R$ and $R'{-}\overset{O}{\overset{\|}{C}}{-}R'$, are formed along with the desired product.

Calcium, barium, and manganese salts of the 6-carbon (adipic acid) and the 7-carbon (pimelic acid) dicarboxylic acids are partially decarboxylated to give good yields of the cyclic ketones, cyclopentanone and cyclohexanone, respectively. This illustrates the familiar rule of organic chemistry that 5- and 6-membered carbon rings are readily formed. The yields of larger ring ketones formed by the pyrolysis of higher molecular weight dicarboxylic acids fall off rapidly as the value of n in $HO{-}\overset{O}{\overset{\|}{C}}{-}(CH_2)_n{-}\overset{O}{\overset{\|}{C}}{-}OH$ increases.

In this experiment, you will prepare cyclopentanone from adipic acid. In recent years, adipic acid has achieved tremendous commercial importance as a starting material in the production of one type of nylon (Nylon 66).

Preparation of Cyclopentanone

Mix 28.3 g. (0.400 mole) of powdered adipic acid intimately with 2.0 g. of finely-powdered barium hydroxide in a mortar. Place the mixture in a 50-ml. distilling flask fitted with a thermometer reaching to within 4 mm. of the bottom of the flask. Connect the flask with a condenser fitted with a curved adapter leading through a cotton plug into a receiver (small Erlenmeyer flask) packed in ice. Heat the flask carefully with a small flame held close to the flask; if necessary, agitate the flask to shake the solid into the melted acid. **0-30**

When all of the solid has melted, heat more rapidly until the thermometer reaches 285°. **30-130**

[Assemble apparatus for Experiment 20 and answer drill questions.]

At this temperature, decarboxylation occurs and cyclopentanone, accompanied by water and a little adipic acid, distills slowly. Heat to maintain the temperature at 285°-295° as long as a liquid distills (Note 1) and until only a small amount of dry residue remains in the distilling flask.

Transfer the two-phase distillate to a small separatory funnel and slowly add just enough solid potassium carbonate to saturate the aqueous layer. Draw off the aqueous layer and add about 0.5 g. of anhydrous potassium carbonate to the cyclopentanone in the separatory funnel. Swirl the funnel occasionally, until the cyclo- **130-170** pentanone is clear. Then decant the ketone through the mouth of the separatory funnel (Note 2) into a small distilling flask, and distill with a small free flame over a wire gauze. Collect the cyclopentanone distilling at 129°-131°. Calculate the percentage yield and store the product in a labeled bottle for testing in the next experiment.

NOTES

1. You will find it possible during this period to assemble your apparatus in preparation for the synthesis of *n*-butyraldehyde to be carried out at the beginning of the next period, and to work on the questions at the end of this experiment.
2. Filter through a small funnel if necessary.

QUESTIONS

1. Assume that you were assigned the project of synthesizing ethyl *n*-propyl ketone by the pyrolysis of a mixture of barium salts. Write the formulas for the two carboxylic acids you would use. In what ratio by weight would you mix them?

What three ketones would you expect to find in the product mixture? On a statistical basis, in what mole ratio should they be formed? In what weight ratio?

2. What is the role of the barium hydroxide in the synthesis of cyclopentanone?
3. Propose another method for the preparation of cyclopentanone. Write the balanced equation for the reaction.
4. If 12 g. of water were formed in the partial decarboxylation of a certain weight of adipic acid, what would be the maximum weight of cyclopentanone that could be obtained?
5. What purposes does the potassium carbonate wash serve in this experiment?

EXPERIMENT 20

I. Preparation of *n*-Butyraldehyde (Butanal)

II. Some Reactions of Aldehydes and Ketones

$$3CH_3CH_2CH_2CH_2OH + Na_2Cr_2O_7 + 4H_2SO_4 \rightarrow 3CH_3CH_2CH_2CHO + Na_2SO_4 + Cr_2(SO_4)_3 + 7H_2O$$

Introduction. Aliphatic aldehydes, $R\text{—}\overset{H}{C}\text{=}O$, can be prepared from primary alcohols, $R\text{—}CH_2\text{—}OH$, and aliphatic ketones, $R\text{—}\overset{\overset{O}{\|}}{C}\text{—}R'$, from secondary alcohols, $R\text{—}CHOH\text{—}R'$, by carefully controlled oxidation. The preferred reagent is an aqueous solution of sodium or potassium dichromate and sulfuric acid. Because of the extreme ease with which aldehydes are oxidized further to carboxylic acids (an aldehyde is much more easily oxidized than the alcohol from which it is formed), an aldehyde must be removed from the reaction mixture as rapidly as it is produced. Fortunately, because of the greater volatility of aldehydes as compared with alcohols, this can be accomplished by distillation of the aldehyde.

It is an interesting generalization that aldehydes, whose molecules lack the hydrogen atom required for association through hydrogen bonding, always boil lower than the corresponding alcohols and acids, the molecules of both of which are extensively associated through hydrogen bonding.

Ketones are more resistant to oxidation than are aldehydes and primary and secondary alcohols. In their synthesis from secondary alcohols, they can be retained in the heated oxidizing medium with almost no loss due to further oxidation.

The oxidation of primary and secondary alcohols with dichromate is highly exothermic, and the reaction is usually controlled by gradual addition of either the alcohol or dichromate.

You will be interested in noting that the net effect of the reaction from the standpoint of the alcohol molecule is simply the removal of two hydrogen atoms. This suggests that a catalytic dehydrogenation would accomplish the same result and this is, indeed, the case. In fact, a number of aldehydes and ketones are produced commercially by dehydrogenation of the corresponding alcohols over copper-zinc catalysts at 200°-350°.

The markedly superior ease of oxidation of aldehydes constitutes the basis for a convenient means of distinguishing between aldehydes and ketones. A number of mild oxidizing reagents, which are reduced only by aldehydes and a few other easily oxidized types of organic compounds, and are unaffected by ketones and alcohols, have been developed. Among such oxidizing reagents, which are commonly used to test for aldehydes, are Tollens' reagent and Fehling's solution. Tollens' reagent is essentially a solution of $Ag(NH_3)_2OH$, and Fehling's solution, of $Cu(OH)_2$ in which the cupric ion is complexed with tartrate ion.

Schiff's reagent is a sensitive reagent for the detection of aldehydes. The test is based, not upon the reducing action of aldehydes, but upon a complex reaction to form a red-purple solution which aldehydes undergo with the almost colorless compound formed by addition of sulfurous acid to the pink dye fuchsin.

I. PREPARATION OF *n*-BUTYRALDEHYDE FROM *n*-BUTYL ALCOHOL

0-100 Fit a 1.5-liter, round-bottomed flask (Note 1) with a rubber stopper carrying a dropping funnel and a fractionating column leading to a condenser and receiving flask, as shown in Figure 22. Disconnect the reaction flask, introduce into it 260 ml. of water, 149 g. (0.50 mole) of sodium dichromate, and a few boiling chips. Add cautiously, with cooling under a water tap, 120 ml. of concentrated sulfuric acid. Mount the flask securely on a ring stand above a wire gauze, and set up the distillation assembly. Add 37 g. (0.50 mole) of *n*-butyl alcohol to the dropping funnel (stopcock closed!).

Heat the reaction mixture moderately so that a drop of *n*-butyl alcohol introduced from the dropping funnel reacts vigorously when it strikes the mixture. Continue to introduce the alcohol, at the rate of about a drop a second, regulating the flow so that distillation takes place regularly and the temperature, as registered by the thermometer, is 75°-90° (Note 2).

From time to time loosen the clamp somewhat and shake the flask gently to insure good mixing of the reactants. When all of the alcohol has been added, heat the mixture with a small flame as long as material distills below 90°.

The two-phase distillate consists of an upper layer of aldehyde with a considerable amount of alcohol and a small lower layer of water. Transfer it to a small separatory funnel and drain off the water. Add 4 g. of anhydrous magnesium sulfate directly to the aldehyde in the funnel and swirl the mixture occasionally. When the liquid is dry, as indicated by disappearance of turbidity, decant it through the mouth of the funnel, filtering if necessary, into a small round-bottomed flask. Distill through a short fractionating column, collecting the fraction boiling at 72°-76° in a tared bottle. Weigh the product and calculate the yield.

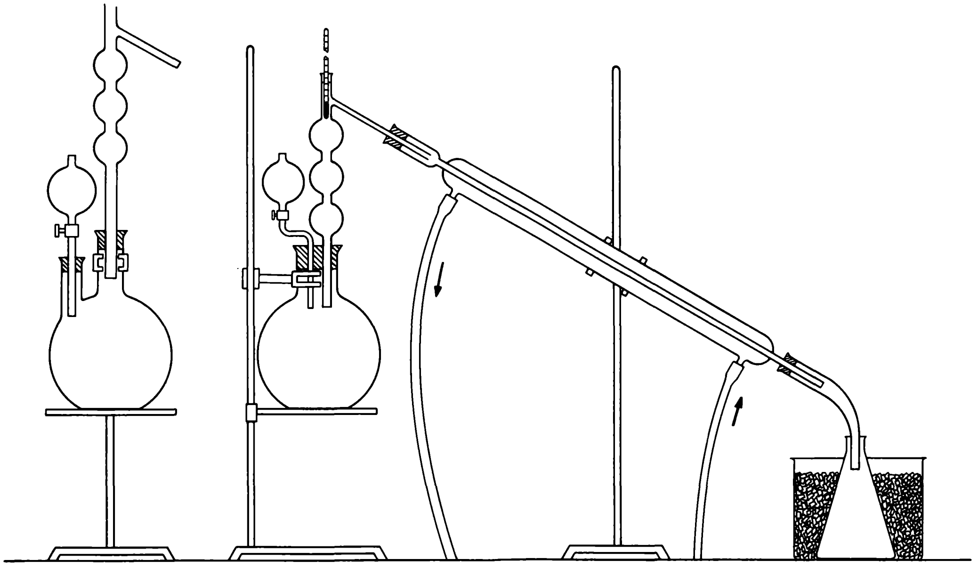


FIG. 22. Assembly for the synthesis of butyraldehyde.

II. SOME REACTIONS OF ALDEHYDES AND KETONES
(Test Tube Experiments)

100-125 A. Oxidation of Aldehydes and Ketones

(*1*) *With Permanganate.* To a few drops of a dilute (10 per cent) (Note 3) aqueous solution of formaldehyde, add 1 or 2 drops of a 0.3 per cent solution of potassium permanganate. Repeat with dilute (about 10 per cent) solutions of acetaldehyde, acetone, and cyclopentanone. If no reaction is observed in 1 minute, add a drop of sodium hydroxide solution. Note the results.

Repeat, using permanganate solution acidified with dilute sulfuric acid.

(*2*) *With Tollens' Reagent.* Place 5 ml. of Tollens' reagent in a *clean* test tube and add a few drops of formaldehyde solution. Repeat with acetaldehyde, acetone, and cyclopentanone. Observe the results both before and after the solution is warmed.

(*3*) *With Fehling's Solution.* To 3 ml. of Fehling's solution Part I, add Part II slowly until the initially formed light-blue precipitate of copper hydroxide dissolves as the dark-blue complex tartrate ion upon shaking. Add 3 drops of formaldehyde solution. Boil gently for 2 minutes. Repeat with solutions of *n*-butyraldehyde, acetone, and cyclopentanone.

125-135 B. Color Test with Schiff's Reagent

To 4 ml. of Schiff's reagent add a few drops of the dilute formaldehyde solution. Repeat with acetaldehyde solution and with pure acetone and cyclopentanone. Note the results.

C. Addition Reaction with Sodium Bisulfite

Shake 1 ml. of butyraldehyde with 5 ml. of a freshly prepared saturated solution of sodium bisulfite. Cool. Note the results.

Repeat with acetaldehyde solution, acetone, cyclopentanone, and diethyl ketone.

D. Aldehyde Resins

Heat about 2 ml. of a solution of acetaldehyde with an equal volume of dilute sodium hydroxide solution. Repeat with acetone. Note any differences.

E. Reactions of Aldehydes with Ammonia

Add 2 ml. of concentrated ammonium hydroxide to 5 ml. of formalin. Evaporate the mixture to dryness on a water bath in the hood. Note the appearance of the product.

NOTES

1. A two-necked flask would be most convenient, if available.
2. If the alcohol is introduced at the proper rate, heating will probably be unnecessary while the alcohol is being added.
3. Ordinary formalin is a 40 per cent aqueous solution of formaldehyde.

QUESTIONS

1. Suggest some possible by-products in the oxidation of *n*-butyl alcohol to *n*-butyraldehyde. How are they re-

moved by the purification procedure? What would be the probable effect of allowing the reaction temperature to go too high?

2. Can you suggest why sodium dichromate is used in place of potassium dichromate?

3. *n*-Butyraldehyde is an oxidation product of *n*-butyl alcohol and a reduction product of *n*-butyric acid, yet it is more easily oxidized than the alcohol and more easily reduced than the acid. Can you recall any analogy from inorganic chemistry?

4. Write balanced equations for the oxidation of formaldehyde and of acetaldehyde with potassium permanganate in neutral and acid solution.

What is the effect of the addition of alkali on the oxidizability of ketones with permanganate? Can you suggest an explanation?

5. Write balanced equations for the reactions of Tollens' reagent and of Fehling's solution with formaldehyde and *n*-butyraldehyde. How is a positive test with each of these reagents recognized in a practical way?

6. Assume that a certain reagent reacts chemically with organic compound A and not with B. Does this in itself make the reagent a good reagent for distinguishing between A and B in simple, clear-cut fashion? Explain.

7. Is sodium bisulfite a perfectly general reagent for the detection of a carbonyl function? What general types of carbonyl compounds form sodium bisulfite addition products?

8. Propose a mechanism for the addition of sodium bisulfite to *n*-butyraldehyde.

9. Could *n*-butyraldehyde be obtained by the catalytic hydration of 1-butyne? Explain.

10. Write balanced equations for the reactions involved in chemical tests you would use to distinguish between:

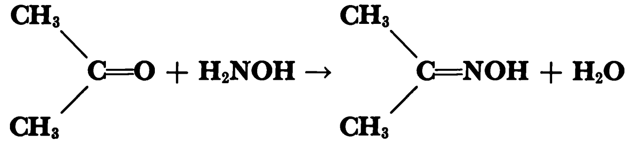
(a) Acetone and acetaldehyde.

(b) Methyl ethyl ketone and di-isopropyl ketone.

EXPERIMENT 21

I. Derivatives of Aldehydes and Ketones
II. Identification of an Unknown Carbonyl Compound

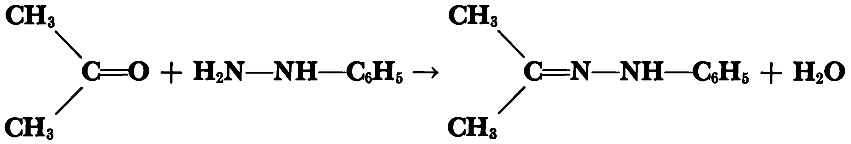
A.



$$(CH_3)_2C{=}O + H_2NOH \rightarrow (CH_3)_2C{=}NOH + H_2O$$

Acetoxime

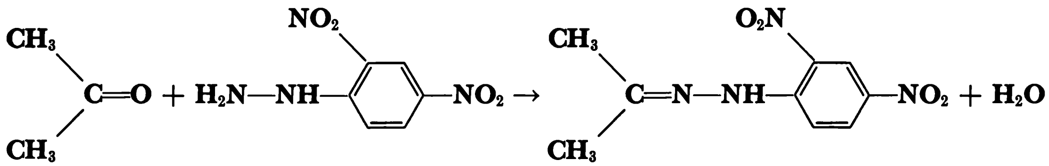
B.



$$(CH_3)_2C{=}O + H_2N{-}NH{-}C_6H_5 \rightarrow (CH_3)_2C{=}N{-}NH{-}C_6H_5 + H_2O$$

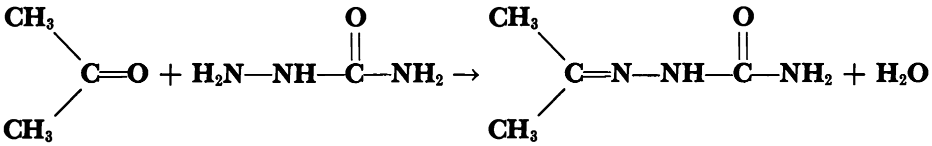
Acetone phenylhydrazone

C.



Acetone 2,4-dinitrophenylhydrazone

D.



$$(CH_3)_2C{=}O + H_2N{-}NH{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}NH_2 \rightarrow (CH_3)_2C{=}N{-}NH{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}NH_2 + H_2O$$

Acetone semicarbazone

Introduction. One of the most frequently encountered problems in organic chemical research is that of identifying an unknown compound. In attacking this problem, organic chemists, to some extent at least, follow a systematic procedure which involves the following steps:

1. Purification of unknown.
2. Qualitative (and sometimes quantitative) analysis for elements.
3. Determination of solubility behavior and other important physical constants.
4. Determination of functional groups present in molecule or of the homologous series to which the unknown belongs.
5. Survey of literature for the purpose of compiling a list of all possibilities (based on data obtained in steps 2-4).
6. Preparation of derivatives.
7. Synthesis of the unknown for comparison purposes by an unequivocal method.

Step 6 (the preparation of derivatives) usually establishes the identity of the unknown with certainty, and step 7 (synthesis) is regarded as conclusive confirmatory evidence. The term "derivative" as used here refers simply to a compound prepared from an unknown for use in identification of the unknown. An ideal derivative should be a crystalline, easily purified solid with a sharp melting point which can be prepared readily from the unknown in one direct and unambiguous step. It should possess properties distinctly different from those of the parent compound and should single out uniquely one compound from among all possibilities.

Carbonyl compounds (aldehydes and ketones) are noteworthy for the number of excellent and conveniently prepared derivatives available for use in their identification. In this experiment, several of the best derivatives of aldehydes and ketones will be studied —oximes, phenylhydrazones, 2,4-dinitrophenylhydrazones, and semicarbazones. You will observe from the equations that the over-all reaction in the preparation of each of these types of derivations involves the elimination of the elements of water between a molecule of the carbonyl compound and a molecule of the reagent. The oxygen of the water molecule is supplied by the carbonyl group and the two hydrogen atoms by the terminal NH_2-group of the reagent molecule.

The phenylhydrazones, 2,4-dinitrophenylhydrazones, and semicarbazones of most aldehydes and ketones are solids. Conversion of the carbonyl compound to each of these derivatives not only effects a large increase in molecular weight but also introduces at least one hydrogen atom capable of forming hydrogen bonds. The molecular weight increase on conversion to oximes is only 15 units; hence it is not surprising that a number of oximes are liquids.

Hydroxylamine, phenylhydrazine, and semicarbazide are not very stable in the free form and are usually stored in the laboratory in the form of their hydrochloride salts. In each case, a basic reagent is used to liberate the free base for reaction with the carbonyl compound. The reaction of 2,4-dinitrophenylhydrazine with aldehydes and ketones is catalyzed by strong mineral acids.

In today's experiment you will prepare several typical derivatives of the model carbonyl compound acetone. Then you will begin the identification of an unknown carbonyl compound. Determination of the melting point of some of the acetone derivatives and complete identification of one (or possibly two) unknown carbonyl compounds will require the next laboratory period, as well.

I. DERIVATIVES OF ACETONE

0-35 *A. Acetoxime.* Dissolve 0.7 g. of hydroxylamine hydrochloride in 1.5 ml. of water in a small Erlenmeyer flask. Place the flask in an ice bath and add slowly a cold solution of 0.5 g. of sodium hydroxide in 1 ml. of water. Then, with the flask still in the ice bath, add slowly 1 g. (25 drops) of acetone (Note 1). The crystals of acetoxime will separate completely within 10-15 minutes (Note 2). Then filter the crystals (Note 3) by means of a small Hirsch (p. 21) or Büchner funnel, and recrystallize from petroleum ether (b.p. 40°-60°). Dry rapidly (Note 4) on filter paper or in a desiccator and determine the melting point. Record the results.

25-60 *B. Acetone Phenylhydrazone.* Add 0.4 g. (10 drops) of acetone dissolved in 5 ml. of 95 per cent ethyl alcohol to 5 ml. of a stock solution of phenylhydrazine hydrochloride (Note 5). Shake the mixture until a clear solution is obtained (Note 1). Heat the mixture on a steam bath for 10 minutes (Note 2). Then cool in an ice bath and filter the crystals (Note 3).

Recrystallize the phenylhydrazone as follows: dissolve it in hot 95 per cent ethyl alcohol, add water to the hot solution until a faint turbidity persists, then add just enough 95 per cent alcohol to give a clear solution, and finally cool and filter the mixture.

40-75 *C. Acetone 2,4-Dinitrophenylhydrazone.* Add 2 ml. of concentrated sulfuric acid to a solution of approximately 0.4 g. of 2,4-dinitrophenylhydrazine in 3 ml. of water contained in a small Erlenmeyer flask. Swirl the flask until solution is complete and then add 10 ml. of 95 per cent ethanol to the warm solution. Dissolve 0.5 g. (25 drops) of acetone in 10 ml. of 95 per cent ethanol. Add the 2,4-dinitrophenylhydrazine solution, and allow the resulting mixture to stand at room temperature. Crystallization of the acetone 2,4-dinitrophenylhydrazone usually occurs almost immediately; other carbonyl compounds may require 5-6 minutes, or even several hours (Note 2). When crystallization is complete, cool the mixture in an ice bath and filter. Recrystallize from 95 per cent ethanol, dry, and determine the melting point of the acetone 2,4-dinitrophenylhydrazone.

60-100 *D. Acetone Semicarbazone.* In an 8-inch test tube, dissolve 1 g. of semicarbazide hydrochloride and 1.5 g.

TABLE 5. CARBONYL UNKNOWNS AND MELTING POINTS OF DERIVATIVES (°C.)

Compound	Formula	B.P.	Sp. Gr.	Water Solubility	Oxime	Phenylhydrazone	2,4-Dinitrophenylhydrazone	Semicarbazone
Acetone	CH_3COCH_3	56	0.79	Completely miscible	60	42	128	190
n-Butyraldehyde	$CH_3CH_2CH_2CHO$	74	0.82	4 g./100 g.	Oil	Oil	123	106
Methyl ethyl ketone	$CH_3CH_2COCH_3$	80	0.81	37 g./100 g.	Oil	Oil	126	187
Diethyl ketone	$CH_3CH_2COCH_2CH_3$	102	0.81	4.7 g./100 g.	69	Oil	156	139
Furfural	$C_4H_3O \cdot CHO$	161	1.16	9 g./100 g.	89	97	229	202
Crotonaldehyde	$CH_3CH{=}CHCHO$	103	0.85	18 g./100 g.	119	56	190	199
Benzaldehyde	C_6H_5CHO	179	1.05	0.3 g./100 g.	35 (dec.)	158	237	224
Cyclohexanone	$C_6H_{10}O$	156	0.95	2.1 g./100 g.	91	81	162	167
2-Heptanone	$CH_3(CH_2)_4COCH_3$	151	0.83	Insol.	Oil	207	89	127
n-Heptaldehyde	$CH_3(CH_2)_5CHO$	156	0.82	Insol.	57	Oil	108	109
Acetophenone	$C_6H_5COCH_3$	202	1.03	Insol.	59	105	250	199
2-Octanone	$CH_3(CH_2)_5COCH_3$	173	0.82	Insol.	Oil	Oil	58	123
Salicylaldehyde	$C_6H_5(OH)CHO$	197	1.15	1.72 g./100 g.	63	143	252	231
Cinnamaldehyde	$C_6H_5CH{=}CHCHO$	252	1.10	Insol.	139	168	255 (dec.)	215

of sodium acetate in 10 ml. of water, add 1 g. (25 drops) of acetone, and shake vigorously (Note 1).

Place the test tube in a beaker of boiling water for 5 minutes and let it cool. Transfer the tube to an ice bath and scratch the sides with a glass stirring rod. Cool until crystallization is complete. Filter the crystals, wash with a few ml. of water, and recrystallize from 95 per cent alcohol. Dry and determine the melting point of the semicarbazone.

100-360

II. Identification of an Unknown Carbonyl Compound

While the various acetone derivatives are drying, obtain a sample of an unknown from your instructor and begin its identification. Proceed as far as you can this period, and complete the identification during the next period. If you work especially efficiently, you may be able to solve two carbonyl unknowns by the end of the second period. Your unknown may be any aldehyde or ketone listed in Table 5, or a noncarbonyl compound. Test for the carbonyl group by means of the phenylhydrazine and 2,4-dinitrophenylhydrazine reactions described in Section I for acetone. In each case, *substitute your unknown for the acetone*. If the test is positive, save the phenylhydrazones formed for later use as one of your derivatives. If your unknown is not a carbonyl compound, obtain a second unknown.

Now by means of physical constants, any tests in Experiment 20 which will be helpful, the iodoform test (Experiment 23) if it will be useful, and appropriate derivatives, identify your unknown. The derivatives may in every case be prepared by the procedures given in Section I. Merely substitute your unknown for the acetone.

When you have completed the identification, submit your derivatives to your instructor, along with your report.

NOTES

1. If the unknown does not dissolve completely or if the solution is turbid at this point, add just enough 95 per cent alcohol to give a clear solution.
2. During this period, proceed with the preparation of the next derivative.
3. If no solid separates on cooling add 3 volumes of water and cool again.
4. Acetoxime has a rather high vapor pressure and evaporates readily in the air.
5. The stock solution of phenylhydrazine hydrochloride can be prepared as follows: add 45.0 g. of crystalline sodium acetate to a solution containing 25.0 g. of colorless phenylhydrazine hydrochloride in 250 ml. of water. Stir until all the sodium acetate has dissolved and store in an amber bottle.

If the phenylhydrazine hydrochloride is dark it should be decolorized. Dissolve the phenylhydrazine hydrochloride in six times its weight of water, add a small amount of decolorizing charcoal, and heat at the boiling point for 10 minutes. Then filter the hot solution, add a volume of concentrated hydrochloric acid equal to one third that of the solution, cool in an ice bath, and filter.

QUESTIONS

1. After a study of Table 5, explain why it is often necessary to prepare more than one derivative in the identification of an aldehyde or ketone.
2. Propose a mechanism for the reaction of hydroxylamine, phenylhydrazine, 2,4-dinitrophenylhydrazine, and semicarbazide with carbonyl compounds. How do these reactions differ in mechanism from the addition of ammonia to acetaldehyde?
3. Point out one important advantage in using low boiling petroleum ether as a solvent for recrystallization.
4. Which of the various derivatives of aldehydes and ketones do you prefer in general? Why?

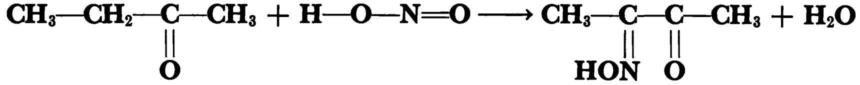
EXPERIMENT 22

Dimethylglyoxime

(1) $$C_2H_5OH + NaNO_2 + H_2SO_4 \longrightarrow C_2H_5ONO + NaHSO_4 + H_2O$$

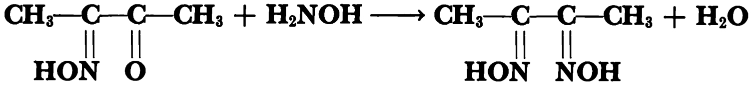
(2) $$C_2H_5ONO + H_2O \xrightarrow{HCl} H-O-N=O + C_2H_5OH$$

(3)



$$CH_3-CH_2-\underset{\underset{O}{\|}}{C}-CH_3 + H-O-N=O \longrightarrow CH_3-\underset{\underset{HON}{\|}}{C}-\underset{\underset{O}{\|}}{C}-CH_3 + H_2O$$

(4)



$$CH_3-\underset{\underset{HON}{\|}}{C}-\underset{\underset{O}{\|}}{C}-CH_3 + H_2NOH \longrightarrow CH_3-\underset{\underset{HON}{\|}}{C}-\underset{\underset{NOH}{\|}}{C}-CH_3 + H_2O$$

Introduction. Dimethylglyoxime is of special interest because of its wide use as a reagent for the qualitative and quantitative analysis of nickel. It is actually the dioxime of the diketone called biacetyl or dimethyl glyoxal $(CH_3-\overset{\overset{O}{\|}}{C}-\overset{\overset{O}{\|}}{C}-CH_3)$ but may be more cheaply prepared from the readily available ketone 2-butanone (methyl ethyl ketone). The key step is the nitrosation of methyl ethyl ketone with nitrous acid to produce the monoxime of biacetyl. This step illustrates a fairly general reaction of a methylene (CH_2) group adjacent to a carbonyl group, which is frequently used to oxidize a carbonyl compound to a 1,2-dicarbonyl compound. The monoxime of biacetyl is then treated with hydroxylamine to form the dioxime, dimethylglyoxime.

In this experiment you will introduce the nitrous acid into the reaction mixture indirectly by passing gaseous ethyl nitrite into an acidified solution of methyl ethyl ketone. The ethyl nitrite is hydrolyzed in the acid medium to nitrous acid and ethyl alcohol.

0-30 A. Preparation of Dimethylglyoxime

Assemble the apparatus as shown in Figure 23. The filter flask, which is to serve as the ethyl nitrite generator, should be 1 liter in size, and the distilling flask, which will be the actual reaction vessel, 125 ml. The two bottles of 5 per cent sodium hydroxide solution serve to remove excess ethyl nitrite (Note 1). As an alternative means of absorbing excess ethyl nitrite the two bottles may be replaced by the type of trap shown at the extreme right in Figure 23.

To the ethyl nitrite generator (filter flask) add a 30-100
solution of 40 g. of commercial sodium nitrite, 300 ml. of water, and 15 ml. of 95 per cent ethyl alcohol. Place in the reaction flask (distilling flask) 45 ml. (36 g., 0.50 mole) of methyl ethyl ketone and 3 ml. of concentrated C.p. hydrochloric acid.

Add to the dropping funnel (be certain that the stopcock is closed!) a solution of 15 ml. of 95 per cent ethyl alcohol in 300 ml. of water which has been acidified with 25 ml. of concentrated sulfuric acid. Be certain that all stoppers are inserted tightly. Then allow the solution in the dropping funnel to drop into the generating flask at the rate of about 1 drop per second so that all of it is introduced during the course of 45-50 minutes. Shake the generating flask frequently during this period.

The heat of reaction soon warms the mixture in the distilling flask to above 40°; raise or lower the cooling bath as needed to maintain the temperature between 45°-55° until all of the ethyl nitrite has been absorbed. During this period prepare a solution of hydroxylamine by dissolving 28 g. (0.4 mole) of hydroxylamine hydro-

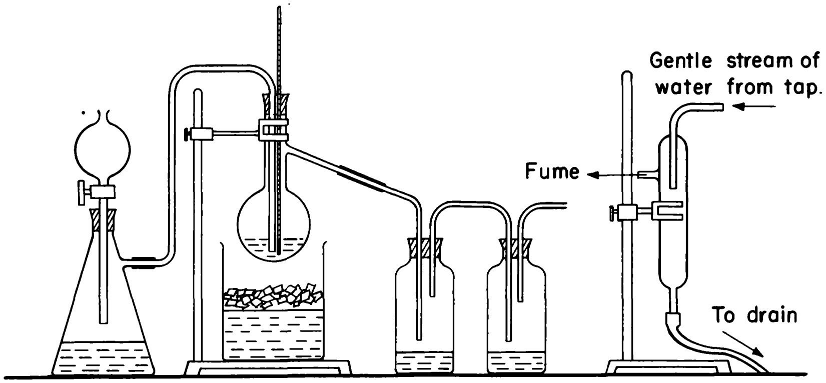


FIG. 23. Ethyl nitrite generator and ethyl nitrite-methyl ethyl ketone reaction flask.

chloride and 33 g. (0.40 mole) of sodium acetate in 300 ml. of water in a 1-liter beaker.

100-130 When all of the ethyl nitrite has been absorbed by the methyl ethyl ketone, pour the biacetyl monoxime solution from the distilling flask into the beaker containing the hydroxylamine solution, with constant stirring. Heat the mixture over a wire gauze on a ring stand to 75° with constant stirring. Remove the burner, and continue to stir for an additional 15 minutes. Then place a large sheet of filter paper over the beaker to keep out dust and store the material overnight to allow the dimethylglyoxime to crystallize.

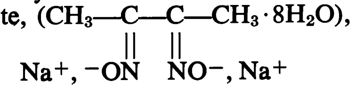
[Use the balance of the period to assemble the apparatus for Experiment 23.]

Collect the crystalline product on a filter, wash with four 25-ml. portions of cold water and then with 15 ml. of ice-cold acetone, and finally dry on filter paper or in an oven at 80°. The yield is about 35 g. of dimethylglyoxime, melting at 235°-240°. Calculate the percentage yield (Note 2) and determine the melting point for reporting to your instructor. This product is suitable for most laboratory purposes but may be recrystallized from glacial acetic acid if a very pure material is desired.

B. Properties of Dimethylglyoxime

(Optional for specially interested students; to be performed during the next laboratory period.)

Solubility in Alkali. Dissolve 1 g. of dimethylglyoxime in 10 ml. of warm 5 per cent sodium hydroxide solution and divide the solution into two parts. Pour one part into 10 ml. of 95 per cent ethyl alcohol. The sodium salt of dimethylglyoxime crystallizes from the alcohol solution as the octahydrate,



$(\mathrm{CH_3}{-}\underset{\underset{\mathrm{Na^+,\,{}^-ON}}{\|}}{\mathrm{C}}{-}\underset{\underset{\mathrm{NO^-,\,Na^+}}{\|}}{\mathrm{C}}{-}\mathrm{CH_3\cdot 8H_2O})$,

upon cooling.

Dilute the second half of the alkaline solution with 5 ml. of water and then acidify with dilute hydrochloric acid. Observe the results.

Tests with Metallic Salts. Dissolve a small crystal of a nickel salt in a few ml. of water, add 1 ml. of sodium acetate solution, and then a few drops of 1 per cent solution of dimethylglyoxime in alcohol. Observe the results. Repeat the test several times, each time diluting the solution of the nickel salts in order to test the sensitivity of the test.

Repeat with copper and cobalt salts. Add the alcoholic solution of dimethylglyoxime to a dilute freshly prepared solution of a ferrous salt and introduce a few drops of ammonium hydroxide. Observe the results.

NOTES

1. The delivery tube leading into the first bottle should extend just below the surface of the sodium hydroxide solution. Ethyl nitrite, like the other lower molecular weight alkyl nitrites, is a vasodilator (an agent which causes dilation of the blood vessels). Isoamyl nitrite, because of this property, is used for treatment of angina pectoris. Inhalation of these nitrites soon produces marked flushing, throbbing in the head, and occasionally nausea.

The fume absorber may be replaced by two wash bottles in series containing an alkaline solution of ethyl alcohol or may be dispensed with if the experiment is performed in an efficient hood.

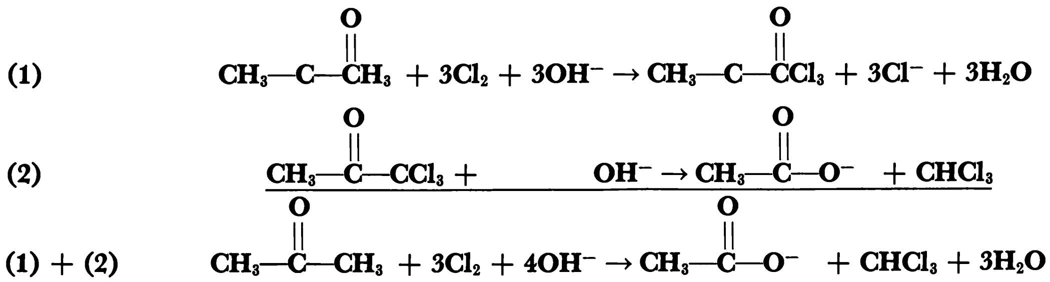
2. It is standard practice, in a multi-step synthesis, to base the yield on the major organic starting material. In this case, for example, the yield should be based on 0.5 mole of methyl ethyl ketone, even though only 0.4 mole of hydroxylamine hydrochloride is later used. At that stage, there is less than 0.4 mole of the biacetyl monoxime, formed in the prior step, available for reaction with the hydroxylamine.

QUESTIONS

1. Show the structure of the compound which precipitates when nickel ion is heated with dimethylglyoxime. What name is given to this general type of compound?
2. How can you account, on the basis of structure, for the acidity of oximes?

EXPERIMENT 23

I. Preparation of Chloroform



$$(1)\quad CH_3-\overset{O}{\overset{\|}{C}}-CH_3 + 3Cl_2 + 3OH^- \rightarrow CH_3-\overset{O}{\overset{\|}{C}}-CCl_3 + 3Cl^- + 3H_2O$$

$$(2)\quad CH_3-\overset{O}{\overset{\|}{C}}-CCl_3 + OH^- \rightarrow CH_3-\overset{O}{\overset{\|}{C}}-O^- + CHCl_3$$

$$(1) + (2)\quad CH_3-\overset{O}{\overset{\|}{C}}-CH_3 + 3Cl_2 + 4OH^- \rightarrow CH_3-\overset{O}{\overset{\|}{C}}-O^- + CHCl_3 + 3H_2O$$

II. Properties of Chloroform

III. The Iodoform Test

Introduction. Chloroform is produced commercially by the chlorination of methane and methyl chloride, by the reduction of carbon tetrachloride with iron and water, and by the action of bleaching powder on acetaldehyde or acetone. In today's experiment, the last of the three methods, with acetone as the starting material, is utilized as a convenient laboratory synthesis of chloroform.

The reaction proceeds in two stages. In the first stage, one of the methyl groups is fully substituted by chlorine[1] to produce trichloroacetone. In alkaline solution the substitution of three chlorine proceeds readily, with each successive chlorine substituting more easily than the one before. The second stage of the synthesis is the alkaline cleavage of the trichloroacetone to form chloroform and sodium acetate.

The preparation of chloroform by the reaction of acetone with chlorine in alkaline solution is an example of an important general type of reaction known as the **haloform reaction.** Whenever (1) an aldehyde or a ketone containing a $CH_3-\overset{O}{\overset{\|}{C}}-$ grouping, or (2) an alcohol which is oxidized by the reagent to give such an aldehyde or ketone, is treated with an alkaline solution of a halogen, the corresponding haloform is formed. This is the haloform reaction.

In general, compounds which contain the $CH_3-\overset{O}{\overset{\|}{C}}-$ grouping joined to a hydrogen or carbon atom, as well as compounds which give such a structure upon oxidation, undergo the haloform reaction.

Specifically, this includes the following groups of compounds:[2]

Aldehydes	$CH_3-\overset{H}{C}=O$	**Acetaldehyde** only
Ketones	$R-\overset{O}{\overset{\|}{C}}-CH_3$	**All methyl ketones**
Primary alcohols	CH_3-CH_2OH	**Ethyl alcohol** (which is oxidized to acetaldehyde) only
Secondary alcohols	$R-\underset{H}{\overset{OH}{\overset{\vert}{C}}}-CH_3$	**All methyl carbinols** (which are oxidized to methyl ketones).

When the halogen used is iodine, the haloform obtained, iodoform or tri-iodomethane (CHI_3), is readily identified by its characteristic odor and bright yellow color and by its melting point of 119°-120°. Formation of iodoform upon treatment of an unknown with iodine and sodium hydroxide is the basis for the **iodoform test,** an important diagnostic test for the structures shown above. It has played an important role in the development of organic chemistry and is widely used in research today.

I. PREPARATION OF CHLOROFORM 0-70

Weigh 100 g. of fresh high test bleaching powder, such as HTH or Perchloron (Note 1) into a 600-ml. beaker and add 300 ml. of water. Stir the mixture into a thin slurry and pour it into a 1-liter round-bottomed flask. Fit a reflux condenser to the flask and mount the

---

[1] Bleaching powder is a mixture whose composition may be represented roughly by the formula CaCl(OCl). In water, it gives chlorine and calcium hydroxide: $CaCl(OCl) + H_2O \rightarrow Cl_2 + Ca(OH)_2$. It therefore constitutes a ready source of chlorine in alkaline solution.

[2] It is understood throughout that the methyl group may already be partially halogenated in every case. Thus, CH_2X-CHO, CHX_2-CHO, and CX_3-CHO, as well as CH_3-CHO, would undergo the haloform reaction with X_2 in alkaline solution.

assembly on a ring stand. Add through the condenser a total of 37 ml. (0.5 mole) of acetone in 2-ml. portions, shaking the flask gently with a rotary motion after each addition. Cool the flask occasionally in cold water if the reaction becomes too vigorous. After all of the acetone has been added, continue to shake the flask at frequent intervals for an additional 10 minutes.

70-130 Arrange the apparatus for steam distillation, as shown in Figure 15, page 33. Begin the steam distillation and continue until droplets of chloroform can no longer be observed in the distillate. Transfer the distillate to a small separatory funnel, draw off the lower chloroform layer into a small Erlenmeyer flask, and wash it once with 20 ml. of water. Dry the moist chloroform over anhydrous calcium chloride with frequent gentle shaking for several minutes.

Decant the dry chloroform from the desiccant into a small distilling flask and distill into a tared bottle, observing and recording the boiling point range. Weigh the chloroform and calculate the percentage yield. The recorded boiling point of chloroform is 61.2° at 760 mm. and its specific gravity 1.49.

NOTE

1. Best results are obtained if fresh bleaching powder specified to have at least "70 per cent available chlorine" is used.

130-150

II. PROPERTIES OF CHLOROFORM

Test the solubility of each of the following in chloroform: ether, ethyl alcohol, water, rubber, vaseline.

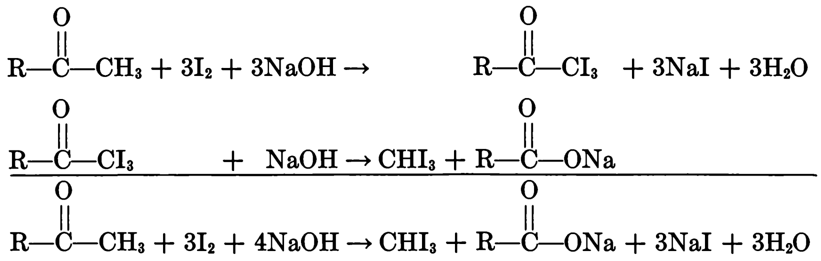
Shake 4 ml. of chloroform with 4 ml. of bromine water in a small separatory funnel and then allow the layers to separate. Observe and record the results.

Test chloroform for flammability.

150-175

III. THE IODOFORM TEST[3]

For acetaldehyde and methyl ketones

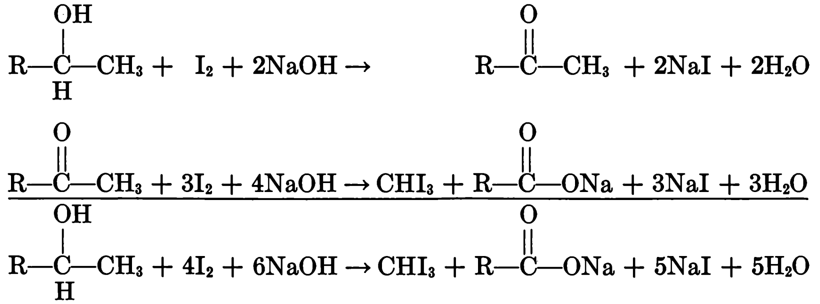


$$R\text{—}\overset{\overset{O}{\|}}{C}\text{—}CH_3 + 3I_2 + 3NaOH \rightarrow R\text{—}\overset{\overset{O}{\|}}{C}\text{—}CI_3 + 3NaI + 3H_2O$$

$$R\text{—}\overset{\overset{O}{\|}}{C}\text{—}CI_3 + NaOH \rightarrow CHI_3 + R\text{—}\overset{\overset{O}{\|}}{C}\text{—}ONa$$

$$R\text{—}\overset{\overset{O}{\|}}{C}\text{—}CH_3 + 3I_2 + 4NaOH \rightarrow CHI_3 + R\text{—}\overset{\overset{O}{\|}}{C}\text{—}ONa + 3NaI + 3H_2O$$

For ethyl alcohol and secondary methyl carbinols



$$R\text{—}\underset{H}{\overset{\overset{OH}{|}}{C}}\text{—}CH_3 + I_2 + 2NaOH \rightarrow R\text{—}\overset{\overset{O}{\|}}{C}\text{—}CH_3 + 2NaI + 2H_2O$$

$$R\text{—}\overset{\overset{O}{\|}}{C}\text{—}CH_3 + 3I_2 + 4NaOH \rightarrow CHI_3 + R\text{—}\overset{\overset{O}{\|}}{C}\text{—}ONa + 3NaI + 3H_2O$$

$$R\text{—}\underset{H}{\overset{\overset{OH}{|}}{C}}\text{—}CH_3 + 4I_2 + 6NaOH \rightarrow CHI_3 + R\text{—}\overset{\overset{O}{\|}}{C}\text{—}ONa + 5NaI + 5H_2O$$

Run the iodoform test on (1) acetaldehyde, (2) acetone, (3) methyl ethyl ketone, (4) methyl alcohol, (5) ethyl alcohol, (6) isopropyl alcohol, and (7) *n*-propyl alcohol as follows:

Add 4 drops of the substance to be tested to 5 ml. of water (in the case of acetaldehyde, merely use the water solution as it comes from the shelf) in a small test tube. Make the solution alkaline by the addition of 12 drops of 10 per cent sodium hydroxide solution. Then add to the mixture, a drop at a time, the iodine in potassium iodide reagent until the solution remains straw-colored after a minute of shaking. In a positive test the brown iodine color disappears and yellow iodoform is precipitated.

Note the odor of the solution and also whether a precipitate forms. If no precipitate develops, warm the solution to about 60° and allow it to stand for a minute. If the solution becomes colorless, add more iodine solution and repeat the warming.

Isolate the iodoform in at least one case as follows: add 3 ml. of chloroform, stopper the test tube and shake vigorously to extract the iodoform in the lower chloroform layer, withdraw this layer with a capillary dropping tube, transfer to a small test tube, and remove the chloroform by evaporation on a steam bath.

---

[3] R (in the general formulas in this section) = a hydrogen atom or an alkyl group.

Recrystallize the iodoform from a 1:1 mixture of methanol and water, dry in a desiccator, and determine the melting point.

QUESTIONS

1. How many grams of chloroform could be obtained theoretically from 100 g. of acetaldehyde? Of acetone? Of ethyl alcohol?

2. What important general commercial use of chloroform is suggested by its properties? What properties make chloroform a useful extraction solvent?

3. Write a general equation for the preparation of a carboxylic acid, RCOOH, from a ketone by means of the haloform reaction. If your interest was only in the preparation of the acid, what halogen would you use? Why?

4. Write a balanced equation for the iodoform reaction as run on 2-butanol (*s*-butyl alcohol).

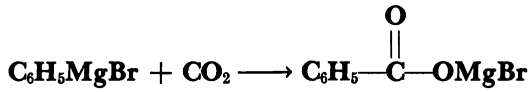
5. Which of the following will give a positive iodoform test: 1-pentanol, 2-pentanol, 3-pentanol, diethyl ketone, methyl *n*-butyl ketone, dimethyl ether, acetic acid? Write balanced equations for the reactions.

6. What weight of iodoform might be obtained theoretically from 1 g. of acetaldehyde?

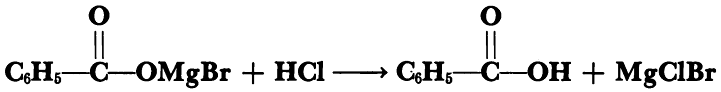
EXPERIMENT 24

Preparation of a Carboxylic Acid (Benzoic Acid) by the Grignard Method

(1) $$C_6H_5Br + Mg \xrightarrow[\text{Ether}]{\text{Dry}} C_6H_5MgBr$$

(2)


$$C_6H_5MgBr + CO_2 \longrightarrow C_6H_5-\overset{\overset{\displaystyle O}{\|}}{C}-OMgBr$$

(3)


$$C_6H_5-\overset{\overset{\displaystyle O}{\|}}{C}-OMgBr + HCl \longrightarrow C_6H_5-\overset{\overset{\displaystyle O}{\|}}{C}-OH + MgClBr$$

Introduction. Some of the common methods for the preparation of carboxylic acids include the oxidation of alcohols, hydrolysis of nitriles and the carbonation of Grignard reagents. The latter procedure will be illustrated in today's experiment.

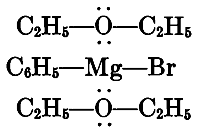
Owing to the fact that a solid carboxylic acid is much easier to isolate and purify than a liquid acid, benzoic acid, m.p. 121°, rather than a liquid aliphatic acid, has been selected for this assignment. It will be prepared by treatment of phenylmagnesium bromide with solid carbon dioxide (Dry Ice) and subsequent acidification of the reaction mixture by the addition of hydrochloric acid.

The Grignard reagent, phenylmagnesium bromide, is to be prepared at the start of the present period by reaction of bromobenzene with metallic magnesium. The entire sequence of steps employed in this synthesis of benzoic acid is shown in the equations at the top of the page.

Since most of the common aliphatic carboxylic acids are liquids at room temperature, such acids are purified by distillation. If one were to prepare such an acid by the Grignard method, not only would the purification by distillation have to be carried out, but also it would be necessary to prepare at least one solid derivative of the acid in order to identify the product in a reasonably certain manner. Hence the entire experiment could not conveniently be completed in a regular 3-hour laboratory period.

However, in the actual practice of organic chemistry in industrial or institutional laboratories, where there are no arbitrary time limits for completing an experiment, the syntheses of certain aliphatic carboxylic acids can better be achieved by the Grignard process than by other methods. For example, trimethylacetic acid, $(CH_3)_3CCOOH$, is readily prepared from *t*-butyl chloride, $(CH_3)_3CCl$, by the Grignard method, whereas the nitrile route would be of no use whatsoever; treatment of *t*-butyl chloride with sodium cyanide gives sodium chloride, hydrogen cyanide and isobutylene rather than trimethylacetonitrile, $(CH_3)_3\,CCN$.

Anhydrous ether is generally used as the solvent in the preparation of a Grignard reagent. Actually, the ether plays a more important role in the reaction than merely that of solvent. Ether molecules combine with the various components of a Grignard reagent to form complex etherates. For example, one of the components present in phenylmagnesium bromide-ether solution is the complex shown below:



As implied in the previous paragraph, a Grignard reagent is actually an equilibrium mixture of different molecular species. One of the equilibria thought to exist in any Grignard reagent is shown in the following equation, which has been simplified in that the ether molecules coordinated with the magnesium are not shown:

$$2RMgX \rightleftarrows R_2Mg + MgX_2$$

Addition of anhydrous dioxane to an ether solution of a Grignard reagent causes RMgX and MgX_2 to precipitate, leaving R_2Mg in solution. Occasionally, for certain specific reactions, it is preferable to use the filtrate from such a mixture rather than the Grignard mixture itself; i.e., there are certain Grignard reactions in which the use of R_2Mg is preferable to the use of the equilibrium mixture of RMgX, MgX_2 and R_2Mg. However, no such complication exists in today's experiment.

Grignard reagents can be prepared successfully only in a completely anhydrous medium and in an atmosphere that is free of oxygen. The presence of water causes hydrolysis of the reagent, and the presence of oxygen causes loss of the reagent by oxidation.

$$RMgX + H_2O \rightarrow RH + Mg(OH)X$$

$$2RMgX + O_2 \rightarrow 2ROMgX$$

Therefore, in carrying out a Grignard reaction, one must take care to dry the apparatus and all of the reagents (magnesium metal, ether, and organic halide) carefully and also to provide an inert atmosphere over the reaction mixture. The latter condition is best realized by passing highly purified nitrogen over the surface of the liquid.

However, in today's experiment, the oxygen-free atmosphere will be attained by keeping the ether solution warm during the preparation of the Grignard reagent. Ether is so highly volatile (boiling point 35°) that a blanket of ether vapor over the warm solution keeps the reagent reasonably well insulated from contact with the air.

Preparation of a Carboxylic Acid

0-30 Fit a dry (Note 1), 500-ml. round-bottomed flask with a dry, water-cooled condenser, using a clean and well-fitting cork; a drying tube filled with calcium chloride is attached to the top of the condenser. (See Figure 18, page 46.) In the flask place 8.0 g. of dry magnesium turnings, a few small crystals of iodine, 20 ml. of anhydrous ether (Note 2), and 10 ml. (15 g.) of anhydrous bromobenzene (Note 3). If reaction does not start immediately, warm the flask on the steam bath so that the ether refluxes gently and then remove the bath. This will usually initiate the reaction. The disappearance of the iodine color, the production of a cloudiness in the solution, and gentle boiling of the ether are all indications that the reaction has started (Note 4).

Replace the drying tube by a separatory funnel containing a solution of 26 ml. (38 g.) of bromobenzene in 140 ml. of ether; fit the separatory funnel into the top of the condenser by use of a cork which has been grooved on each side by rubbing a triangular file vertically along the sides. Place the calcium chloride drying tube in the mouth of the separatory funnel. Allow
30-60 the bromobenzene solution to run into the flask at such a rate that the ether refluxes vigorously because of the exothermic nature of the reaction. (Begin to answer the questions at the end of this unit of work.)

When all of the solution of bromobenzene has been introduced into the reaction flask, replace the separatory funnel by the calcium chloride tube and heat the mixture under gentle reflux on the steam bath for 30 minutes
60-90 (continue with the questions). By the end of this period, the solution should be somewhat cloudy and almost all of the magnesium should have gone into solution.

90-130 Place about 80 g. of crushed solid carbon dioxide (Note 5) in a large beaker and decant the ether solution of the Grignard reagent slowly and steadily onto the carbon dioxide; be sure to leave any unreacted magnesium metal behind in the round-bottomed flask. Stir the mixture with a glass rod as the Grignard solution is being added to the Dry Ice. The reaction is vigorous, and the mixture sets to a stiff mass. Continue stirring the mixture until all of the excess of carbon dioxide has evaporated. Add about 200 g. of crushed ice and then 60 ml. of 6 *M* hydrochloric acid. Stir the mixture until most of the solid mass has disintegrated.

Pour the mixture into a separatory funnel, and wash the last of the material from the beaker into the funnel with the aid of several small portions of ordinary ether. Draw off the lower aqueous layer and discard it. Wash the ether layer with two 25-ml. portions of water, and discard the wash solutions. Extract the ether solution with two 100-ml. portions of 5 per cent sodium hydroxide solution and collect the alkaline solution in a clean Erlenmeyer flask. Warm the alkaline solution with about 1 g. of decolorizing carbon and filter the mixture with suction. If necessary, filter the solution a second time to remove the last of the carbon. Cool the filtrate in ice and acidify it with 6 *M* hydrochloric acid. Collect the precipitate of benzoic acid on a Büchner funnel by suction filtration. Recrystallize about 1 g. of the acid from hot water and determine its melting point. **130-160**

Dry the remainder of the acid by spreading it out on filter paper or a paper towel and allowing it to stand in the air for the remainder of the period. In the meantime place the ether remaining in the separatory funnel in a bottle which will be provided by the instructor.

Weigh the benzoic acid and calculate the yield. **160-170**

NOTES

1. The flask should be dried in an oven at about 100° for several minutes before the apparatus is assembled. The condenser, apparently dry, should be rinsed with a little absolute ether.

2. Anhydrous ether should be prepared by one of the methods described in Experiment No. 10 (page 46).

3. The bromobenzene, if not already dry, must be dried over anhydrous calcium chloride and redistilled before it can be used.

4. If the reaction does not start after this treatment, add some more iodine and crush an iodine crystal together with a magnesium turning against the wall of the flask by use of a stirring rod that has a flattened end. If the reaction still does not start, it will be necessary for you to try the whole procedure again, this time taking even greater care than before to dry the apparatus and all the reagents.

5. The solid carbon dioxide should not be handled with the fingers. Place a few lumps on a towel with the aid of tongs, wrap the towel around the solid and pound the towel and its contents with some blunt object such as a mallet or block of wood to powder the Dry Ice.

QUESTIONS

1. In what way does carbon dioxide resemble an aldehyde, ketone, or ester?

2. Write a detailed mechanism for the condensation of phenylmagnesium bromide with carbon dioxide.

3. Write equations to show what products are formed in the reaction of ethylmagnesium bromide with each of the following reagents:

(a) H_2O
(b) C_2H_5OH
(c) O_2
(d) acetone
(e) ethyl acetate
(f) acetaldehyde
(g) CO_2
(h) capronitrile

4. Would a Grignard reagent be formed on treatment of 4-bromo-1-butanol with magnesium in anhydrous ether? Explain your answer.

5. In the electrolysis of a Grignard solution, ions containing magnesium migrate to both the anode and cathode. How can this result be explained?

6. Write equations to show how *t*-amyl chloride can be converted to dimethylethylacetic acid.

7. Name several types of organometallic reagents other than Grignard reagents.

8. Describe an analytical method making use of a Grignard reagent whereby the number of "active hydrogen" atoms in a molecule may be determined.

9. Write equations to show how primary, secondary, and tertiary alcohols may be produced by the action of Grignard reagents on aldehydes or ketones.

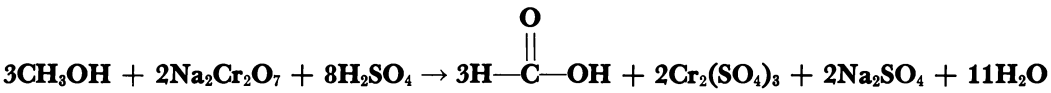
10. A student was instructed to prepare triethylcarbinol by treatment of ethyl propionate with ethylmagnesium bromide. Inadvertently he used methyl propionate rather than the ethyl ester. How would this affect his results?

11. When alcohols are prepared by a Grignard reaction, ammonium chloride solution rather than hydrochloric acid is ordinarily used to hydrolyze the reaction mixture. Why is this the case?

12. Which is more reactive toward a given Grignard reagent, a ketone or an ester? Explain your answer.

EXPERIMENT 25

Formic Acid



$$3CH_3OH + 2Na_2Cr_2O_7 + 8H_2SO_4 \rightarrow 3H-\overset{\overset{\displaystyle O}{\|}}{C}-OH + 2Cr_2(SO_4)_3 + 2Na_2SO_4 + 11H_2O$$

Introduction. The first member of a homologous series frequently possesses some properties that are not characteristic of the series as a whole. This is particularly true of formic acid. Examination of its structure reveals that it is, in a sense, both an aldehyde and a carboxylic acid. The aldehyde properties are reflected in the ease of oxidation of formic acid by mild reagents such as Tollens' solution or mercuric chloride. The acid properties are apparent in the acidity of the compound. ($Ka = 2.1 \times 10^{-4}$ at 25°) and in its ability to form esters with alcohols and salts with suitable bases. The latter property tends to mask certain of the properties of the aldehyde function.

For example, reagents such as hydroxylamine and phenylhydrazine form salts with formic acid rather than the oxime or phenylhydrazone, respectively. The large resonance energy and consequent stability of the formate anion precludes further reaction with a second molecule of hydroxylamine or phenylhydrazine.

Other unusual chemical properties of formic acid include its sulfuric acid-catalyzed decomposition to water and carbon monoxide and also its inability to form the acid chloride, formyl chloride, on treatment with phosphorus trichloride; hydrogen chloride and carbon monoxide are formed instead, presumably by decomposition of the unstable and nonisolable acid chloride.

As a part of today's assignment, formic acid will be prepared in two different ways. One of these involves the oxidation of methanol with sodium dichromate and sulfuric acid in which, as might well be expected, the yield is low owing to the ease of oxidation of the desired product. In the second method of preparation of formic acid, glyceryl monooxalate is first formed by reaction of glycerol with oxalic acid. On being heated to a temperature of 90°-115°, glyceryl monooxalate loses carbon dioxide to form glyceryl monoformate. Hydrolysis of the latter compound affords formic acid.

0-10 *Preliminary Operation.* Before beginning the preparation of formic acid by oxidation of methanol, make preparations for the oxalic acid-glycerol method by placing about 60 g. of commercial oxalic acid in an oven maintained at 110°. The oxalic acid will be anhydrous by the time that it is needed.

I. PREPARATION OF FORMIC ACID FROM METHANOL

10-30 *Procedure.* Place a solution containing 16 g. of sodium dichromate, 50 ml. of water, and 10 ml. of concentrated sulfuric acid in a 125-ml. distilling flask and immerse the flask in a pan of cold water. Add 10 ml. of methanol dropwise, with continuous shaking of the flask. After the initial spontaneous reaction has subsided, attach a glass tube 50 cm. in length to the distilling flask to serve as a reflux condenser (see Figure 24a), and set the flask in a beaker of hot water for 5 minutes. Attach the flask to a condenser and distill 25-30 ml. of the liquid. The distillate consists of an aqueous solution of formic acid and may be used for the tests described below. **30-50**

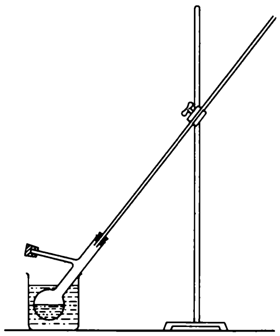


FIG. 24a. Use of a glass tube as an air condenser in the oxidation of methanol.

Formic Acid as a Reducing Agent

(*a*) *Reduction of Tollens' Solution.* Add about 1 ml. of the formic acid solution to 5 ml. of Tollens' reagent. Warm the solution gently and note the result. Write the equation for the reaction. **50-60**

(*b*) *Reduction of Mercuric Chloride.* Heat 5 ml. of the formic acid solution with an equal volume of a saturated solution of mercuric chloride. What is the initial white precipitate? Why does it gradually darken? Write the equation for the reaction. **60-70**

Decomposition of Formic Acid **70-80**

(CAUTION: Carbon monoxide, a poisonous gas, is evolved in this experiment. Carry out the experiment in the hood.) Warm 1 g. of sodium formate with 5 ml. of concentrated sulfuric acid. Note the result, and write the equation for the reaction. Why must sodium formate be used in this experiment rather than the aqueous solution of formic acid prepared earlier?

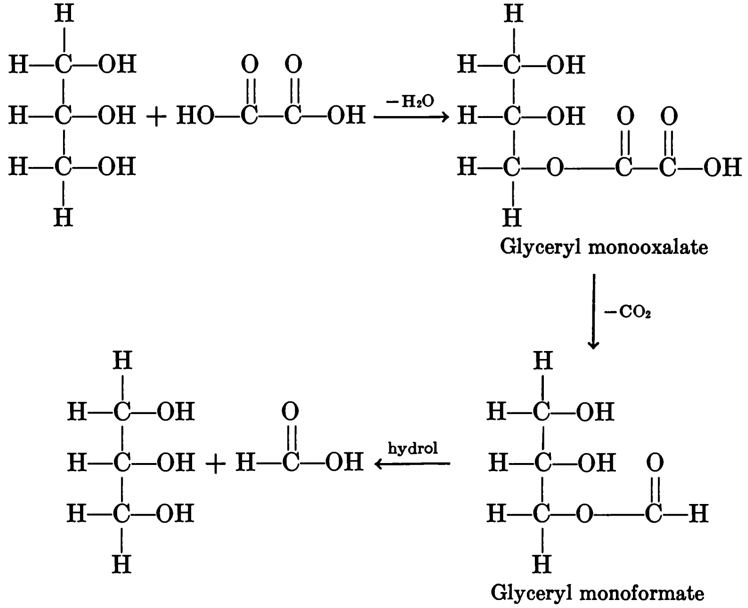
Salts of Formic Acid

(*a*) *Hydrolysis of Sodium Formate.* Dissolve 1 g. of sodium formate in 5 ml. of water, and test the solution with litmus paper. Explain the result. **80-90**

90-100 (*b*) *Preparation of Lead Formate.* Boil 10 ml. of formic acid solution with about 2 g. of litharge (PbO) for 2 minutes and filter the hot solution rapidly. Lead formate crystallizes as the filtrate cools. Write the equation for the reaction between formic acid and PbO.

100-120 Answer the questions at the end of today's assignment as anhydrous glycerol is being prepared for the next experiment.

II. FORMIC ACID FROM OXALIC ACID BY THE AID OF GLYCEROL



Procedure. Heat 50 ml. of glycerol in an evaporating
100-120 dish or a beaker until a thermometer inserted in the
liquid registers a temperature of 180°. By this time,
most of the water present in ordinary glycerol will have
120-140 been driven off. When the vessel has cooled somewhat
transfer the anhydrous glycerol to a 500-ml. distilling flask and add 50 g. of the oxalic acid that has been drying in the oven since the start of the period. Fit the flask with a stopper and thermometer, the bulb of which is immersed in the reaction mixture. Support the flask by clamping it loosely at the neck, and connect it with a water-cooled condenser as shown in Figure 24b.

Heat the flask gently by waving a slightly luminous flame of the Bunsen burner beneath it, and agitate the flask frequently in order to obtain a uniform melt. The use of a wire gauze is not necessary. Raise the temperature of the reaction mixture to 110°-115° and maintain that temperature for about 7 minutes. Evolution of carbon dioxide begins at about 90°, and a large volume of the gas is given off during the period of heating at 110°-115°. Finally, apply heat at such a rate that the temperature of the reaction mixture rises from 115° to 130° during the course of 15 minutes.

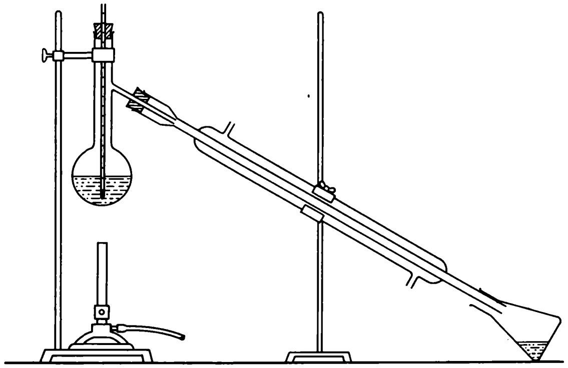


FIG. 24b. Distillation assembly for the preparation of formic acid from glycerol monooxalate.

During this period of time about 20 ml. of aqueous 140-155
formic acid (approximately 50 per cent formic acid)
collects in the receiver. To obtain a rough measure of
the amount of formic acid present in the distillate, dis- 155-165
solve 10 ml. of the distillate in 50 ml. of water, add a few drops of phenolphthalein indicator and determine how many ml. of 10 per cent sodium hydroxide solution are needed to neutralize the solution. Inasmuch as the result is only an approximate one in this crude titration, the use of a graduated cylinder suffices for the measurement of volumes.

QUESTIONS

1. What is the approximate pH of a 0.01 *M* solution of formic acid in water at 25°?
2. Calculate the approximate pH of a 0.01 *M* solution of sodium formate in water at 25°.
3. Would it be proper to say that glycerol functions

as a catalyst for the conversion of oxalic acid to formic acid? Explain.

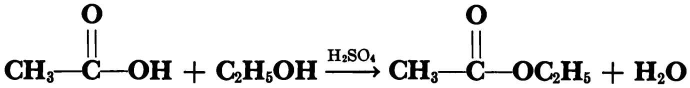
4. Why is less than the theoretical quantity of sodium dichromate used in the preparation of formic acid from methanol?

5. Is it likely that the aqueous distillate from the oxidation of methanol contains some formaldehyde? How would it be possible to separate formaldehyde from formic acid?

6. How may pure formic acid be obtained from an aqueous solution of the acid?

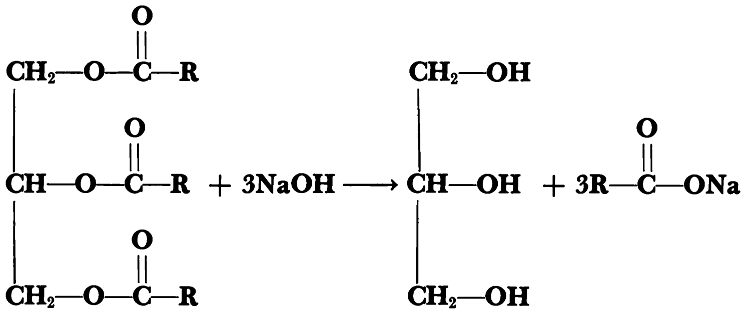
EXPERIMENT 26

I. Ethyl Acetate



$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-OH + C_2H_5OH \xrightarrow{H_2SO_4} CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-OC_2H_5 + H_2O$$

II. Preparation of Soap and Glycerol



Introduction. The reaction of a carboxylic acid with an alcohol to produce an ester plus water is known as the Fischer esterification reaction. A mineral acid, usually sulfuric acid or hydrochloric acid, is used as a catalyst. Since the reaction is reversible the law of mass action is applicable. This law states that *when equilibrium is attained in a reversible reaction at constant temperature, the product of the concentration of the substances formed, divided by the product of the concentration of the reacting substances, each concentration being raised to that power which is the coefficient of the substance in the chemical equation, is a constant.*

$$RCOOH + ROH \rightleftarrows RCOOR + H_2O$$

$$K = \frac{C_{ester} \times C_{water}}{C_{acid} \times C_{alcohol}}$$

For most Fischer esterification reactions, K has a value of approximately four ($K = 4$). Thus, if equal concentrations of alcohol and carboxylic acid are used, the yield of ester, under equilibrium conditions, is about 67 per cent. This yield may be improved either by use of an excess of one of the reactants or by removal of the water as it is formed.

Today's experiment consists of the preparation of ethyl acetate from acetic acid and ethyl alcohol, sulfuric acid being used as the catalyst. While the reaction mixture is being heated under reflux and also during the period that the product is being treated with anhydrous magnesium sulfate prior to distillation, one of the fats will be subjected to alkaline hydrolysis. It may be well to explain here that fats belong to the family of esters. Ordinary solid fats, such as tallow, consist chiefly of esters of glycerol with saturated carboxylic acids of high molecular weight. The glyceryl esters of unsaturated carboxylic acids are liquids at ordinary temperature and, although they too are fats, are usually referred to as *oils.* The alkaline hydrolysis of any fat results in the formation of glycerol and a soap; hence, the terms "alkaline hydrolysis" and "saponification" have become synonomous.

I. Ethyl Acetate

Procedure. Into a 500-ml. round-bottomed flask place **0-20**
60 g. (1 mole) of glacial acetic acid and 75 ml. of 95
per cent ethanol. Then, with constant shaking of the
flask, slowly add 10 ml. of concentrated sulfuric acid.
Connect the flask to a water cooled reflux condenser
and heat the mixture under reflux for 30 minutes on the **20-50**
steam bath.

[During the period of refluxing proceed with Part II.]

At the end of the period of refluxing, cool the flask **50-100**
and its contents (Note 1) and rearrange the flask and condenser for distillation, the connection being made by a bent glass tube about 7 mm. in diameter. A filter flask, whose side arm is joined to a rubber tube leading over the edge of the laboratory bench as shown in Figure 21 (page 64), is used as a receiver (Note 2). Put a few boiling chips (Note 3) in the flask and distill the ethyl acetate from the steam bath. A small residue of dilute sulfuric acid remains in the flask. The distillate (Note 4) is shaken with sodium carbonate solution until the upper layer is no longer acid to litmus. Separate the upper layer and wash it with a cool solution of 40 g. of calcium chloride in 40 ml. of water. Dry the product for 30 minutes over anhydrous magnesium sulfate
(Note 5). **100-130**

[While the product is being dried, continue with Part II.]

After the product has been dried over anhydrous **130-170**
magnesium sulfate, filter the liquid through a dry filter

and distill it (Note 6). Collect the portion boiling from 75°-78° separately. The fractions of higher and lower boiling point are fractionated again, the portion of boiling point 75°-78° being collected and added to the first lot (Note 7). Weigh your product and calculate the percentage yield based upon the amount of acetic acid used (Note 8).

In preparation for Part II of Experiment 28, the production of acetamide, place 50 ml. of ethyl acetate and 70 ml. of concentrated ammonium hydroxide in an Erlenmeyer flask and stopper the flask. The mixture should be permitted to stand for at least 48 hours before an attempt is made to isolate acetamide.

NOTES

1. If the flask and its contents are not cooled sufficiently, there will be some loss of material by evaporation.
2. Ethyl acetate is highly flammable. Therefore any vapors should be conducted off the table and toward the floor.
3. Broken pieces of clay plate may be used.
4. The distillate consists mainly of ethyl acetate, but impurities such as water, alcohol, ether, acetic acid and sulfurous acid are also present.
5. If no anhydrous magnesium sulfate is on hand, it can be prepared by heating 20 g. of Epsom salts in an evaporating dish.
6. It would be preferable to use a small column, such as a Vigreux column (see page 14), for this distillation.
7. Pure ethyl acetate boils at 77°. However, ethyl acetate forms an azeotrope of minimum boiling point with water and also with ethanol. Furthermore, the three-component system, ethyl acetate-ethanol-water, forms a ternary azeotrope of minimum boiling point. The compositions (in percentage by weight) of these three azeotropes and their boiling points are as follows:

Ethyl Acetate 93.9%—Water 6.1%, b.p. 70.4°
Ethyl Acetate 69.1%—Ethanol 30.9%, b.p. 71.8°
Ethyl Acetate 83.3%—Ethanol 8.9%—Water 7.8%, b.p. 70.3°

The necessity for removing water and ethanol from the crude ethyl acetate is obvious. If your product should distill at 70°-72°, dry it again with anhydrous magnesium sulfate and refractionate it.

8. Ordinarily the yield is about 50 g.

II. PREPARATION OF SOAP AND GLYCEROL

20-40 *Procedure.* Weigh 25 g. of cottonseed oil, lard, or other fat, into a beaker and add to it 25 ml. of ethyl alcohol and 6 g. of sodium hydroxide dissolved in 25 ml. of water. Set the beaker in a pan of hot water placed
40-100 on a wire gauze over a Bunsen burner (Note 1). Heat the water occasionally in order to maintain its temperature at 80°-90° (Note 2). Stir the mixture frequently and continue heating for at least an hour.

[In the meantime, proceed with Part I.]

If so much of the water and alcohol should evaporate that the contents of the flask become almost solid, add a little distilled water. After this period of heating add **100-130**
200 ml. of saturated salt solution. Cool the mixture and filter it through a double thickness of cheesecloth. Rinse the soap on the filter with 50 ml. of cold water and preserve the filtrate and washings for the recovery of glycerol. Press the soap into a small evaporating dish which will serve as a mold.

Recovery of Glycerol. Separate the salt solution, which contains the glycerol, from particles of soap by filtration. Neutralize or slightly acidify the filtrate with hydrochloric acid and evaporate it to dryness. Remove the glycerol from the salt by extraction with 20 ml. of absolute ethyl alcohol. Decant the alcohol solution from the salt and evaporate the alcohol on the steam bath. A small residue of glycerol remains.

NOTES

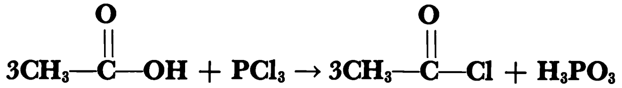
1. The apparatus should be mounted on a ring stand, all of the equipment being adequately supported.
2. Keep the flame of the Bunsen burner well removed from the ethyl acetate being prepared in Part I.

QUESTIONS

1. Write the equation for the preparation of soap, assuming that the fat is pure glyceryl stearate.
2. How would you expect an aqueous solution of soap to react toward litmus?
3. What happens if a soap solution is treated with solutions of copper sulfate, magnesium sulfate, or calcium chloride?
4. If soap is dissolved in hot water, then cooled and acidified with hydrochloric acid, what is the nature of the precipitate which forms?
5. Name three acids which can usually be obtained from soap.
6. Give a qualitative explanation for the ability of soap to bring about formation of an emulsion of water and oil.
7. What excess of one mole of ethanol was used in the preparation of ethyl acetate? Why is an excess of one of the reagents employed?
8. Suggest several ways in which the equilibrium reaction of a Fischer esterification may be shifted to the right.

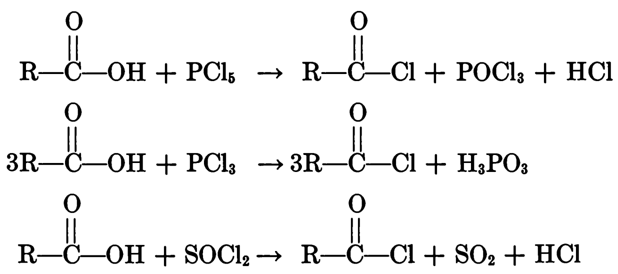
EXPERIMENT 27

Preparation and Properties of Acetyl Chloride



$$3CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-OH + PCl_3 \rightarrow 3CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-Cl + H_3PO_3$$

Introduction. Carboxylic acids may be converted to acid chlorides by treatment with phosphorus pentachloride, phosphorus trichloride, or thionyl chloride. Equations for the three reactions are given below:



$$R-\overset{\overset{\displaystyle O}{\|}}{C}-OH + PCl_5 \rightarrow R-\overset{\overset{\displaystyle O}{\|}}{C}-Cl + POCl_3 + HCl$$

$$3R-\overset{\overset{\displaystyle O}{\|}}{C}-OH + PCl_3 \rightarrow 3R-\overset{\overset{\displaystyle O}{\|}}{C}-Cl + H_3PO_3$$

$$R-\overset{\overset{\displaystyle O}{\|}}{C}-OH + SOCl_2 \rightarrow R-\overset{\overset{\displaystyle O}{\|}}{C}-Cl + SO_2 + HCl$$

Inasmuch as the acid chlorides are generally purified by distillation from the reaction mixture, the choice of reagent for the preparation of a particular acid chloride is dictated, at least in part, by the ease of separation of the acid chloride from the reagent or by-products.

For example, when phosphorus pentachloride is used as the reagent, the inorganic by-product is phosphorus oxychloride, which has a boiling point of 107°. The major purification problem, therefore, is the separation of the acid chloride from phosphorus oxychloride by fractional distillation. Obviously, phosphorus pentachloride would not be used to convert a carboxylic acid to the corresponding acid chloride if the latter should have a boiling point close to 107°.

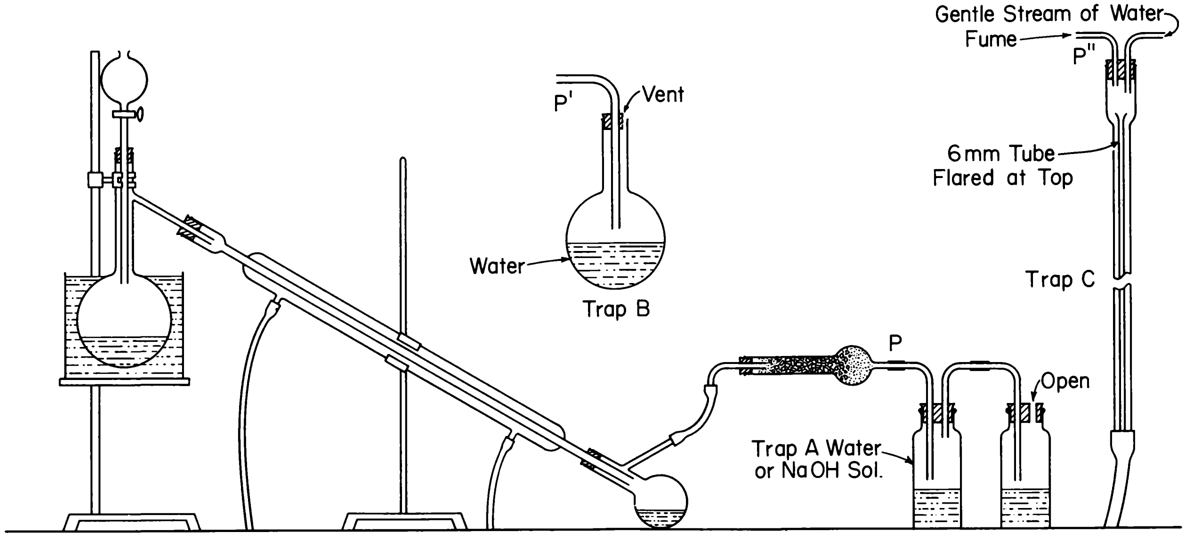


FIG. 25. Apparatus for the preparation and distillation of acetyl chloride with absorption of hydrogen chloride (three different types of trap shown).

Similarly, thionyl chloride, having a boiling point of 79°, would not be used to prepare an acid chloride having about the same boiling point. Although the inorganic by-products are gases, the resulting acid chloride must be separated from unreacted thionyl chloride by fractional distillation.

In the major part of today's experiment, acetyl chloride will be prepared by the action of phosphorus trichloride on acetic acid. In the purification step, acetyl chloride (boiling point 52°) is readily separated from a small amount of unreacted phosphorus trichloride (boiling point 76°) and orthophosphorous acid (decomposes at 200°) by distillation. The reactions of acetyl chloride with water, alcohols, and amines will be investigated in a qualitative manner during the latter part of the laboratory period.

I. PREPARATION OF ACETYL CHLORIDE

Procedure. Assemble the apparatus as shown in Figure 25. The escaping hydrogen chloride must be absorbed by a suitable trap such as A, B, or C. If type A is used be sure that the glass tubes leading into the bottles or flasks terminate about 1 cm. above the surface of the sodium hydroxide solution; otherwise there is

0-30

danger that the solution might be sucked back into the acetyl chloride causing a violent reaction. A similar precaution applies to type B. In type C the stream of water entering the top of the vertical tube must not exceed the rate of flow from the bottom of the tube. The idea is simply to keep a moving film of water spread over a large surface for absorption of the hydrogen chloride.

In all cases a tube of calcium chloride protects the acetyl chloride in the receiving flask from the moist vapors in the absorption apparatus. Note also that the pan of water completely covers the bulb of the distilling flask.

To 60 g. (1 mole, 58 ml.) of glacial acetic acid contained
30-70 in the 500-ml. distilling flask add slowly from
the dropping funnel 30 ml. of phosphorus trichloride
and shake the flask to mix the reactants. Warm the
water bath to 40°-50° until the evolution of hydrogen
chloride ceases. By this time the liquid will have separated
into two layers. Heat the water bath to boiling
and continue the heating until all of the acetyl chloride
70-130 has distilled. Redistill the acid chloride and collect the
fraction boiling from 50°-60°. Weigh the distillate and
calculate the percentage yield.

While the acetyl chloride is being purified by distillation, answer some of the questions at the end of the assignment.

II. Properties of Acetyl Chloride

Procedure. Carry out the following experiments in the hood.

(*1*) *Hydrolysis.* Carefully add 1 ml. of acetyl chloride
130-135 to 5 ml. of water. Record your observations, and
write the equation for the reaction.

(*2*) *Esterification.* Cautiously add 1 ml. of acetyl
chloride to 2 ml. of ethyl alcohol. Pour the resulting 135-140
solution into 50 ml. of water and note the odor. Write
the equation for the reaction.

Carry out the same procedure with amyl alcohol in 140-145
place of ethyl alcohol. Equation.

(*3*) *Reaction with Aniline.* Slowly mix 1 ml. of
acetyl chloride with an equal volume of aniline. When 145-160
the initially vigorous reaction has subsided, add 15 ml.
of water to the tube and shake the mixture vigorously.
To crystallize the precipitate which has formed heat the
contents of the tube to boiling, filter, and allow the filtrate
to cool. Collect the crystals by filtration, press out
a few mg. on a clay plate and determine the melting
point. What is the product? Write the equation for the
reaction.

QUESTIONS

1. Would it be wise to prepare benzoyl chloride (boiling point 199°) by reaction of benzoic acid with phosphorus trichloride? Would the use of phosphorus pentachloride be more satisfactory? Explain your answers.

2. Look up in a handbook or elsewhere the boiling, sublimation, or decomposition points of phosphorus pentachloride, phosphorus oxychloride, phosphorus trichloride, orthophosphorous acid, and thionyl chloride.

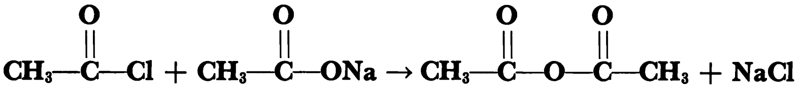
3. In the preparation of acid chlorides, why is it not practical to destroy excess of reagents (phosphorus pentachloride, phosphorus trichloride, and thionyl chloride) by pouring the reaction mixtures into water?

4. Write equations for the reactions of acetyl chloride with each of the following reagents:

(a) *n*-amylamine
(b) diethylamine
(c) *n*-butyl alcohol
(d) ethanolamine

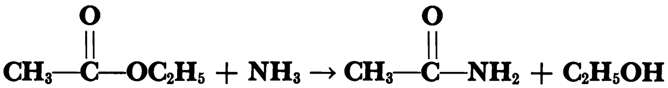
EXPERIMENT 28

I. Preparation of Acetic Anhydride



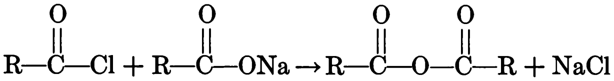
$$CH_3-\overset{O}{\overset{\|}{C}}-Cl + CH_3-\overset{O}{\overset{\|}{C}}-ONa \rightarrow CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3 + NaCl$$

II. Preparation of Acetamide



$$CH_3-\overset{O}{\overset{\|}{C}}-OC_2H_5 + NH_3 \rightarrow CH_3-\overset{O}{\overset{\|}{C}}-NH_2 + C_2H_5OH$$

Introduction. The anhydrides of carboxylic acids are usually obtained in the laboratory by reaction of the acid chlorides with the sodium salts of the acids. Acid anhydrides are useful acylating agents.



$$R-\overset{O}{\overset{\|}{C}}-Cl + R-\overset{O}{\overset{\|}{C}}-ONa \rightarrow R-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-R + NaCl$$

They undergo reaction with alcohols to produce esters, with ammonia or amines to produce amides, and with aromatic hydrocarbons, in the presence of anhydrous aluminum chloride, to give ketones.

In the experiment to be carried out during this laboratory period, acetic anhydride will be prepared by reaction of acetyl chloride with sodium acetate. After the acetic anhydride has been purified by distillation, some of the characteristic reactions of acid anhydrides will be studied in a qualitative manner. At the same time, acetamide will be prepared according to the directions given in Part II, and some of the characteristic properties of the amide will be tested.

I. Acetic Anhydride

0-30 *Procedure.* Fit a 500-ml. distilling flask with a condenser and dropping funnel as shown in Figure 26a.

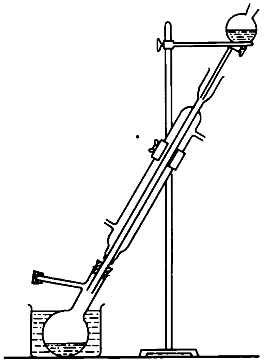


Fig. 26a. Reflux assembly for preparation of acetic anhydride.

Notice that there is no stopper in the top of the condenser. Introduce 35 g. of freshly fused sodium acetate into the distilling bulb and pour 20 ml. (22 g.) of acetyl chloride into the dropping funnel. Immerse the bulb of the distilling flask in cold water and allow about one fourth of the acetyl chloride to flow slowly into it. Do not allow the mixture to become hot enough to boil. Agitate the mixture as much as possible, and, after a few minutes, disconnect the flask from the condenser and shake it carefully to obtain a uniform mixture. When the reaction has subsided, add another portion of acetyl chloride, cooling the flask and shaking it as before.

When all of the acetyl chloride has been added, arrange the apparatus as shown in Figure 26b. The distillate is protected from the moist vapors of the 5 per cent solution of sodium hydroxide in the absorption bottle by a tube of calcium chloride.

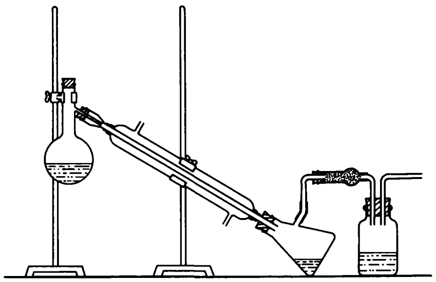


Fig. 26b. Apparatus for distillation of acetic anhydride with absorption of volatile acids.

Heat the flask with a slightly luminous flame until 30-60
all of the acetic anhydride has distilled. The distillate consists of acetic anhydride containing a little acetyl chloride. Transfer the distillate to a clean distilling flask and mix it with 2 g. of fused sodium acetate and redistill it in order to convert any remaining acetyl chloride to the anhydride. Use a thermometer during the second distillation to determine the boiling point of the liquid (Note 1). Weigh your product and calculate the percentage yield on the basis of the acetyl chloride used.

[Proceed to Part II of today's assignment. While the 60-160
acetamide is being purified by distillation, carry out the qualitative experiments described below.]

Properties of Acetic Anhydride

The following short experiments show the characteristic properties of acetyl chloride.

(*1*) *Comparative Ease of Hydrolysis of Acetyl Chloride, Acetic Anhydride, and Ethyl Acetate.* Place 1 ml. of acetyl chloride, acetic anhydride and ethyl acetate into each of three dry test tubes, respectively. Add 5 ml. of water cautiously to each tube. Compare the violence of the reaction in each case. Write equations for the reactions.

(*2*) *Reaction of Acetic Anhydride with Ethyl Alcohol.* Add 1 ml. of acetic anhydride to 5 ml. of ethyl alcohol. After 2 minutes pour the solution into 50 ml. of water and note the odor. Write an equation for the reaction.

(*3*) *Reaction of Acetic Anhydride with Aniline.* Slowly add 1 ml. of acetic anhydride to 2 ml. of aniline. Add 15 ml. of water to the tube and shake it vigorously. Note the formation of a solid product. Recrystallize this solid by heating the contents of the tube to boiling, then filter and allow the filtrate to cool. Collect the crystalline product by filtration and determine its melting point (Note 2). Write an equation for the reaction.

II. ACETAMIDE

60-120 *Procedure.* Transfer the reaction mixture of ethyl acetate and ammonia water from Part I of Experiment 26 to a 500-ml. distilling flask (Note 3). Add a few boiling chips, and connect the receiver in such a way that the escaping ammonia gas will be absorbed in dilute sulfuric acid solution, Figure 25, page 88 (Note 4). (The calcium chloride tube shown in Figure 25 is not needed in the present experiment.)

Distill the liquid, using a water condenser, until the thermometer reading reaches 180°. At this point, interrupt the distillation, replace the water condenser with an air condenser, and use a small flask as a receiver.

It will also be of advantage to transfer the acetamide solution to a 100-ml. distilling bulb before carrying out the rest of the distillation. Proceed with the distillation, heating the flask directly with a slightly luminous Bunsen flame, and collect the distillate in two fractions: I, 150°-210° and II, 210°-225°. The second fraction is mainly acetamide (Note 5). The liquid collected between 150° and 210° should be refractionated and the acetamide thus obtained added to the first lot.

Throughout the distillation any acetamide that solidifies in the condenser should be removed by warming the tube. Otherwise the flask may burst if the tube becomes clogged. Crystallize a small portion of the acetamide from chloroform and determine its melting point (Note 6). Determine the percentage yield of the product. Note the odor of your sample of acetamide. This odor is due to the presence of an impurity, as pure acetamide is odorless. Save the bulk of your acetamide for Experiment 29.

Properties of Acetamide

120-160 The following qualitative tests are designed to demonstrate some of the characteristic reactions and properties of amides in general and acetamide in particular.

(*1*) *Hydrolysis in Acid Solution.* Boil about 1 g. of acetamide with 10 ml. of a 10 per cent solution of sulfuric acid. Test the vapor with litmus paper. Write the equation for the reaction.

(*2*) *Hydrolysis in Alkaline Solution.* Boil about 1 g. of acetamide with 10 ml. of a 10 per cent solution of sodium hydroxide. Test the escaping gas with litmus paper. Write the equation for the reaction.

(*3*) *Reaction of Acetamide with Nitrous Acid.* Dissolve 1 g. of acetamide in 10 ml. of water. Acidify the solution by the addition of 1 ml. of concentrated hydrochloric acid and add dropwise a 5 per cent solution of sodium nitrite. Note the evolution of a gas. Write the equation for the reaction.

(*4*) *Test with Litmus.* Test a solution of acetamide in water with litmus paper. How do you explain your observed result?

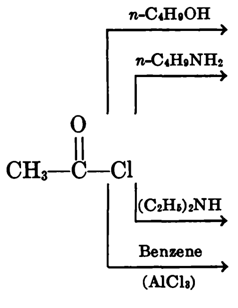
NOTES

1. The boiling point of acetic anhydride is about 137° at atmospheric pressure.
2. The melting point of acetanilide is 114°.
3. This should be a homogeneous solution after the 48-hour reaction period.
4. As an alternative method of absorbing the ammonia, a trap such as B or C of Figure 25 on page 88 may be used.
5. The boiling point of acetamide is 222°.
6. The melting point of acetamide is 82°.

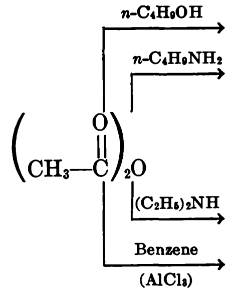
QUESTIONS

1. Why is an excess of sodium acetate employed in the preparation of acetic anhydride? How many grams of sodium acetate in excess of the theoretical quantity were used in today's experiment?

2. Complete the following outline equations:



$CH_3-\overset{\overset{O}{\|}}{C}-Cl$



$\left(CH_3-\overset{\overset{O}{\|}}{C}\right)_2O$

3. Explain why acetyl chloride is more reactive than acetic anhydride in each of the reactions given in your answer to question 2.

4. Would it be reasonable to look upon both acetyl chloride and acetic anhydride as being essentially acid anhydrides?

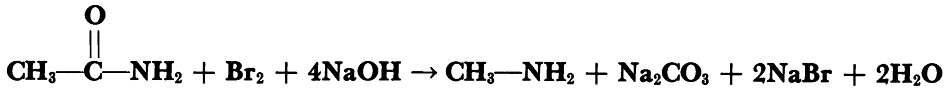
5. Write a detailed mechanism for the reaction of ethyl acetate with ammonia to produce acetamide plus ethanol.

6. Why is acetamide essentially neutral? Keep in mind the fact that ammonia and amines are basic compounds; i.e., aqueous solutions of these compounds turn litmus paper blue.

7. Does the evolution of ammonia on boiling an amide with sodium hydroxide solution serve as a qualitative test to distinguish amides from all other classes of neutral compounds which contain nitrogen? Explain.

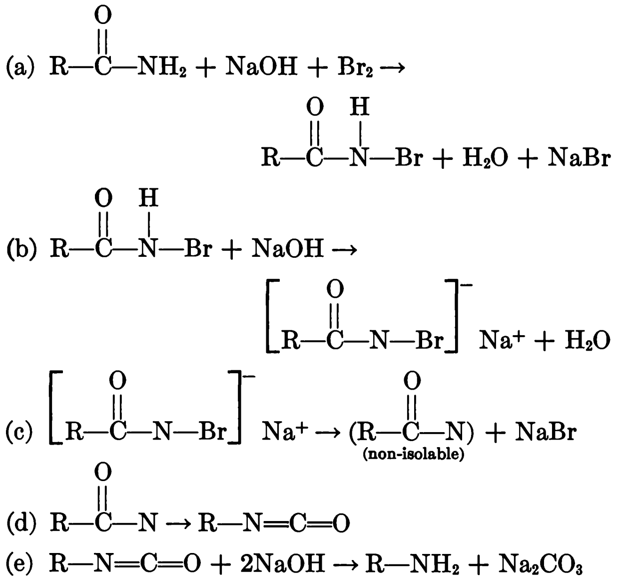
EXPERIMENT 29

Preparation and Properties of Methylamine



$$CH_3-\overset{\overset{O}{\|}}{C}-NH_2 + Br_2 + 4NaOH \rightarrow CH_3-NH_2 + Na_2CO_3 + 2NaBr + 2H_2O$$

Introduction. Primary aliphatic amines are frequently prepared from acid amides by application of the Hofmann hypobromite reaction. A molecular rearrangement occurs in one step of the overall process; specifically, an alkyl group migrates from the carbon atom to which it is bonded to an adjacent electron-deficient nitrogen atom. The steps in the accepted mechanism for the Hofmann hypobromite reaction are shown below:



$$(a)\ R-\overset{\overset{O}{\|}}{C}-NH_2 + NaOH + Br_2 \rightarrow R-\overset{\overset{O}{\|}}{C}-\overset{\overset{H}{|}}{N}-Br + H_2O + NaBr$$

$$(b)\ R-\overset{\overset{O}{\|}}{C}-\overset{\overset{H}{|}}{N}-Br + NaOH \rightarrow \left[R-\overset{\overset{O}{\|}}{C}-N-Br\right]^- Na^+ + H_2O$$

$$(c)\ \left[R-\overset{\overset{O}{\|}}{C}-N-Br\right]^- Na^+ \rightarrow \underset{\text{(non-isolable)}}{(R-\overset{\overset{O}{\|}}{C}-N)} + NaBr$$

$$(d)\ R-\overset{\overset{O}{\|}}{C}-N \rightarrow R-N=C=O$$

$$(e)\ R-N=C=O + 2NaOH \rightarrow R-NH_2 + Na_2CO_3$$

During the latter part of the distillation of methylamine, some characteristic reactions of primary aliphatic amines will be investigated.

I. Preparation of Methylamine

0-30 *Procedure.* CAUTION: Bromine vapor must not be allowed to escape into the laboratory. Await the instructor's directions.

Into a 500-ml. round-bottomed flask place 15 g. of acetamide and 12 ml. (37 g.) of bromine. Add to this mixture a cold solution of 10 g. of sodium hydroxide in 120 ml. of water in portions of about 5 ml. at a time. After each addition wait until the reaction ceases before adding more alkali. The flask should be shaken and cooled continuously in cold water. When all of the alkali has been added, the liquid should have a bright yellow color due to the formation of acetobromoamide, $CH_3CONHBr$. If any precipitate should form during this process, add a little water to bring it into solution because it might clog the dropping funnel in the next part of the experiment.

Fit a 500-ml. distilling flask with a thermometer, dropping funnel, and condenser as shown in Figure 27.

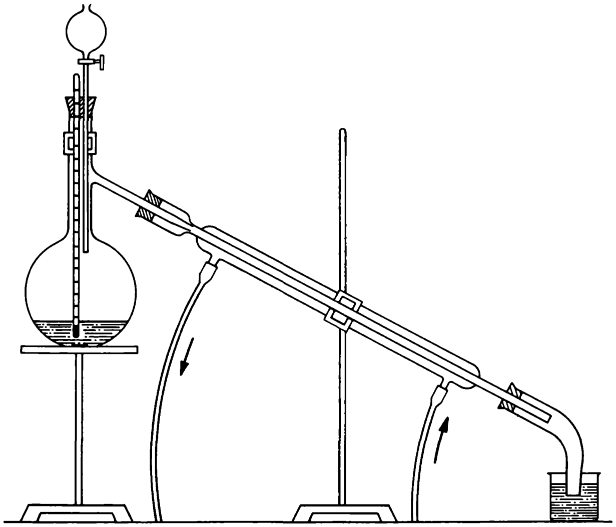


Fig. 27. Apparatus for preparation of methylamine, the gaseous product being collected in water or dilute hydrochloric acid.

Pour into the distilling flask a solution of 25 g. of sodium hydroxide in 150 ml. of water. Transfer the solution of acetobromoamide prepared as described above to the separatory funnel and allow it to drop slowly into the sodium hydroxide solution. Meanwhile shake the flask frequently and warm its contents to a temperature of 80°-90°. The reaction is exothermic and the application of heat should be stopped if the solution begins to boil.

When all of the acetobromoamide solution has been added, introduce a few chips of unglazed porcelain and heat the flask gently over an asbestos gauze. Methylamine escapes as a gas along with water vapor and a little ammonia. During the first 5 minutes of the distillation collect the methylamine in 25 ml. of distilled water. Continue the distillation, absorbing the remainder of the methylamine in 25 ml. of dilute (1-1) hydrochloric acid solution.

[During this latter period of distillation and also while
the hydrochloric acid solution is being evaporated to 60-120
dryness (see below), begin Part II of the assignment.]

When the distillate plus the original hydrochloric 120-160
acid solution amounts to 100 ml., the distillation is

stopped, and the hydrochloric acid solution is evaporated to dryness on the water bath. Transfer the residue of methylamine hydrochloride, which also contains some ammonium chloride, to a small flask fitted with a glass tube about 60 cm. in length which serves as an air condenser, and boil it for 2 minutes with 25 ml. of absolute ethanol. Remove the solution of methylamine hydrochloride (methylammonium chloride) from the undissolved ammonium chloride by filtration. Evaporation of the alcohol on the steam bath leaves the methylamine hydrochloride as a white solid.

II. PROPERTIES OF METHYLAMINE

60-160 *Procedure.* Make use of the 25 ml. of methylamine solution obtained from the first part of the distillate of Part I for the following experiments.

1. Tests for Primary Amines

The following reactions represent convenient qualitative tests for the detection of primary amines in general. Of course, the specific reactions will be carried out on methylamine.

(*a*) *Nitrous Acid.* To 5 ml. of the methylamine solution contained in a test tube add sufficient dilute hydrochloric acid to make the solution acid to litmus. Add dropwise about 2 ml. of a 5 per cent solution of sodium nitrite. If no gas evolution is observed, warm the test tube gently. Write the equation for the reaction.

(*b*) *Isocyanide Reaction.* Add 3 ml. of a 10 per cent solution of sodium hydroxide and 2 drops of chloroform to 1 ml. of the methylamine solution contained in a test tube. Warm the mixture and note the odor. Write the equation for the reaction.

(*c*) *Complex Ion Formation with Cupric Ion.* To 3 ml. of copper sulfate solution add 1 ml. of methylamine solution. Note the change in color of the copper sulfate solution. Write the equation for the reaction.

2. Methylamine as a Base

Amines in general are moderately strong organic bases. The following experiments illustrate this property of methylamine.

(*a*) *Behavior of Aqueous Solution Toward Litmus.* Place a drop of the methylamine solution on a strip of red litmus paper. Note the color change. Write the equation for the reaction of methylamine with water.

(*b*) *Reaction with Hydrogen Chloride.* Wet a glass rod with the methylamine solution and bring the rod close to an open bottle of concentrated hydrochloric acid. Note the result, and write the equation for the reaction.

(*c*) *Reaction with Ferric Chloride.* To 3 ml. of ferric chloride solution add methylamine solution until a precipitate appears. Write the equation for the reaction.

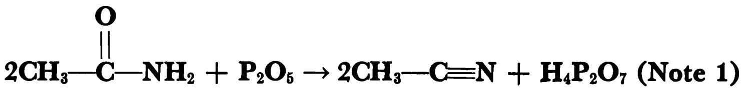
[During the remaining part of the laboratory period answer the questions that follow.]

QUESTIONS

1. What volume (S.T.P.) of methylamine gas is theoretically obtainable from 14.75 g. of acetamide by application of the Hofmann hypobromite reaction?
2. If the theoretical amount of methylamine obtainable from 14.75 g. of acetamide by the Hofmann hypobromite reaction were dissolved in sufficient distilled water to bring the total volume of the solution to 100 ml., what would be the molar concentration of methylamine in this solution?
3. What volume of 0.5 *M* hydrochloric acid solution would be required to neutralize the 100 ml. of solution described in question 2?
4. Write balanced equations for the preparation of isopropylamine from isobutyramide and of aniline from benzamide by the Hofmann hypobromite reaction.
5. What is the approximate pH of a 0.1 *M* solution of ethylamine at 25°? $K_B = 5.6 \times 10^{-4}$.
6. What qualitative tests may be used to distinguish among primary, secondary, and tertiary aliphatic amines?
7. In what way does an aqueous solution of a quaternary ammonium hydroxide differ from an aqueous solution of a primary, secondary, or tertiary amine?
8. How may a water-insoluble amine be isolated when it is present in a mixture with several neutral, water-insoluble organic compounds?

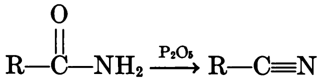
EXPERIMENT 30

Preparation and Properties of Acetonitrile



$$2CH_3{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}NH_2 + P_2O_5 \rightarrow 2CH_3{-}C{\equiv}N + H_4P_2O_7 \text{ (Note 1)}$$

Introduction. Nitriles are neutral compounds that may be prepared by reaction of primary alkyl halides with sodium cyanide or by dehydration of acid amides. The latter procedure will be followed in the experiment for today.



$$R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}NH_2 \xrightarrow{P_2O_5} R{-}C{\equiv}N$$

A nitrile may be hydrolyzed either in acid or alkaline medium to the carboxylic acid and ammonia. It is also possible in an acid-catalyzed hydrolysis of a nitrile to stop the reaction at an intermediate stage, thus permitting isolation of the acid amide. Reduction of nitriles affords primary amines. Several of these typical reactions will be carried out in a qualitative manner in Part II of this day's assignment.

I. Preparation of Acetonitrile

Procedure. Place 30 g. of phosphoric anhydride **0-30** (Note 2) in a dry, 125-ml. distilling flask, and add 20 g. of dry acetamide. Mix the compounds as thoroughly as possible by shaking the flask. Attach a water-cooled condenser to the side arm and heat the flask gently with a small, slightly luminous flame. The mixture tends to foam during this operation. After the mixture has been heated in this manner for about 5 minutes, gradually **30-60** raise the temperature until the nitrile distills. To the distillate add one half of its volume of water and about 10 g. of potassium carbonate in small portions, with swirling and cooling of the flask and its contents in a pan of water. Decant the mixture of liquids into a separatory funnel. Draw off the lower aqueous layer and discard it.

Transfer the upper layer of acetonitrile to a small dis- **60-90** tilling flask, add about 1 g. of phosphoric anhydride, 2 or 3 boiling chips, and then distill the liquid. Collect the distillate having a boiling point range of 77°-82° (Note 3) in a weighed bottle. Determine the weight of the distillate and calculate the percentage yield.

NOTES

1. Actually a mixture of phosphoric acids is produced, but the major component is pyrophosphoric acid, $H_4P_2O_7$.
2. Phosphoric anhydride can cause a bad burn if it gets on the skin. In case of accident, wash the area well with water and apply a paste of sodium bicarbonate.
3. The boiling point of acetonitrile is 81°. The yield usually amounts to about 8-10 g.

II. Properties of Acetonitrile

1. Hydrolysis of Acetonitrile

(*a*) *Acid Solution.* To 10 ml. of a 25 per cent sul- **90-115** furic acid solution add 1 ml. of acetonitrile and heat the solution to boiling. Test the escaping vapor with litmus paper. Cool the solution and make it alkaline by addition of sodium hydroxide solution. Heat the solution and test the escaping gas with litmus paper. Write equations for the reactions described above.

(*b*) *Alkaline Solution.* Add 1 ml. of acetonitrile to **115-125** 10 ml. of a 10 per cent sodium hydroxide solution. Heat the solution and test the escaping gas with litmus paper. Write the equation for the reaction.

2. Reduction of Acetonitrile **125-140**

To 10 ml. of commercial absolute ethanol add 1 ml. of acetonitrile. Add a piece of sodium about one half the size of a pea. When the reaction subsides and the sodium has gone into solution, cool the mixture and add a second piece of sodium. After the sodium has dissolved, apply the isocyanide test for a primary amine to the resulting solution (see page 94). Write equations for the reactions described above.

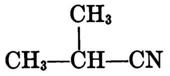
[During the remainder of the laboratory period answer the questions that follow.]

QUESTIONS

1. Write equations to show how *n*-butyl alcohol may be converted into (a) *n*-butyronitrile and (b) *n*-valeronitrile.
2. Give both "nitrile" and "cyanide" names to each of the following compounds:

(a) $CH_3CH_2CH_2CN$

(b)

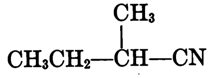


$$CH_3{-}\overset{\overset{\displaystyle CH_3}{|}}{C}H{-}CN$$

(c) $(CH_3)_3C{-}CN$

(d) $CH_3CH(CH_3)CH_2CN$

(e)



$$CH_3CH_2{-}\overset{\overset{\displaystyle CH_3}{|}}{C}H{-}CN$$

(f) $CH_3{-}(CH_2)_8{-}CN$

3. Can trimethylacetonitrile be prepared by reaction of *t*-butyl chloride with sodium cyanide? Write equations for an alternative method of preparation of the nitrile from *t*-butyl chloride.
4. How may lactic acid be prepared from acetaldehyde?
5. Would it be best to employ the nitrile route or the Grignard route for the conversion of 4-chloro-1-butanol to 5-hydroxy-pentanoic acid? Explain.
6. Write equations to show how *n*-propyl alcohol may be converted to (a) *n*-butylamine, (b) ethylamine, and (c) *n*-propylamine.

EXPERIMENT 31

Some Chemical Properties of Ethylene Glycol and Glycerol

Introduction. Many of the chemical properties of 1,2-diols are simply the properties to be expected of alcohols in general. However, there are other reactions which are specific for the 1,2-diol unit. For example, the formation of esters by the action of acid chlorides, acid anhydrides, or carboxylic acids under the catalytic influence of mineral acids and the liberation of hydrogen with formation of the corresponding alkoxide salts on treatment with metallic sodium represent reactions common to most alcohols, whereas the oxidative cleavage of 1,2-diols to aldehydes and/or ketones by the action of periodic acid or lead tetraacetate and the formation of relatively highly acidic complexes with boric acid represent specific reactions of the 1,2-diol group.

The outstanding physical properties of 1,2-diols are their relatively high boiling points, viscosities, and solubilities in water. All of these characteristics are a direct consequence of hydrogen bonding. In order to separate the diol molecules in the process of distillation, it is necessary to supply sufficient heat to overcome the electrostatic attraction, mainly owing to hydrogen bonding, between the molecules.

Thus it is apparent why glycols (diols) have decidedly higher boiling points than most other organic compounds of about the same molecular weight. Glycols have higher boiling points than simple alcohols of about the same molecular weight because glycols, having two hydroxyl groups per molecule, can enter into a greater degree of hydrogen bonding than the simple alcohols.

The relatively high viscosity of glycols reflects the fact that two glycol molecules can slide by one another only with difficulty owing to the making and breaking of hydrogen bonds in the process of flow; the hydroxyl groups attached to the glycol molecule can be likened to small hooks which, by forming hydrogen bonds, tend to catch the similar hooks attached to the other molecules and thus impede the passage of one molecule past the other. The relatively high solubility of glycols in water is the consequence of the favorable decrease in energy (increase in stability) of the system when glycol molecules are attracted to water molecules with formation of hydrogen bonds.

I. Properties of Ethylene Glycol

Procedure. Distill 50 ml. of commercial ethylene gly-
0-20 col (or Eveready, Prestone or Zerex) from a 125-ml.
distilling flask connected to an air condenser. Collect the portion boiling from 185°-200° for use in the following experiments:

(*a*) *Taste.* Taste a drop of ethylene glycol. How would you classify the taste?

20-40 (*b*) *Viscosity.* Pour 15-ml. samples of ethyl alcohol, ethylene glycol, and glycerol into small beakers and allow the samples to attain room temperature if they are not already at that temperature. Draw the ethyl alcohol into a 10-ml. pipette up to the mark and then determine the number of seconds required for the alcohol to flow from the pipette. Use a stop watch, if one is available, or use a watch having a second hand to time the flow. Make a duplicate observation. Wash the pipette with water and acetone and dry it either by blowing air through it from the compressed air line or by warming it gently over the Bunsen burner while drawing air through it by means of a tube attached to the aspirator. Repeat the experiment, first with ethylene glycol and then with glycerol. Record the relative viscosities of these three liquids.

(*c*) *Ethylene Glycol as an "Anti-freeze" Compound.* **45-65** Fill a 500-ml. beaker with an intimate mixture of salt and crushed ice and stir the mixture for a few minutes. The temperature of this freezing mixture will be between −15° and −20°. Add 2 ml. of ethylene glycol to 8 ml. of water contained in a test tube and set the tube in the freezing bath for several minutes. Does the solution freeze? Try several other concentrations and record your observations.

(*d*) *Action of Metallic Sodium.* Add a piece of so- **65-75** dium about the size of a small pea to 3 ml. of ethylene glycol. Note the result. Write the equation for the reaction. To destroy any unreacted sodium, add a few ml. of alcohol, wait until the reaction subsides, then pour the mixture into the sink.

(*e*) *Action of Acetyl Chloride.* In the hood add 2 **75-85** ml. of acetyl chloride dropwise to an equal volume of ethylene glycol. Pour the product into 50 ml. of water contained in a small beaker. Note the sweet odor of ethylene glycol diacetate. Write the equation for the reaction.

(*f*) *Benzoylation* (*Schotten-Baumann Reaction*). **85-105** Carry out this experiment in the hood. Dissolve 2 ml. of ethylene glycol in 8 ml. of 10 per cent sodium hydroxide solution contained in a test tube and add a total of 2 ml. of benzoyl chloride in 0.5-ml. portions, with shaking of the tube for about a minute after each addition. Pour the reaction mixture into 10 ml. of cold water and collect the solid ester by filtration. Crystallize the ester from 50 per cent ethanol and determine its melting point. Look up the melting point of ethylene glycol dibenzoate and record this value also. Write the equation for the reaction.

(*g*) *Oxidation to Oxalic Acid.* Add 3 drops (no **105-115** more) of ethylene glycol to 3 ml. of concentrated nitric acid contained in a test tube. Carry the tube to the hood and warm the solution until the evolution of brown fumes begins. Remove the flame and allow the reaction to proceed spontaneously. When the evolution of oxides of nitrogen ceases, pour the solution into 10 ml. of water and neutralize it with ammonium hydroxide solution. Add a few drops of calcium chloride solution and note the result. Write equations for the three reactions involved in this experiment.

115-130 (*h*) *Cleavage by Action of Periodic Acid.* Dissolve 0.1 g. of para-periodic acid (H_5IO_6) in 20 ml. of distilled water. Place 2 ml. of this reagent in a small test tube, add 1 drop of concentrated nitric acid, and shake the solution thoroughly. Add 1 drop of ethylene glycol to the solution and shake the tube for 15 seconds. Then add 2 drops of 3 per cent silver nitrate solution. The instantaneous formation of a white precipitate of silver iodate ($AgIO_3$) indicates that the ethylene glycol has been cleaved to two molecules of formaldehyde by the periodic acid, which is thereby reduced to iodic acid. Repeat this test with glycerol and D(+)-glucose. Write equations for the sequence of reactions starting with periodic acid and ethylene glycol.

II. PROPERTIES OF GLYCEROL

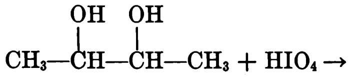
130-140 (*a*) *Solubility.* Test the solubility of glycerol in water, ether, and petroleum ether. Record your results. How does glycerol compare with ethylene glycol with regard to its solubility in these solvents?

140-150 (*b*) *Formation of a Complex with Boric Acid.* Add a few drops of phenolphthalein indicator solution to 5 ml. of 1 per cent borax solution, and note the color. Add 1 ml. of glycerol to the solution and note the change in color. Explain this result by writing equations for the reactions taking place.

150-160 (*c*) *Dehydration of Glycerol.* Add 6 drops of glycerol to 1 g. of potassium hydrogen sulfate contained in a test tube. Heat the mixture strongly and note the odor. Write the equation for the reaction.

QUESTIONS

1. Complete and balance each of the following equations:

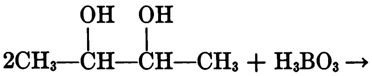
(a)


$$\mathrm{CH_3{-}\overset{\overset{OH}{|}}{C}H{-}\overset{\overset{OH}{|}}{C}H{-}CH_3 + HIO_4 \rightarrow}$$

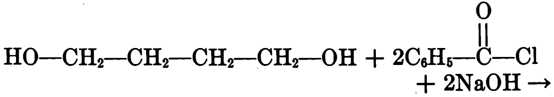
(b) $\mathrm{HO{-}CH_2{-}CH_2{-}OH + Pb(OCOCH_3)_4 \rightarrow}$

(c)


$$\mathrm{HO{-}CH_2{-}CH_2{-}CH_2OH + 2CH_3{-}\overset{\overset{O}{\|}}{C}{-}Cl \rightarrow}$$

(d)


$$\mathrm{2CH_3{-}\overset{\overset{OH}{|}}{C}H{-}\overset{\overset{OH}{|}}{C}H{-}CH_3 + H_3BO_3 \rightarrow}$$

(e)


$$\mathrm{HO{-}CH_2{-}CH_2{-}CH_2{-}CH_2{-}OH + 2C_6H_5{-}\overset{\overset{O}{\|}}{C}{-}Cl + 2NaOH \rightarrow}$$

2. Write equations to show three different methods for effecting the conversion of cyclohexene to adipaldehyde.

3. In analytical chemistry, titration of boric acid with standard sodium hydroxide solution can be carried out satisfactorily only if a considerable quantity of mannitol, glycerol, glucose, or other polyhydric alcohol is added to the boric acid solution. Why is this true?

EXPERIMENT 32

Oxalic Acid

Introduction. Oxalic acid is one of the oldest known carboxylic acids. Gay-Lussac obtained the sodium salt of the acid in 1829 by fusing sawdust with sodium hydroxide, and Scheele prepared the acid in 1776 by the oxidation of cane sugar with nitric acid. Both procedures were used for the commercial manufacture of oxalic acid in the nineteenth century, but most of the acid used today is manufactured by heating sodium formate to drive off hydrogen and then liberating oxalic acid from the resulting sodium salt by the action of mineral acid. Oxalic acid crystallizes from aqueous solution as a dihydrate, and it is thought that the dihydrate is actually ortho-oxalic acid. Oxalic acid forms both normal and acid salts with alkali metal hydroxides. Potassium acid oxalate and oxalic acid dihydrate combine to form a crystalline compound known as potassium tetroxalate, $KHC_2O_4 \cdot H_2C_2O_4 \cdot 2H_2O$. Either oxalic acid dihydrate or potassium tetroxalate may be used in quantitative analysis for the standardization of potassium permanganate solution.

Oxalic acid readily forms esters with the simple alcohols. Most of these esters are liquids, but the methyl ester, which is to be prepared as a part of today's assignment, is a solid. Hydrogen chloride is used as the catalyst in this esterification reaction. The carbon atoms of the carbonyl groups present in methyl oxalate are highly electrophilic in reactivity, and accordingly nucleophilic substitution reactions occur rapidly. For example, methyl oxalate is converted to oxamide almost instantaneously on treatment with ammonia.

0-10 *Procedure.* Place an evaporating dish containing 60 g. of oxalic acid dihydrate in an oven maintained at 100° and allow it to remain there for about 1½ hours. Anhydrous oxalic acid obtained in this manner will be used for the preparation of methyl oxalate.

I. Preparation of Sodium Oxalate from Sodium Formate

10-30 Place 1 g. of sodium formate in a test tube and heat the tube until the crystals melt and decompose with evolution of hydrogen. When the evolution of hydrogen ceases, cool the tube and dissolve the fused mass in water. To about 2 ml. of the solution add a few drops of calcium chloride solution and acidify it by the addition of acetic acid. Note the result. As a control experiment, add calcium chloride solution and acetic acid to aqueous sodium formate solution. Write equations for the preparation of sodium oxalate and calcium oxalate by the procedure described above.

II. Preparation of Oxalic Acid from Sucrose

30-70 To 50 ml. of concentrated nitric acid (sp. gr. 1.42) contained in a 1-liter flask add 10 g. of sucrose (cane or beet sugar). Support the flask on a ring stand in the hood. Warm the mixture gently with the slightly luminous flame of the Bunsen burner, removing the flame when the evolution of brown fumes begins. Allow the reaction to proceed spontaneously until it is ended. Transfer the acid solution to an evaporating dish and heat it on the steam bath in the hood until the solution has evaporated to about one third of its original volume.

[Proceed with the next part of today's assignment while the solution is being concentrated.]

Set the solution aside until the next laboratory period, when a deposit of crystalline oxalic acid will have formed. Collect the solid by filtration through a porcelain funnel or a glass funnel fitted with a perforated porcelain plate (Witt plate). Crystallize the solid from the least possible quantity of hot water and determine the melting point of the product.

III. Properties of Oxalic Acid

(*a*) *Reducing Action of Oxalic Acid.* Dissolve about 0.5 g. of oxalic acid in 5 ml. of water and add 3 drops **70-80** of concentrated sulfuric acid. Then add a few drops of a dilute aqueous solution of potassium permanganate and warm the solution. Record your observations. Write the equation for the reaction.

(*b*) *Decomposition of Oxalic Acid.* Heat 2 g. of oxalic acid with 5 ml. of concentrated sulfuric acid in **80-90** the hood. What gases are evolved? Write the equation for the reaction.

IV. Preparation of Methyl Oxalate

To 50 ml. of methanol contained in a 250-ml. Erlenmeyer flask add 45 g. (0.5 mole) of the oxalic acid **90-150** that has been drying in the oven since the start of the period. Equip the flask with a two-holed rubber stopper bearing two bent glass tubes, one extending only a few millimeters below the stopper and the other extending to within 1 cm. of the surface of the methanol-oxalic acid mixture. Gaseous hydrogen chloride, generated in a filter flask by dropping concentrated sulfuric acid onto a slurry of sodium chloride and concentrated hydrochloric acid, is passed through the longer tube into the Erlenmeyer flask. Shake the flask frequently to facilitate dissolution of the hydrogen chloride.

The smaller tube extending into the Erlenmeyer flask serves as an exit tube. Although most of the hydrogen chloride is absorbed by the methanol solution, some of the gas escapes through the exit tube. Therefore, that tube should be connected by rubber tubing to a suitable apparatus for the absorption of excess hydrogen chloride (see page 88). As the introduction of hydrogen chloride proceeds, the Erlenmeyer flask and its contents become warm and the oxalic acid passes into solution. Absorption of the gas is continued until the solution is practically saturated or at least until the flask has increased 10 g. in weight.

Filter the hot solution into a second Erlenmeyer flask, and allow the filtrate to stand for 10 minutes. Then place the flask in a pan of ice and water, and stir the solution as methyl oxalate crystallizes. When the mixture has been thoroughly chilled, collect the crystals in a Büchner funnel and press them out with a large, flat-topped glass stopper. Place the crystals in a beaker, stir with 25 ml. of ice-cold methanol and again filter the mixture and press out the crystals.

Most of the hydrogen chloride has now been removed and the methyl oxalate is recrystallized from 50 ml. of hot methanol by cooling in ice. Once again, collect the crystals by filtration, press them out, and finally dry them on a clay plate or between pieces of filter paper. Weigh the dried material, and, inasmuch as methyl oxalate is somewhat volatile, transfer the compound to a stoppered bottle. Determine the melting point of your product. The recorded melting point is 54°. Calculate the percentage yield.

V. Conversion of Methyl Oxalate to Oxamide

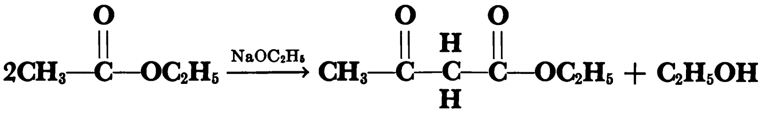
Dissolve about 1 g. of methyl oxalate in a few ml.
150-160 of methanol and add about 1 ml. of concentrated ammonium hydroxide solution. What do you observe? Write the equation for the reaction.

QUESTIONS

1. Can you suggest an explanation for the fact that the carbonyl group carbon atoms of methyl oxalate have a high degree of electrophilic reactivity (i.e., add bases rapidly)?
2. If titration of a dilute sulfuric acid solution containing 0.6165 g. of oxalic acid requires 17.70 ml. of potassium permanganate solution, what is the molarity of the permanganate solution?
3. Write a sequence of equations to show how oxalic acid may be prepared from carbon monoxide, sodium hydroxide, and sulfuric acid as the fundamental starting materials.
4. Why does oxalic acid tend to form a hydrate?
5. Propose a mechanism for the acid-catalyzed decomposition of oxalic acid.
6. What are two types of salts that may be formed on reaction of oxalic acid with an amine?
7. Which would be larger, the first or the second ionization constant of oxalic acid? Why?
8. How may diethyl phenylmalonate be prepared from ethyl oxalate and ethyl phenylacetate as the organic starting materials?

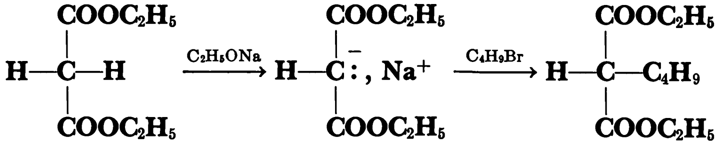
EXPERIMENT 33

I. Preparation of Ethyl Acetoacetate (Part A)



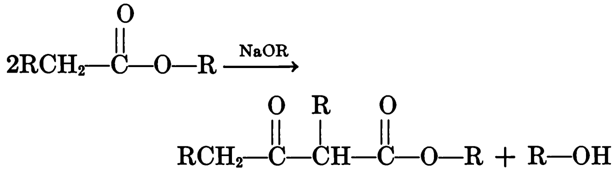
$$2CH_3-\overset{O}{\overset{\|}{C}}-OC_2H_5 \xrightarrow{NaOC_2H_5} CH_3-\overset{O}{\overset{\|}{C}}-\underset{H}{\overset{H}{C}}-\overset{O}{\overset{\|}{C}}-OC_2H_5 + C_2H_5OH$$

II. Alkylation of Ethyl Malonate (Part A)



$$\begin{array}{c} COOC_2H_5 \\ | \\ H-C-H \\ | \\ COOC_2H_5 \end{array} \xrightarrow{C_2H_5ONa} \begin{array}{c} COOC_2H_5 \\ |\,- \\ H-C:, Na^+ \\ | \\ COOC_2H_5 \end{array} \xrightarrow{C_4H_9Br} \begin{array}{c} COOC_2H_5 \\ | \\ H-C-C_4H_9 \\ | \\ COOC_2H_5 \end{array}$$

Introduction. β-Ketoesters may be prepared by application of the Claisen condensation reaction. Usually it is necessary to employ esters having at least two α-hydrogen atoms when a sodium alkoxide is used as the catalyst. The condensation always takes place at the α-carbon, as shown in the following equation.



$$2RCH_2-\overset{O}{\overset{\|}{C}}-O-R \xrightarrow{NaOR} RCH_2-\overset{O}{\overset{\|}{C}}-\overset{R}{\overset{|}{C}}H-\overset{O}{\overset{\|}{C}}-O-R + R-OH$$

You will note that the condensation of two molecules of ethyl acetate yields a β-ketoester in which a methylene group (CH_2) is located between two carbonyl (CO) groups. A methylene group so placed is particularly reactive and is called an "active methylene group"; likewise its two hydrogen atoms are referred to as "acid methylene hydrogen atoms."

The two classic examples of compounds containing an "acid methylene group" are ethyl acetoacetate and ethyl malonate, compounds being studied in today's assignment. In each compound an acidic hydrogen atom of the methylene group may be replaced by sodium, yielding a sodio derivative whose sodium atom, in turn, may be replaced by an alkyl group through reaction with an alkyl halide. Hence the two-step process results in the formation of an alkyl derivative of the compound containing the acid methylene group and is known as an alkylation reaction. In Part II of today's experiment and also in the assignment for the next laboratory period, such an alkylation reaction is illustrated by the preparation of the *n*-butyl derivative of ethyl malonate (ethyl *n*-butylmalonate).

(a) $CH_2(CO_2C_2H_5)_2 + NaOC_2H_5 \rightarrow NaCH(CO_2C_2H_5)_2 + C_2H_5OH$

(b) $NaCH(CO_2C_2H_5)_2 + C_4H_9Br \rightarrow C_4H_9CH(CO_2C_2H_5)_2 + NaBr$

In order to prepare ethyl sodiomalonate, it is necessary to use high-grade absolute ethanol. This will be prepared during today's period and utilized during the next laboratory period. A convenient method for the preparation of anhydrous ethanol is to treat commercial absolute ethanol with sodium metal and then with diethyl phthalate. After the solution has been heated for a short time, pure ethanol can be distilled from the mixture. When sodium metal dissolves in commercial absolute ethanol, the small amount of water present is converted to sodium hydroxide with evolution of hydrogen, and some ethanol is converted to sodium ethoxide, also with hydrogen evolution. The sodium hydroxide produced saponifies diethyl phthalate to give sodium phthalate and sodium ethyl phthalate, which are nonvolatile, and ethanol. Pure ethanol can be distilled from this mixture, leaving behind the various sodium salts and any unchanged diethyl phthalate (boiling point 298°).

I. PREPARATION OF ETHYL ACETOACETATE (PART A)

Procedure. Place 200 ml. of commercial ethyl acetate **0-20**
in a separatory funnel and shake the ester with an equal
volume of 5 per cent sodium carbonate solution (Note
1). After removal of the sodium carbonate solution,
shake the ethyl acetate with 50 ml. of saturated calcium
chloride solution, then dry the ester over anhydrous **20-80**
potassium carbonate for an hour.

[While the ethyl acetate is being dried, proceed with Part II.]

Decant the ethyl acetate from the drying agent and **80-120** distill it, taking care that all of the apparatus used is completely dry. Weigh the purified ester (Note 2) and pour it into a 500-ml. round-bottomed flask equipped with a water-cooled reflux condenser and a calcium chloride drying tube.

Place 2 or 3 lumps of clean sodium having a com- **120-160** bined weight of 16 g. in a beaker and cover the metal with kerosene. Cut off about a 2-g. piece of sodium, dry it with a paper towel or a piece of filter paper, and cut it into thin slices. As quickly as possible, disconnect the flask of ethyl acetate from the condenser and add the slices of sodium (Note 3). Join the flask to the condenser once again and wait until the reaction subsides before adding another 2-g. quantity of sliced sodium. All of the metal may be added to the ester in the course of about 20 minutes.

After the initial vigorous reaction has diminished, place the flask with its attached condenser on the steam bath and heat it for the remainder of the period. At the end of the laboratory period, remove the apparatus from the steam bath, and allow the reaction mixture to stand until the next laboratory period. Leave the flask attached to the reflux condenser but shut off the stream of water through the condenser.

NOTES

1. The sodium carbonate solution neutralizes any acetic acid present in the ethyl acetate. Since carbon dioxide is liberated in the neutralization reaction, be prepared to release the pressure in the separatory funnel at frequent intervals while shaking the mixture.

2. At this stage, the ethyl acetate is free of acetic acid and water, but it does contain some ethyl alcohol. The presence of this alcohol is necessary in order to initiate the reaction. Sodium reacts with the alcohol to produce sodium ethoxide, the catalyst for the reaction.

3. Owing to the increased surface area, thin shavings of sodium may inflame if left in contact with air for too long a time. If this should happen, smother the metal with dry sand, scrape the material into a pan and take it out of doors. Do not use a fire extinguisher! Of course, the main portion of sodium should be kept in the beaker of kerosene and portions removed and sliced only as needed.

II. ALKYLATION OF ETHYL MALONATE (PART A)

20-80 *Procedure.* To 300 ml. of commercial absolute ethanol contained in a 500-ml. round-bottomed flask add 3 g. of sodium, in small pieces. After all of the sodium has dissolved, add 10 g. of diethyl phthalate to the solution, connect the flask to a water-cooled reflux condenser, the top of which bears a calcium chloride tube to exclude moisture, and heat the mixture on the steam bath for about 30 minutes (don't forget the standard procedure of adding 1 or 2 boiling chips). Distill the ethanol into a dry bottle, the distillate being protected from moisture by a calcium chloride tube, and stopper the bottle tightly. Save the anhydrous ethanol for the next laboratory period. Continue with Part I as the ethanol is being distilled.

QUESTIONS

1. Write equations for the Claisen condensation of ethyl propionate; of ethyl *n*-butyrate.

2. Would it be a good idea to use sodium methoxide to catalyze the Claisen condensation of ethyl acetate? Explain.

3. At the completion of the experiment, before the hydrolysis step, does ethyl acetoacetate exist mainly as the free β-ketoester or as some derivative? Of what significance is this?

4. Write a detailed mechanism for the Claisen condensation as applied to ethyl acetate.

5. One method for preparing absolute ethanol was given in Part II of today's assignment. What are some other methods?

6. Why does the Claisen condensation fail when applied to ethyl isobutyrate, with sodium ethoxide as the catalyst? How might a successful reaction be brought about?

7. What is the easiest way to prepare absolute methanol? Why isn't the same method used for the preparation of absolute ethanol?

8. What is the commercial method for the manufacture of ethyl acetoacetate?

9. How might a β-aldehydoester be prepared by a Claisen condensation reaction? In general, under what circumstances are "mixed" Claisen condensation reactions useful in synthesis?

10. What is the product of the sodium ethoxide-catalyzed reaction of acetone with ethyl acetate? May the same compound be prepared under conditions of acid-catalysis? What acid catalyst could be used?

EXPERIMENT 34

I. Preparation of Ethyl Acetoacetate (Part B)

II. Alkylation of Ethyl Malonate (Part B)

Introduction. During the previous laboratory period the Claisen condensation of ethyl acetate was carried out. Today, the product, ethyl acetoacetate, will be isolated and purified by distillation.

The absolute ethanol prepared last time will be utilized today for the preparation of a sodium ethoxide solution, which, in turn, will be used to prepare ethyl sodiomalonate. The latter reagent, on treatment with n-butyl bromide, affords ethyl n-butylmalonate.

I. Preparation of Ethyl Acetoacetate (Part B)

0-40 *Procedure.* The reaction mixture left from the previous period should contain a large quantity of precipitate consisting of sodium ethoxide and the sodium salt of ethyl acetoacetate. Some unreacted sodium will probably also be present. Add 5 ml. of the anhydrous ethanol prepared during the previous period and heat the mixture under reflux for 30 minutes.

[Proceed with Part II.]

Cool the mixture somewhat, then add, in small
40-70 portions, a total of 25 ml. of anhydrous ethyl alcohol, with swirling of the contents of the flask, and watch for any evidence of unused sodium. If metallic sodium is present in the reaction mixture, wait until it dissolves before proceeding with the next step. When there appears to be no further evidence of the metal, add a few drops of a 50 per cent solution of acetic acid and swirl the mixture. If, in spite of the previous treatment, any sodium comes to the surface at this point, stir the mixture thoroughly and do not add any more acetic acid solution until the metal dissolves.

Gradually add 50 per cent acetic acid solution until all of the precipitate has dissolved and the resulting solution is faintly acidic to litmus. About 110 ml. of the acetic acid solution will be required. Add to the mixture an equal volume of saturated sodium chloride solution and separate the upper layer of mixed esters (ethyl acetoacetate and unreacted ethyl acetate) from the lower aqueous layer.

Dry the ester layer over calcium chloride for about
10 minutes, filter the liquid into a 125-ml. distilling **70-80**
flask, add some boiling chips and distill the liquid
in the usual manner (Note 1). Collect three fractions: **80-130**
I, up to 95°; II, 95°-175°; III, 175°-185°. The last fraction consists of ethyl acetoacetate (Note 2) and the first fraction is mainly ethyl acetate. Redistill the intermediate fraction in order to obtain additional ethyl acetoacetate (Note 3).

After the ethyl acetoacetate has been purified by distillation, continue with Part II of the laboratory assignment.

NOTES

1. It would be preferable to distill the ethyl acetoacetate at reduced pressure in order to minimize thermal decomposition of the ester, but, in order to save time, the distillation is carried out at atmospheric pressure in this experiment. An assembly of apparatus for vacuum distillation is shown in Figure 28.
2. The boiling point of ethyl acetoacetate is 181°.
3. The yield of ethyl acetoacetate should be about 10-15 g.

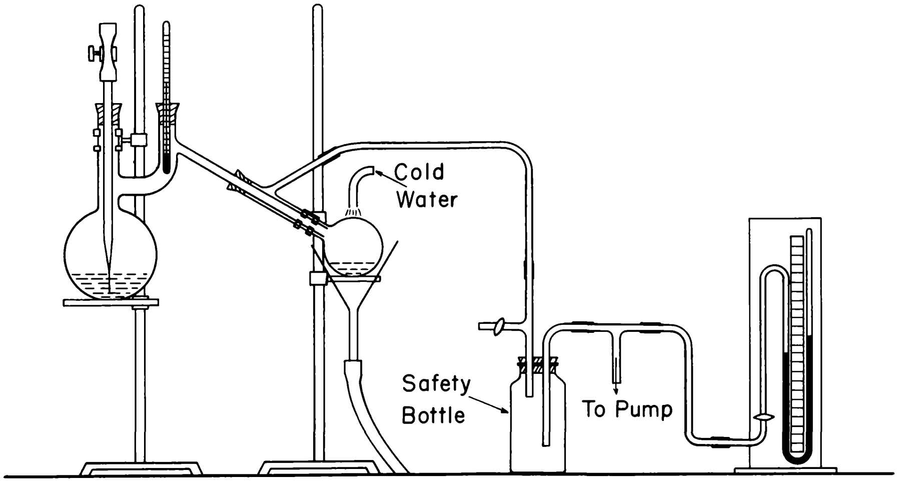


Fig. 28. Apparatus for distillation at reduced pressure.

II. ALKYLATION OF ETHYL MALONATE (PART B)

10-40 *Procedure.* Pour 150 ml. of the absolute ethanol prepared during the last period into a dry 500-ml. round-bottomed flask and attach a reflux condenser equipped with a calcium chloride drying tube. Weigh out 5.8 g. of clean sodium in a small beaker containing sufficient kerosene to cover the metal. Add the sodium, in small pieces, through the condenser tube, to the ethanol at such a rate that the alcohol solution refluxes gently. When all of the sodium has dissolved, cool the solution to about 50°, and add, in the course of 5 minutes, 40 ml. (44 g.) of ethyl malonate. Warm the solution of ethyl sodiomalonate on the steam bath and, through the condenser, add dropwise from a separatory funnel 27 ml. (34.3 g.) of *n*-butyl bromide in the course of 10 minutes. Add some boiling chips to the reaction
40-130 mixture and allow it to reflux for 90 minutes (Note 1).
130-160 Filter the hot solution to remove sodium bromide, and then distill off as much ethanol as possible from the steam bath. Cool the residue by running tap water over the flask, add 100 ml. of water and 3 ml. of concentrated hydrochloric acid to the contents of the flask, and pour the mixture into a separatory funnel. Discard the aqueous layer, wash the organic layer with a small amount of water, and pour the crude ethyl *n*-butylmalonate into a bottle containing anhydrous magnesium sulfate.

At a subsequent laboratory period purify the dried ethyl *n*-butylmalonate by one of the following methods, as directed by the instructor:

(a) Distill the ester at atmospheric pressure collecting the fraction boiling at 210°-240°. This involves some thermal decomposition of the ester.

(b) Distill the ester at diminished pressure provided a sufficient number of sets of apparatus is available.

(c) The laboratory instructor will distill several collected lots of the ester at diminished pressure as a demonstration experiment.

The ethyl *n*-butylmalonate will be used in Experiment 35 for the preparation of *n*-caproic acid.

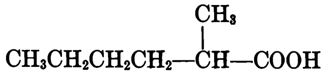
NOTE

1. Violent bumping may occur when sodium bromide precipitates during the course of the refluxing.

QUESTIONS

1. Write equations to show how the following compounds may be prepared from ethyl malonate and any alkyl halides containing not more than four carbon atoms per molecule.

(a) $CH_3CH_2CH_2CH_2CH_2COOH$



(b) $CH_3CH_2CH_2CH_2{-}\overset{CH_3}{\overset{|}{C}}H{-}COOH$

(c) $HOOCCH_2CH_2CH_2CH_2CH_2CH_2COOH$

2. Can ethyl phenylmalonate be prepared by reaction of ethyl sodiomalonate with bromobenzene? Explain.

3. Using any materials that have been studied throughout this course write equations for six common nucleophilic displacement reactions involving fundamentally different bases as the displacing agents.

4. Write equations to show how the following compounds may be prepared from ethyl acetoacetate and any alkyl halides containing not more than four carbon atoms per molecule.

(a) $CH_3\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2CH_2CH_3$

(b) $CH_3CH_2CH_2CH_2CH_2COOH$

5. What is barbital? How may barbital be prepared from ethyl malonate as one of the main starting materials?

6. The crude ethyl acetoacetate prepared in Part I of today's assignment is dried over anhydrous calcium chloride prior to being distilled. If, through careless handling, some water containing dissolved calcium chloride should remain with the ethyl acetoacetate, what reaction will occur as the mixture is heated?

7. What volume (S.T.P.) of carbon dioxide would be evolved on acid-catalyzed hydrolysis of 15 g. of ethyl acetoacetate?

EXPERIMENT 35

I. *n*-Caproic Acid (Part A)

$$CH_3(CH_2)_3CH(COOC_2H_5)_2 \xrightarrow{NaOH} CH_3(CH_2)_3CH(COONa)_2 \xrightarrow{H_2SO_4} CH_3(CH_2)_3CH(COOH)_2 \xrightarrow{heat} CH_3(CH_2)_4COOH + CO_2$$

II. Reactions of Ethyl Acetoacetate

Introduction. Malonic acid, an alkylmalonic acid, or a dialkylmalonic acid, when heated, undergoes decarboxylation to give acetic acid, an alkylacetic acid or a dialkylacetic acid, respectively. Thus, alkylation of ethyl malonate, followed by saponification of the product and decarboxylation of the corresponding malonic acid, provides a general method for the preparation of an alkylacetic acid or a dialkylacetic acid.

$$RCH(COOR)_2 \xrightarrow{NaOH} RCH(COONa)_2 \xrightarrow{H_2SO_4} RCH(COOH)_2 \xrightarrow{heat} RCH_2COOH$$

$$R_2C(COOR)_2 \xrightarrow{NaOH} R_2C(COONa)_2 \xrightarrow{H_2SO_4} R_2C(COOH)_2 \xrightarrow{heat} R_2CHCOOH$$

In today's work the ethyl *n*-butylmalonate prepared in Experiment 34 will be hydrolyzed to *n*-butylmalonic acid which, by removal of one mole of carbon dioxide, yields *n*-caproic acid.

At one point, in which the production of the specimen of *n*-caproic acid will require little attention for about an hour, the properties of ethyl acetoacetate will be studied.

I. Preparation of *n*-Caproic Acid (Part A)

$$CH_3CH_2CH_2CH_2CH(COOC_2H_5)_2 \xrightarrow{NaOH} CH_3CH_2CH_2CH_2CH(COONa)_2 \xrightarrow{H_2SO_4} CH_3CH_2CH_2CH_2CH(COOH)_2 \xrightarrow{heat} CH_3CH_2CH_2CH_2CH_2COOH$$

0-30 *Procedure.* Place 30 g. of potassium hydroxide in a 500-ml. round-bottomed flask, add 30 ml. of water and shake the mixture until the potassium hydroxide dissolves. Add 30 g. of ethyl *n*-butylmalonate to the hot alkaline solution in small portions, with thorough shaking of the flask. The reaction is usually vigorous, and some of the ethanol formed in the saponification reaction boils off. To avoid spattering of the alkaline solution upon the skin, hold the flask in a towel, be
30-90 sure to add the ester in small portions, and shake the flask thoroughly after each addition. After all the ester has been added, place the flask on a wire gauze, attach a reflux condenser, and boil the mixture for an hour.

> [While the mixture is being heated under reflux, proceed with Part II.]

90-120 Add 80 ml. of water to the reaction mixture, rearrange the apparatus for distillation, and distill off about 65 ml. of water and ethyl alcohol. Cool the distillation residue to room temperature, then attach a reflux condenser to the flask and place it on a wire gauze. Through the condenser tube slowly add a solution of 33 ml. of cold, concentrated sulfuric acid in 65 ml. of water. Foaming of the reaction mixture can be kept under control by slow addition of the sulfuric acid and shaking of the flask. Add some boiling chips and heat the 120-180
mixture under reflux for the remainder of the period. Allow the mixture to stand until the next laboratory period.

> [While the acid solution is being heated under reflux, finish Part II of today's assignment and answer the questions at the end of Part II.]

II. Reactions of Ethyl Acetoacetate 30-35

Introduction. In the molecular structure of ethyl acetoacetate, as in that of ethyl malonate, a reactive methylene (CH_2) group is located between two carbonyl groups. In each substance reaction with sodium ethoxide followed by the addition of an alkyl halide successively replaces one or both of the two methylene hydrogen atoms by alkyl groups. The monoalkylation of ethyl malonate has been illustrated in our former preparation of ethyl *n*-butylmalonate which is being converted into *n*-caproic acid in today's experiment. Ethyl acetoacetate may be alkylated in a similar manner yielding an alkylated ester which is useful not only for the synthesis of acids but of certain ketones as well.

Hydrolysis of ethyl acetoacetate with dilute alkali (5 per cent) gives sodium acetoacetate, which undergoes decarboxylation to furnish acetone (ketone split). Use of concentrated alkali (30 per cent) gives two moles of sodium acetate (acid split). Since ethyl sodioacetoacetate is readily prepared and undergoes alkylation with appropriate alkyl halides, and since the substituted acetoacetic esters also undergo the ketone split with dilute alkali or the acid split with concentrated alkali, alkylacetic acids or alkyl-substituted acetones are readily prepared from ethyl acetoacetate.

β-Ketoesters in general, and ethyl acetoacetate in particular, exist as tautomeric mixtures of the *keto* and *enol* forms. The *enol* form of ethyl acetoacetate undergoes characteristic reactions with ferric chloride, ammoniacol copper sulfate and bromine water.

Short Experiments with Ethyl Acetoacetate

(*a*) *Ferric Chloride Test*. Add a drop of ethyl acetoacetate to 10 ml. of water contained in a test tube and shake the mixture. Then add a drop of ferric chloride solution. Record your observation.

35-45 (*b*) *Formation of the Copper Salt*. To 10 ml. of ammoniacal copper sulfate solution contained in a test tube add 1 ml. of ethyl acetoacetate, and shake the mixture vigorously. The precipitation of the copper salt begins in about 1 minute, and the amount of salt becomes quite abundant after about 4 minutes.

45-50 (*c*) *Bromine Water*. Add 1 ml. of ethyl acetoacetate to 10 ml. of water contained in a test tube, and shake the mixture. To the resulting suspension add 10 ml. of bromine water and shake the mixture for a minute. Record your observations and explain the result by writing the equation for the reaction.

50-60 (*d*) *Cleavage to Produce Acetic Acid*. Add 5 ml. of ethyl acetoacetate to 15 ml. of a 30 per cent aqueous sodium hydroxide solution contained in a small round-bottomed flask. Ethyl sodioacetoacetate usually precipitates a short time after the reagents are mixed. Attach a reflux condenser to the flask and place the
60-90 flask on a wire gauze. Heat the mixture under reflux for 30 minutes. If the precipitate does not dissolve when the flask is heated, add a small quantity of water. Cool
120-135 the flask, add 15 ml. of water and acidify the solution by addition of 30 per cent sulfuric acid. Arrange the condenser for distillation and collect 15 ml. of distillate.
135-160 Note the odor of the distillate, and test it with litmus paper. Neutralize the distillate with dilute sodium hydroxide solution and evaporate the solution to dryness. Note the residue. Write the equation for this type of cleavage of ethyl acetoacetate.

(*e*) *Cleavage to Produce Acetone*. Place 5 ml. of 120-160
ethyl acetoacetate and 25 ml. of 10 per cent sodium hydroxide solution in a small flask equipped with a reflux condenser and boil the mixture for 15 minutes. Cool the flask, arrange the condenser for distillation and collect about 10 ml. of distillate. Note the odor of the distillate. Test for acetone in the distillate by the addition of a drop of a freshly prepared solution of sodium nitroprusside and a drop of ammonium hydroxide. The appearance of a red-violet coloration indicates the presence of acetone. Write the equation for the cleavage reaction.

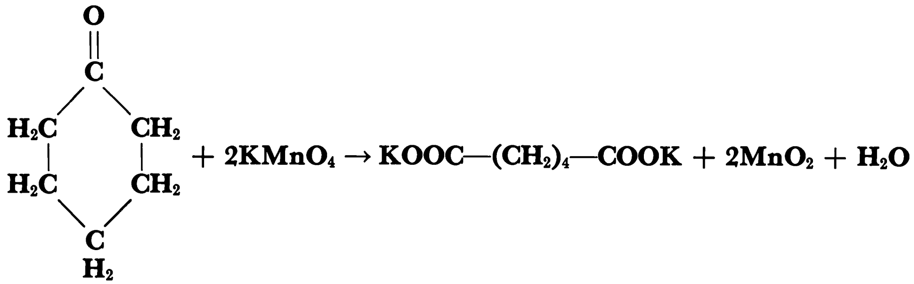
QUESTIONS

1. How may the *keto* and *enol* forms of ethyl acetoacetate be isolated in pure form?
2. List the properties of the *keto* and *enol* forms of ethyl acetoacetate.
3. Suggest an analytical procedure for determining the concentration of *enol* in a *keto-enol* tautomeric mixture.
4. What is the theoretical volume of carbon dioxide liberated on hydrolysis and decarboxylation of 30 g. of ethyl *n*-butylmalonate?
5. Can *t*-butylacetic acid be prepared by alkylation of ethyl sodiomalonate, followed by hydrolysis and decarboxylation of the corresponding malonic acid? Explain.

EXPERIMENT 36

I. *n*-Caproic Acid (Part B)

II. Preparation of Adipic Acid



Introduction. The preparation of *n*-caproic acid, begun in Experiment 35, by saponification of ethyl *n*-butylmalonate and decarboxylation of the corresponding malonic acid will be completed today. Inasmuch as *n*-caproic acid is a liquid, a portion of it may be converted to the anilide, a solid derivative, in some subsequent period. The reactions used to prepare the anilide are summarized in the following equations:

(a)

$$CH_3CH_2CH_2CH_2CH_2COOH + SOCl_2 \rightarrow CH_3CH_2CH_2CH_2CH_2COCl + SO_2 + HCl$$

(b)

$$CH_3CH_2CH_2CH_2CH_2COCl + 2C_6H_5NH_2 \rightarrow CH_3CH_2CH_2CH_2CH_2CONHC_6H_5 + C_6H_5NH_2 \cdot HCl$$

As Part II of the laboratory assignment, adipic acid will be prepared by oxidation of cyclohexanone with potassium permanganate. This experiment illustrates the opening of a ring by oxidation. Adipic acid, which may also be prepared by oxidation of cyclohexanol with hot nitric acid, is used commercially in the manufacture of one type of Nylon (Nylon 66).

I. Preparation of *n*-Caproic Acid (Part B)

0-10 *Procedure.* Heat the acid mixture which has been
10-70 standing since the last laboratory period to boiling and
reflux for an additional hour..

[While the solution is being heated under reflux proceed with Part II.]

70-90 Cool the hot acid solution to room temperature, pour
the mixture into a separatory funnel, draw off the lower
sulfuric acid solution, and pour the upper layer of
n-caproic acid into a 500-ml. Erlenmeyer flask. Extract
the sulfuric acid solution with three 100-ml. portions
of benzene and combine the benzene extracts with the
original *n*-caproic acid layer. Wash the resulting so-
lution with about 20 ml. of water, then dry the benzene
90-110 solution over anhydrous magnesium sulfate for 20 min-
utes.

[Meanwhile continue with Part II.]

Filter the solution into a 500-ml. distilling flask, attach 110-130
a water-cooled condenser, and distill off the benzene.
Transfer the residue to a small distilling flask, attach 130-150
an air-cooled condenser and distill the liquid. Collect
the portion boiling from 196°-206° (Note 1) in a
tared bottle and determine the amount of *n*-caproic
acid obtained. Calculate the percentage yield of product.
Stopper the bottle and save the compound for some
future period when the anilide can be prepared.

n-Caproanilide (Optional). In a small flask mix 3 g. of *n*-caproic acid with 4.5 ml. of pure thionyl chloride, attach a reflux condenser and boil the solution under reflux for 30 minutes. Cool the liquid, dissolve it in 30 ml. of anhydrous benzene, and pour the solution in portions, with shaking, into a solution of 6 ml. of aniline in 50 ml. of anhydrous benzene. Warm the solution on the steam bath for a few minutes, pour the liquid into a separatory funnel and wash it successively with small amounts of 5 per cent hydrochloric acid, 5 per cent sodium hydroxide solution, and water. Distill the benzene from the solution and crystallize the residue from 70 per cent ethanol. Collect the crystals and determine the melting point of the *n*-caproanilide (Note 2).

NOTES

1. The boiling point of *n*-caproic acid is 202°.
2. The melting point of *n*-caproanilide is 95°.

II. Preparation of Adipic Acid

Procedure. To a solution of 15 g. of potassium
permanganate in 130 ml. of water contained in a 10-25
250-ml. Erlenmeyer flask add 5 g. of cyclohexanone
and 1 ml. of 10 per cent potassium hydroxide solution.
Place a thermometer in the reaction mixture and ob-
serve the rise in temperature. When the temperature

reaches 50°, immerse the flask in cold water until the temperature drops to 45°.

25-45 Keep the mixture at a temperature of 45°-50° for 20 minutes by alternately cooling the flask to 45° in water and allowing it to warm up to 50° again outside the water bath. Place the flask on a wire gauze and heat the contents to the boiling point, then cool slightly, add a few crystals of sodium bisulfite and filter the mixture with suction. Wash the precipitate with two 30-ml. portions of water and concentrate the combined filtrate and wash solution to about 40 ml. by boiling in an evaporating dish. Allow the solution to cool slightly, add a small amount of decolorizing carbon and filter the hot solution, collecting the filtrate in an Erlenmeyer flask.

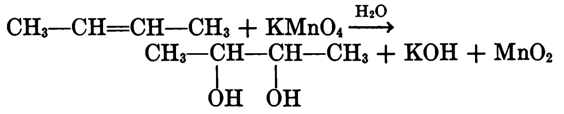
70-90 Acidify the hot filtrate with concentrated hydrochloric acid and allow it to stand in a bath of ice and water for 15-20 minutes. Collect the crystals of adipic acid by suction filtration and determine the melting point of the compound (Note 1). After the crystals have been dried, determine their weight (Note 2) and calculate the percentage yield.

NOTES

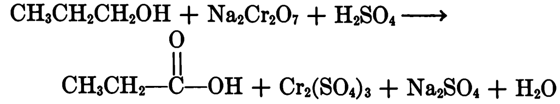
1. The melting point of adipic acid is 152°.
2. The weight of adipic acid obtained in this experiment is usually about 3 g.

QUESTIONS

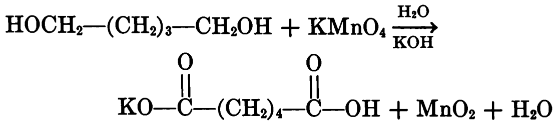
1. Balance each of the following equations and show your method for doing so.

(a) 

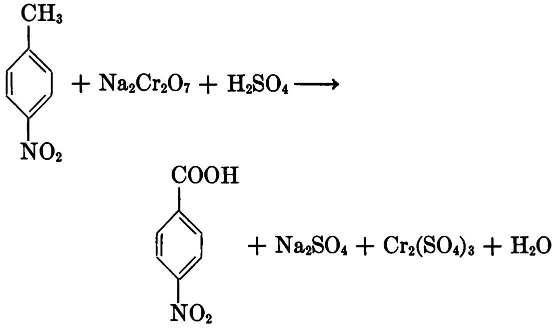
$$CH_3-CH=CH-CH_3 + KMnO_4 \xrightarrow{H_2O} CH_3-\underset{\underset{OH}{|}}{C}H-\underset{\underset{OH}{|}}{C}H-CH_3 + KOH + MnO_2$$

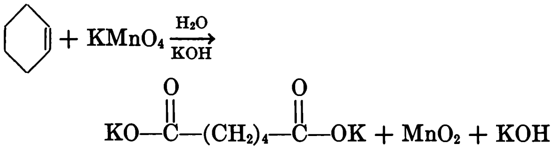
(b) 

$$CH_3CH_2CH_2OH + Na_2Cr_2O_7 + H_2SO_4 \longrightarrow CH_3CH_2-\overset{\overset{O}{\|}}{C}-OH + Cr_2(SO_4)_3 + Na_2SO_4 + H_2O$$

(c) 

$$HOCH_2-(CH_2)_3-CH_2OH + KMnO_4 \xrightarrow[KOH]{H_2O} KO-\overset{\overset{O}{\|}}{C}-(CH_2)_4-\overset{\overset{O}{\|}}{C}-OH + MnO_2 + H_2O$$

(d) 

(e) 

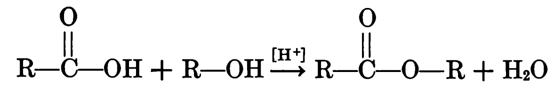
2. Write equations to show how Nylon-66 may be prepared from adipic acid and hexamethylenediamine.
3. Write equations to show the preparation of Nylon-6 from cyclohexanone.
4. What is the purpose in adding a small amount of sodium bisulfite before the initial filtration of the above preparation?
5. What are the commercial sources of cyclohexanol?
6. Would it make any difference if sodium hydroxide solution rather than potassium hydroxide solution was used to catalyze the oxidation reaction described in the above preparation?

EXPERIMENT 37

I. Diethyl Adipate (Azeotropic Esterification)

II. Properties of Lactic, Tartaric, and Citric Acids

Introduction. As mentioned previously (Experiment 26), the Fischer esterification is an equilibrium reaction, and the yield of ester is usually about 67 per cent if equimolar quantities of alcohol and carboxylic acid are caused to react and no scheme is used to displace the equilibrium to the right.



$$\mathrm{R{-}\overset{\overset{\Large O}{\|}}{C}{-}OH + R{-}OH \xrightarrow{[H^+]} R{-}\overset{\overset{\Large O}{\|}}{C}{-}O{-}R + H_2O}$$

However, the yield of ester can be made to approach 100 per cent by the simple expedient of removing water as it is formed. Most often this is accomplished by a process of azeotropic distillation. A third compound is added to the mixture of alcohol and carboxylic acid such that an azeotrope of minimum boiling point, including water as one of the components, will be formed. The reaction is carried out in a flask joined to a distilling column. As water is formed in the esterification process, the azeotrope of minimum boiling point is distilled through the column, thus displacing the esterification equilibrium to the right.

A typical boiling point-composition curve for a binary azeotrope of minimum boiling point is shown in Figure 9, page 15. If a solution of composition L_1 is heated to the temperature T_1, the mixture will begin to boil, and the composition of the vapor which first distills is V_1. If distillation is permitted to continue for a short period of time, the temperature of the liquid in the distilling flask rises from T_1 to T_2 and the distillate possesses the composition ranging from V_1 to V_2. If the distillate were redistilled, the vapor would approach the composition of the system of minimum boiling point. Therefore fractional distillation with the aid of a column will afford a distillate of composition C_M, the residue in the distilling flask approaching the composition A as the distillation progresses. A similar situation would prevail if the starting liquid had a composition falling in the right-hand portion of the curve shown in Figure 9. A few examples of binary azeotropic mixtures of minimum boiling point are given below:

1st Component	*2nd Component*	*B.p. of Azeotropic Mixture*	*Per Cent by Weight of 1st Component in the Mixture*
Water (b.p. 100°)	Ethanol (b.p. 78.3°)	78.15°	4.4
Water (b.p. 100°)	Pyridine (b.p. 115.5°)	92.6°	43.0
Ethanol (b.p. 78.3°)	Ethyl Acetate (b.p. 77.2°)	71.8°	31.0
Ethanol (b.p. 78.3°)	Toluene (b.p. 110.6°)	76.7°	68.0

Ternary azeotropes of minimum boiling point are also known. Although the phase diagram for such a system, being 3-dimensional, is necessarily more complex than that shown in Figure 9 for a binary mixture, the principles involved in a fractional distillation are the same.

In today's experiment, diethyl adipate will be prepared from adipic acid and ethanol, with toluene serving as the agent for azeotropic removal of water. Inasmuch as a ternary azeotrope containing toluene, ethanol, and water is formed, it will be necessary to treat the initial distillate with anhydrous potassium carbonate in order to remove most of the water and then to filter the mixture and return the filtrate to the reaction flask; otherwise excessive quantities of toluene and ethanol would have to be employed.

While the ternary azeotrope is being removed by distillation and also during the purification of diethyl adipate by distillation, certain of the properties of some common hydroxyacids will be examined.

I. DIETHYL ADIPATE (AZEOTROPIC ESTERIFICATION)

$$\mathrm{HOOC{-}(CH_2)_4{-}COOH + 2C_2H_5OH \rightarrow C_2H_5OOC{-}(CH_2)_4{-}COOC_2H_5 + 2H_2O}$$

Procedure. Place 73 g. (0.5 mole) of adipic acid, 180 ml. (142 g., 3.1 moles) of absolute ethanol, 90 ml. **0-30**
of toluene, and 1 ml. of concentrated sulfuric acid in a 500-ml. round-bottomed flask. Attach a short Vigreux or packed column (Note 1) to the flask and connect a water-cooled condenser set for distillation to the head of the column. Partially immerse the flask in an oil bath and raise the temperature of the bath to 115°. As the temperature of the bath is raised, adipic acid dissolves in the reaction mixture, and the ternary azeotrope of ethanol, toluene, and water begins to distill at a temperature of 75°. Collect the distillate in a flask containing 75 g. of anhydrous potassium carbonate. **30-60**

[While the distillation is in progress, work on Part II of the assignment for today.]

Continue the distillation until the thermometer at the top of the column attains a reading of 78°. At this point, discontinue heating the oil bath. When the dis- **60-80**
tillation ceases, shake the distillate which has been collected with the anhydrous potassium carbonate for 1-2 minutes, then filter the mixture through a Büchner funnel with suction, and return the filtrate to the distilling flask. Connect the column with its attached condenser to the flask once again, raise the temperature of the oil bath to about 110°, and continue the distillation **80-100**

until the overhead vapor attains a temperature of 78°-80°.

[Continue with Part II of the assignment.]

100-120 Discontinue heating the oil bath, allow the solution in
the flask to cool somewhat, then transfer the liquid to
a distilling flask, attach a water-cooled condenser, and,
with heating of the flask by the oil bath, remove the
120-170 solvents by distillation. Replace the water-cooled condenser
by an air condenser and purify the diethyl
adipate by distillation.

[Continue with Part II.]

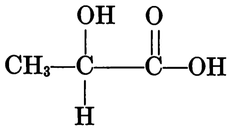
Use the slightly luminous flame of the Bunsen burner to heat the flask in the latter operation. Collect the material boiling from 225°-240° (Note 2). Weigh the ester and calculate the percentage yield.

NOTES

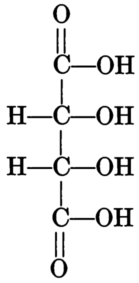
1. A Vigreux column about 1 foot long or a packed column of the same length containing glass beads or helices is adequate for this operation.

2. The recorded b.p. of diethyl adipate is 239° at 760 mm. pressure. Less charring of the ester would result if the distillation were carried out *in vacuo* (see Figure 28, page 102). It is recommended that the distillation be conducted at 20 mm. pressure if suitable apparatus for conducting such a vacuum distillation is available. The recorded b.p. of diethyl adipate at 20 mm. pressure is 138°.

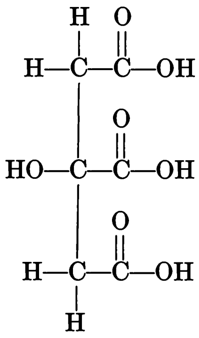
II. Properties of Lactic, Tartaric, and Citric Acids



Lactic acid



meso-Tartaric acid



Citric acid

Properties of Lactic Acid

30-35 (*a*) *Action on Litmus.* Dilute 1 ml. of syrupy lactic acid with 5 ml. of water and test the solution with litmus paper. What is the result?

35-45 (*b*) *Ferric Chloride Test for an α-Hydroxy Acid.* To the dilute solution of lactic acid prepared as described above add 1 drop of ferric chloride solution. Compare the color with that produced in a test with water alone. The color is best observed by looking down through the test tube against a white background. In this test ferric ion is reduced to the ferrous state. To show the presence of ferrous ion, warm the tube and its contents and add a few drops of potassium ferricyanide solution. Record your observations.

(*c*) *Decomposition with Sulfuric Acid.* Add 7 ml. of syrupy lactic acid to 20 ml. of 30 per cent sulfuric acid contained in a distilling flask. Fit the flask with a water-cooled condenser and distill the liquid until about 8 ml. of distillate has been obtained. Divide the distillate into two portions. Test one portion for acetaldehyde with Tollens' solution without the application of heat and test the other portion for formic acid by warming it with a solution of mercuric chloride and sodium acetate. Write the equation for the acid-catalyzed cleavage of lactic acid. 45-60

Properties of Tartaric Acid

(*a*) *Ferric Chloride Test.* Dissolve 1 g. of tartaric acid in 100 ml. of water. To 10 ml. of this solution add 1 drop of ferric chloride solution. Note the depth of the color on looking down through the test tube. Prepare a control solution by adding 1 drop of ferric chloride solution to 10 ml. of a 2 per cent acetic acid solution. Record your observations. 80-90

(*b*) *Potassium Salts of Tartaric Acid.* To 5 ml. of a cold saturated solution of tartaric acid in water add a solution of potassium hydroxide dropwise until a precipitate forms. Then add more potassium hydroxide solution until the precipitate dissolves. Write equations for the two reactions. What is cream of tartar? 90-100

(*c*) *Reducing Action of Tartrates.* Determine whether Rochelle salt will reduce Tollens' solution. What is Rochelle salt? 120-130

(*d*) *Preparation of Fehling's Solution.* To 2 ml. of copper sulfate solution add sodium hydroxide solution until a heavy precipitate forms. Now add a solution of Rochelle salt until the precipitate dissolves. Write equations for these reactions. 130-140

(*e*) *Tartar Emetic.* Dissolve 5 g. of potassium hydrogen tartrate in 50 ml. of water. Add approximately 1 g. of antimony trioxide and boil the solution for 2-3 minutes. Filter the mixture, concentrate the filtrate to about one third of its original volume, and set it aside. What product eventually crystallizes from the solution? 140-150

Properties of Citric Acid

(*a*) *The Use of Ferric Ammonium Citrate in Blue Print Paper.* Add 10 ml. of a 5 per cent aqueous solution of ferric ammonium citrate to an equal volume of a 5 per cent solution of potassium ferricyanide and moisten a sheet of filter paper with this solution. Dry the sheet in an oven at 100° for about 20 minutes. 150-155

[Proceed with the next portion of the assignment.]

When the paper is dry expose it to sunlight under a sheet of cardboard or heavy paper in which a design has been cut. After 3 minutes dip the paper in water. 175-180

Record your observations and explain what reactions have taken place.

155-160 (*b*) *Thermal Decomposition.* Heat 0.5 g. of citric acid in a test tube and note the odor. Write structural formulas and names of three possible organic decomposition products.

160-165 (*c*) *Reducing Power of Citrates.* Determine whether citric acid will reduce Tollens' reagent.

165-175 (*d*) *Solubility of Calcium Citrate.* Dissolve 0.5 g. of citric acid in about 10 ml. of cold water and add a small amount of a thick aqueous suspension of lime. Shake the tube for about 2 minutes, then remove undissolved material by filtration. Heat the filtrate to boiling and note the result. Is calcium citrate more soluble in hot or cold water?

QUESTIONS

1. Select any point on the solution curve of the right-hand portion of Figure 9 and explain briefly what would happen if a solution of that composition were subjected to fractional distillation.
2. Are azeotropic mixtures of maximum boiling point known? Give the names of the components, the boiling point of the azeotropic mixture, and the per cent composition of several such mixtures.
3. Would the composition and boiling point of an azeotropic mixture vary as the pressure over the liquid is changed?
4. Name one important industrial procedure for the purification of a common organic compound that involves an azeotropic distillation.
5. What are several methods that may be used for separating the components of azeotropic mixtures?
6. Compare the behavior of α-, β- and γ-hydroxy-acids on heating.
7. How may ethyl acetonedicarboxylate be prepared from citric acid?
8. Of what biochemical importance is lactic acid?

EXPERIMENT 38

Proteins

Introduction. The three classes of foods—proteins, fats, and carbohydrates—are so interdependent in animal and plant metabolism that it is impossible to list them in any order of importance. However, there can be no question about the relative structural complexities of the three classes of foods; proteins are by far the most complex. In elementary composition the fats and carbohydrates are compounds of carbon, hydrogen, and oxygen; whereas proteins always contain nitrogen in addition to these elements, and often contain sulfur and phosphorus as well. Protein molecules have high molecular weights; values range from about 40,000-45,000 for egg albumin and gliadin up to 40,000,000 reported for the tobacco mosaic virus.

In today's experiments the protein gliadin will be isolated from wheat flour, and an aqueous solution of albumin will be prepared from egg white. Certain color reactions, coagulation tests, and precipitation reactions, characteristic of proteins in general, will be carried out on these proteins and also on milk casein and gelatin.

The acid-catalyzed hydrolysis of a protein to its component amino acids requires a long period of refluxing. In preparation for some experiments on amino acids, to be conducted during the next laboratory period, the hydrolysis of a sample of gelatin will be begun during this period and allowed to continue until the next period.

Acid-Catalyzed Hydrolysis of Gelatin

Add 20 g. of gelatin to 100 ml. of 25 per cent sulfuric
0-20 acid contained in a round-bottomed flask. Place the
flask on a wire gauze, attach a water-cooled reflux
condenser to the flask, and support the apparatus on
a ring stand. Heat the solution under reflux with a
20-155 Bunsen burner for the remainder of the period while
155-165 you are carrying out other experiments, then cool the
solution somewhat, replace the water-cooled condenser
with an air-condenser, and heat the mixture at about
90° in the multiple unit bath shown in Figure 31, page
139, until the next laboratory period.

Isolation of Gliadin from Wheat Flour

15-30 Gradually add sufficient water to 1000 g. of high-
grade wheat flour to make a stiff dough. Allow the
30-90 dough to "age" by standing at room temperature for an
hour.

[Proceed with the next section.]

90-105 Knead the dough in your hands under a stream of cold water until the wash water no longer has a turbid appearance and the residue is a gummy mass. The material obtained in this way is called "gluten" and consists of a mixture of different proteins from the wheat.

105-130 To obtain the protein gliadin in fairly pure form from the gummy mass of gluten, cut it into small pieces, mix the pieces with 200 ml. of 70 per cent ethanol, heat the mixture on the steam bath for a few minutes, and filter the hot solution. Repeat the operation, then combine the filtrates and evaporate the solution to a volume of 100 ml. Cool this solution, add with stirring 10 ml. of 10 per cent sodium chloride solution to "salt out" the protein, allow the precipitate to settle, and wash it twice by decantation with 95 per cent ethanol. The residue is the protein, gliadin.

Preparation of an Albumin Solution

Prepare an aqueous solution of egg albumin by beating the white of an egg for a short time, then mixing it with five times its volume of water. Filter the mixture through cheesecloth and save the filtrate for the various tests described below. **30-45**

Coagulation of Albumin

Place about 2 ml. of egg-white solution in each of five test tubes. Heat one tube gradually and note the approximate temperature at which coagulation takes place. To another tube add 4 ml. of ethanol. To a third add a few drops of concentrated hydrochloric acid, to the fourth nitric acid, and to the fifth concentrated sodium hydroxide solution. Note the cases in which coagulation occurs. **45-60**

Precipitation of a Protein by Cations

Introduce into six test tubes the following solutions: **60-75**

I. 5 ml. of water.
II. 5 ml. of egg-white solution.
III. 5 ml. of water and 4 drops of 10 per cent hydrochloric acid.
IV. 5 ml. of egg-white solution and 4 drops of 10 per cent hydrochloric acid.
V. 5 ml. of water and 4 drops of 10 per cent sodium hydroxide solution.
VI. 5 ml. of egg-white solution and 4 drops of 10 per cent sodium hydroxide solution.

Next introduce into each tube 2 ml. of 10 per cent copper sulfate solution and note the results. The control experiments in which no protein is used are necessary to determine whether the observed effect in each case is actually due to the precipitation of the protein or rather to precipitation of the metal hydroxide. Is the precipitate formed in tube VI simply copper hydroxide? How is the difference in the behavior of acidic, neutral, and alkaline solutions of proteins toward cation precipitants accounted for? What factor is important in determining the effectiveness of a cation precipitant, aside from the atomic weight of the cation?

Precipitation of Proteins by Anions

75-90 Prepare solutions identical with II, IV, and VI of the previous section. To each add 2 drops of potassium ferricyanide solution and note in which tube the precipitate forms most readily. Explain this result.

Action of Formaldehyde on Proteins

130-150 Place a little gliadin in a 20 per cent formaldehyde solution and allow it to stand for 15 minutes.

[Proceed with the following experiments.]

150-155 Remove the gliadin and compare its solubility in 70 per cent ethanol with that of untreated gliadin. Indicate how formaldehyde reacts with amino groups in proteins.

Biuret Color Reaction for Proteins

135-140 Add to an egg-white solution an equal volume of 10 per cent sodium hydroxide solution. Then add 1 drop of a 1 per cent copper sulfate solution. Note the color produced.

Formaldehyde Color Reaction for Proteins

140-145 To a small amount of egg-white solution contained in a test tube add 1 drop of dilute formaldehyde solution. Pour concentrated sulfuric acid down the tube in such a manner that it forms a separate layer in the bottom of the tube. What do you observe? Repeat the test with a gelatin solution. Note the result.

Millon's Test for Proteins

145-150 Add 5 drops of Millon's reagent to an egg-white solution, heat, and note the color. A protein when tested in this manner gives a reddish-orange color provided that a tyrosine, phenylalanine, or tryptophane moiety is present; otherwise the test is negative. Repeat the test with gelatin. What are your conclusions?

Xanthoproteic Reaction for Proteins

Add a small piece of wool or silk to about 1 ml. of **165-170** concentrated nitric acid contained in a test tube and heat the tube. Note the color of the material. Make the mixture alkaline by the addition of sodium hydroxide solution and note the change in color.

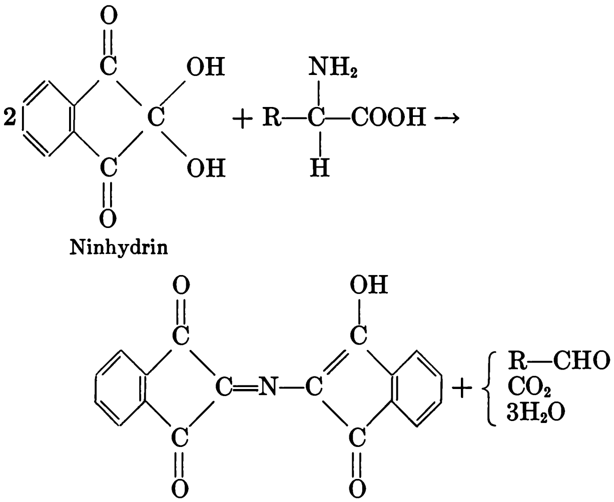
QUESTIONS

1. What is the essential chemical reaction involved in Millon's test?
2. Describe Heller's ring test. What is its main use?
3. What is a conjugated protein?
4. Casein is known to contain phosphorus in addition to the other common elements found in proteins. Does this fact indicate that casein is a conjugated protein?
5. What is the total number of isomers, including optical isomers, possible for a tripeptide containing the alanine, phenylalanine, and tryptophane moieties?
6. Hemoglobin contains 0.335 per cent of iron. What is the minimum possible molecular weight of hemoglobin? The actual molecular weight is four times this value.
7. Why does nitric acid produce a yellow color when it comes in contact with the skin?
8. Why is egg white frequently used as an antidote for various poisons?

EXPERIMENT 39

Amino Acids

Introduction. The hydrolysis of gelatin, started last period, should have been completed by now. However, in order to make sure of this point, the hydrolysate should be subjected to the biuret test at the start of this period. If the test is positive, indicating the presence of protein molecules, the solution must be refluxed for an additional period of time. Following completion of the hydrolysis, studies will be made of the buffer action of amino acids. Also, the action of nitrous acid on amino acids and the ninhydrin color test of such acids will be investigated. Ninhydrin is the common name for triketohydrindene hydrate, which undergoes reaction with an amino acid to form a blue compound according to the following equation:



The ninhydrin test represents an important part of the analysis of the components of a protein hydrolysate by the technique of paper chromatography. The amino acids present in the hydrolysate are partitioned between water absorbed on the cellulose of the paper and an organic solvent, only partially soluble in water, which is caused to travel along the strip of paper by either ascending or descending flow. The absorbed water represents the stationary phase and the organic solvent the moving phase. Butanol or phenol may be used as the organic solvent.

The more hydrophilic the amino acid, the more it tends to be retained in the stationary phase; the more lipophilic the acid, the greater is its tendency to travel with the moving organic phase. The ratio of the distance traveled by the amino acid to that traveled by the organic solvent is called the R_f value, a constant characteristic of each amino acid. When the chromatographic separation of the amino acids has been completed, the location of the various amino acids is determined by spraying the dried paper with ninhydrin solution. Well defined spots appear wherever the reagent comes in contact with an amino acid.

Acid-Catalyzed Hydrolysis of Gelatin (Continued from Experiment No. 38)

Apply the biuret test (page 112) to the gelatin solution that has been heated in the multiple unit bath since **0-15**
the last period. If the test is positive, indicating the presence of unhydrolyzed protein, heat the solution under reflux for the remainder of this period and proceed with another laboratory assignment according to the directions of your laboratory instructor. If the test is
negative, however, continue with this experiment. Di- **15-30**
lute the solution to about 300 ml. and add enough of a solution of barium hydroxide [$Ba(OH)_2 \cdot 7H_2O$] in hot water to neutralize all of the sulfuric acid originally used. Use litmus paper to detect the end point of the neutralization.

When the hot solution containing much barium sulfate is approximately neutral, filter it through a porcelain funnel using hardened filter paper. Test the filtrate with litmus paper and adjust the pH as nearly as possible to a value of seven. Add a small amount of
decolorizing charcoal, heat the mixture to boiling, filter **30-60**
and evaporate the filtrate to dryness in an evaporating dish. The residue consists of a mixture of amino acids including glycine, L(−)-hydroxyproline, L(−)-proline, L(+)-arginine, L(+)-alanine, L(−)-leucine, L(+)-lysine, L(+)-glutamic acid, L(−)-aspartic acid, L(−)-phenylalanine, L(−)-cystine and L(−)-tyrosine. While the solution is being evaporated to dryness, answer the questions at the end of this experiment.

Paper Chromatography of Amino Acids

With the aid of a pipette, place about 0.2 ml. of **60-75**
freshly prepared 80 per cent phenol in the bottom of a 25 x 200 mm. test tube without wetting the walls of the tube. Cut a piece of Whatman No. 1 filter paper into a 0.5 x 8 inch strip and fold it along its long axis. Use a clean spatula to crease the paper and handle only the upper 1 inch of the paper with the fingers. Cut the paper and crease it on a clean paper towel or sheet of writing paper in order to avoid contact with the laboratory desk.

Moisten the bottom of a clean glass rod in a dilute aqueous solution of the amino acids obtained by hydrolysis of gelatin and touch the rod to the strip of filter paper about ½ inch from the bottom. Cut off the top inch of the paper strip, the part that has been touched with the fingers, and with the aid of forceps lower the strip into the test tube containing the 80 per cent phenol solution so that only the bottom and top of the strip touch the test tube. Cork the tube, place it in an Erlen-

75-135 meyer flask at a slight angle, and allow it to stand for an hour.

Meanwhile, proceed with the remaining parts of today's assignment and continue with the questions at the end of this unit of work.

135-155 Remove the strip of paper from the test tube with the aid of forceps and measure the distance that the solvent front has traveled along the strip of paper. Wash the paper with a stream of acetone from a polyethylene wash bottle, and hang it from a hook made from a piece of wire and attached to a clamp on the ring stand.

155-165 Allow it to dry for 15 minutes, then spray it lightly with a solution prepared by dissolving 0.4 g. of ninhydrin and 1.5 ml. of pyridine in 100 ml. of 95 per cent ethanol. The paper should be made moist but not so wet that it drips. Spots indicating the positions of the various amino acids usually begin to appear within 5 to 10 minutes.

Of the amino acids found in gelatin hydrolysate, L(−)-proline, L(−)-phenylalanine, and L(+)-arginine will have traveled the farthest along the paper strip, while L(−)-cystine, L(−)-aspartic acid, L(+)-glutamic acid, and glycine will have traveled the least distance. Assume that the spot farthest removed from the point at which the mixture of amino acids was applied to the paper represents L(−)-proline, and then calculate the R_f value for this amino acid. Your result will be only approximate inasmuch as a more carefully designed experiment than the one described here would have to be carried out before accurate R_f values could be measured. The reported R_f value for L(−)-proline is 0.85.

Ninhydrin Reaction for Proteins and Amino Acids

75-90 Although the ninhydrin test is applied in the development of the paper chromatogram of the previous experiment, it is desirable to make a few preliminary test tube experiments with the reagent. The contents of a 0.1-g. vial of ninhydrin is dissolved in 30 ml. of water. Two drops of this solution are added to 2-3 ml. of the solution to be tested and the mixture is heated to boiling for about a minute. Cool the solution and note the result. Make the test on a solution of the amino acids obtained by hydrolysis of gelatin and on gelatin itself.

Buffer Action of Amino Acids

90-115 Add a drop of congo red indicator solution to 5 ml. of distilled water contained in a test tube and also to 5 ml. of a 1 per cent aqueous solution of the amino acids obtained by hydrolysis of gelatin. Is there any marked difference in the colors of the two solutions? Add approximately 0.1 *N* hydrochloric acid to each tube drop by drop and note the difference in behavior. Repeat the experiment with phenolphthalein as the indicator and 0.1 *N* sodium hydroxide solution. How are the results explained?

Action of Nitrous Acid on Amino Acids

Add 1 ml. of a 5 per cent aqueous solution of sodium nitrite to 5 ml. of an ice-cold solution which contains 5 per cent of hydrochloric acid and 2 per cent of the amino acid mixture obtained by the hydrolysis of gelatin. As a control experiment add the same amount of sodium nitrite solution to 5 ml. of ice-cold 5 per cent hydrochloric acid. Note the results. Write equations for the action of nitrous acid on glycine and alanine. **115-130**

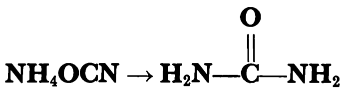
QUESTIONS

1. Write structural formulas for each of the amino acids listed as being among the hydrolysis products of gelatin.
2. Write equations to show how ninhydrin may be synthesized from phthalic acid and ethyl acetate as the organic starting materials.
3. R_f values vary with the solvent system and type of filter paper employed. Therefore the R_f values given below for various amino acids represent values for one particular system only: glycine, 0.42; alanine, 0.59; α-aminobutyric acid, 0.70; norleucine, 0.81; ornithine, 0.67; lysine, 0.71; arginine, 0.76; serine, 0.43; threonine, 0.51; tyrosine, 0.62; aspartic acid, 0.32; glutamic acid, 0.40. Plot each of these R_f values as ordinate vs. molecular weights of the amino acids as abscissa. Do the various amino acids seem to fall into certain natural groups in this plot? Draw any conclusions you can with regard to the relationship between R_f values and structures of the amino acids.
4. Would you expect the R_f value of ornithine to be higher or lower than the R_f value of its conjugate acid? Explain. Answer the same question with regard to aspartic acid and its conjugate base.
5. Would you expect lysine hydrochloride and lysine perchlorate to give different R_f values in the type of experiment carried out as a part of today's assignment?

EXPERIMENT 40

Preparation and Properties of Urea

$$(NH_4)_2SO_4 + 2KOCN \rightleftharpoons 2NH_4OCN + K_2SO_4$$



$$NH_4OCN \rightarrow H_2N{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}NH_2$$

Introduction. Urea is an important chemical, both with respect to its industrial uses and its role in biological processes. The compound is also of interest in the history of organic chemistry inasmuch as Wohler's synthesis of urea in 1828 represented an early synthesis of a typically organic compound from inorganic reagents. The first part of today's laboratory assignment consists of a synthesis of urea which is quite similar to Wohler's original preparation of the compound. The second part of the period will be devoted to a study of the properties of urea including: (1) hydrolysis reactions conducted under various conditions; (2) the formation of a salt with nitric acid; (3) degradation reactions with nitrous acid and sodium hypobromite; (4) thermal decomposition to isocyanic acid which forms biuret by further reaction with urea; (5) trimerization of isocyanic acid; and (6) formation of a resin by the action of formaldehyde on urea.

A. Preparation of Urea from Potassium Cyanate and Ammonium Sulfate

0-15 Place 10 g. of potassium cyanate and 35 g. of ammonium sulfate in an evaporating dish, and dissolve the salts in 25 ml. of hot water. Evaporate the solution
15-45 to dryness on the steam bath.

[During this interim answer some of the questions at the end of today's assignment.]

The residue consists mainly of a mixture of urea, which
45-75 is soluble in absolute ethanol, and potassium sulfate, which is insoluble in alcohol. Place the solid material in an Erlenmeyer flask, add 25 ml. of absolute alcohol, and heat the mixture on the steam bath until the solvent begins to boil. Decant the liquid into a filter funnel. Repeat the alcohol extraction of the residue and combine the filtrates. Evaporate the solution to dryness, and determine the weight and the melting point of the crystalline residue. Calculate the per cent yield of product.

B. Hydrolysis of Urea

75-85 (*1*) *In Alkaline Solution.* Add 5 ml. of 5 per cent sodium hydroxide solution to about 0.5 g. of urea contained in a test tube, and warm the solution gently. Note the odor of the escaping gas. Write the equation for the reaction.

85-95 (*2*) *In Acid Solution.* Dissolve about 0.5 g. of urea in 5 ml. of 5 per cent hydrochloric acid and boil the solution for about 2 minutes. Make the solution alkaline and note the odor of the vapor above the solution. Test the vapor with litmus paper. Write the equation for the reaction.

C. Formation of Urea Nitrate

To a solution of 2 g. of urea in a small amount of water add a few ml. of concentrated nitric acid. What is the precipitate which forms? Write the equation for the reaction. 95-100

D. Reaction of Urea with Nitrous Acid

Add 1 ml. of 5 per cent sodium nitrite solution to an ice-cold solution of about 0.1 g. of urea in 5 ml. of 5 per cent hydrochloric acid. Note the evolution of a gas. As a control experiment add the same amount of sodium nitrite to 5 ml. of ice-cold 5 per cent hydrochloric acid alone. Is there any gas evolution in this experiment? Write the equation for the reaction of urea with nitrous acid. 100-110

E. Reaction of Urea with Sodium Hypobromite

Add a small amount of sodium hypobromite solution to about 5 ml. of a dilute aqueous solution of urea. Note the evolution of a gas. If sodium hypobromite solution is not available in the laboratory, it may be prepared by adding bromine to a 10 per cent sodium hydroxide solution until a yellow color persists. Write the equation for the reaction of urea with sodium hypobromite. 110-120

F. Biuret and Cyanuric Acid

Place 1 g. of urea in a test tube and heat the tube and its contents until evolution of gas has almost ceased and the mass has resolidified. What is the gas? Cool the tube and stir the contents with 5 ml. of cold water to dissolve the biuret which resulted from the pyrolysis reaction. Cyanuric acid, which is also present, is less soluble. Filter the mixture, make the filtrate alkaline by addition of 10 per cent sodium hydroxide solution, and add 2 drops of 1 per cent copper sulfate solution. What do you observe? 120-135

Wash the insoluble portion of the pyrolysis mixture with another 5 ml. of water, then dissolve the residual cyanuric acid in the minimum amount of boiling water. Add 1 ml. of an ammoniacal solution of copper sulfate. Note the formation of a precipitate of copper cyanurate.

Write two equations for the pyrolysis of urea, one showing the formation of biuret and the other showing the formation of cyanuric acid.

G. Urea Resin

135-160 Prepare in an 8-inch test tube a solution containing 3 g. of urea and 5 ml. of concentrated hydrochloric acid in 30 ml. of water. Place a few drops of methyl orange indicator in the solution in order to color it, then add 3 ml. of formalin and mix the reagents by shaking the tube. Allow the tube to stand for several minutes. What is your observation? Write an equation for a partial reaction.

QUESTIONS

1. Write equations to show how urea may be prepared from ammonia and each of the following reagents: (a) phosgene, (b) ethyl carbonate, (c) ethyl carbamate, (d) ethyl chloroformate, (e) carbon dioxide.

2. Write equations to show how urea and any other needed reagents may be used for the synthesis of each of the following compounds: (a) semicarbazide, (b) parabanic acid, (c) barbituric acid, (d) amytal, (e) phenobarbital, (f) uric acid, (g) guanidine.

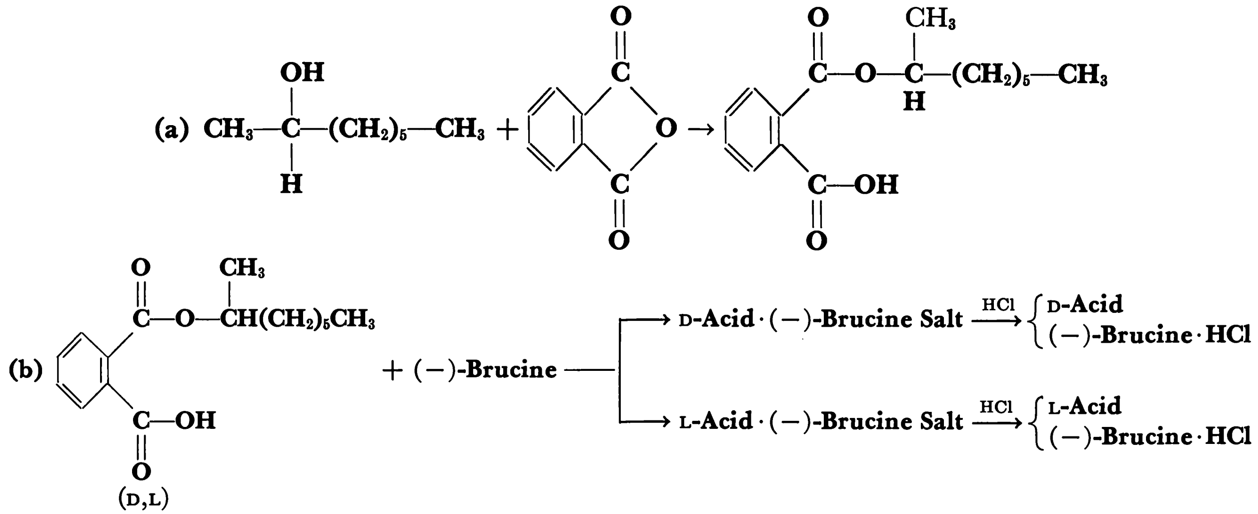
3. In the formation of the conjugate acid of urea, why is it more likely that the proton becomes bonded to oxygen rather than to nitrogen?

4. Would you expect guanidine or urea to be the stronger base? Why does but one proton add to these bases? Justify your answers.

5. How may urea be prepared from calcium cyanamide?

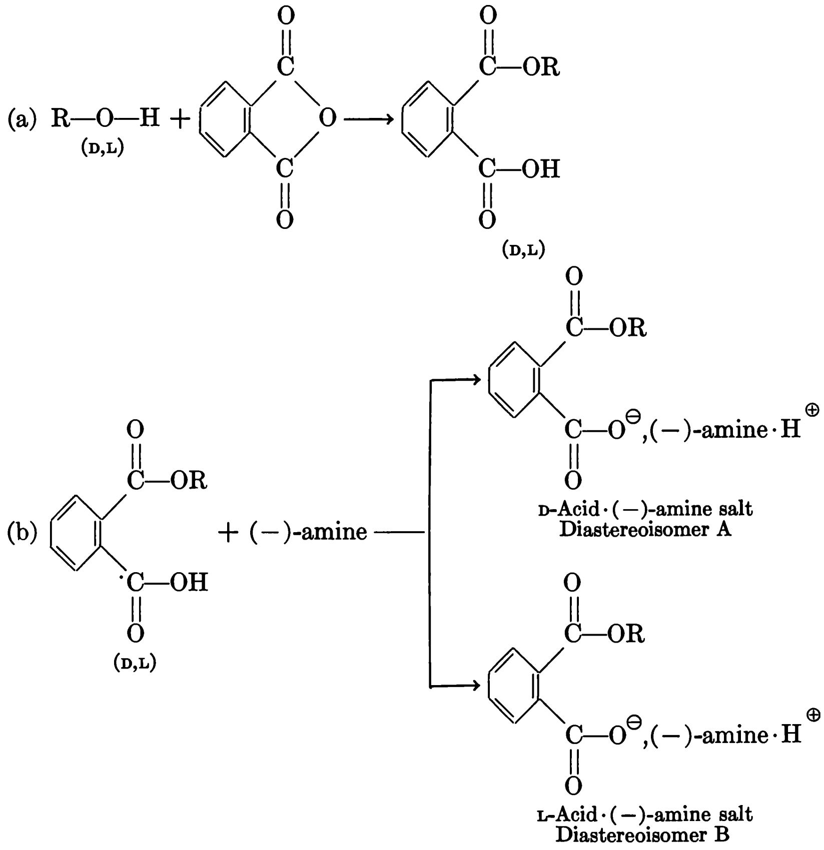
EXPERIMENT 41

I. Preparation and Resolution of D,L-*s*-Octyl Hydrogen Phthalate

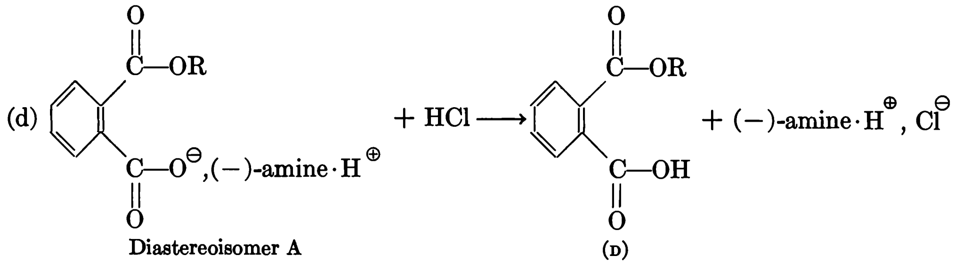


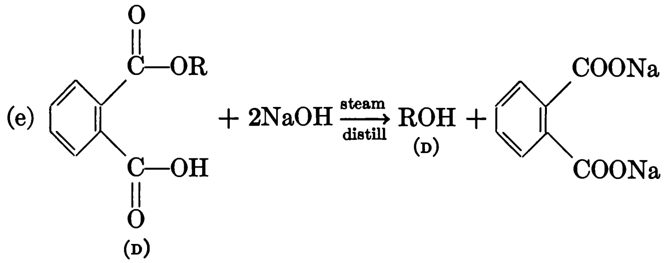
II. Optical Properties of Some Common Carbohydrates

Introduction. One of the classical methods for resolution of a racemate is to convert the enantiomorphs to diastereoisomers by reaction with a suitable optically active compound, separate the diastereoisomers by fractional crystallization, then regenerate the individual enantiomorphs. In the experiments for today and the next period, this classical general scheme is adapted to the resolution of a D,L-alcohol as shown below:



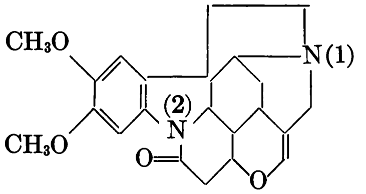
(c) Diastereoisomers A and B are separated by fractional crystallization.





(f) The same procedure as shown in (d) and (e) is used for the isolation of the L-alcohol.

The D,L-alcohol which is to be resolved is 2-octanol, and the resolving agent is the levorotatory alkaloid (−)-brucine, which is obtained from the bark of *Strychnos nux vomica*. The structure of brucine is shown below. Despite its structural complexity, the functional groups present in the molecule are easily recognizable. Note that one nitrogen atom (1) is part of a tertiary amino group, whereas the other nitrogen atom (2) belongs to an acid amide group.



(−)-Brucine

I. PREPARATION AND RESOLUTION OF D,L-s-OCTYL HYDROGEN PHTHALATE

(a) Preparation of D,L-s-Octyl Hydrogen Phthalate

0-70 *Procedure*. Mix 32.5 g. of anhydrous D,L-2-octanol, 37 g. of pure phthalic anhydride (Note 1) and 20 g. of anhydrous pyridine (Note 2) in a 125-ml. Erlenmeyer flask, and heat the mixture on the steam bath for an hour. The flask should be stoppered after the contents have attained the temperature of the bath.

[While the flask is being heated, proceed with Part B of today's laboratory assignment.]

70-120 Dissolve the viscous mass in an equal volume of acetone and add slowly, with stirring, 28 ml. of concentrated hydrochloric acid diluted with an equal volume of crushed ice. If an oil separates before all of the hydrochloric acid solution has been added, add sufficient acetone to make a homogeneous solution.

Pour the solution into a 1000-ml. steam distillation flask, add water until an oil separates, and subject the mixture to steam distillation until the distillate is no longer cloudy. Pour the contents of the steam distillation flask, containing the octyl hydrogen phthalate, into an Erlenmeyer flask and allow the mixture to cool.

Collect the solid D,L-*s*-octyl hydrogen phthalate by suction filtration, wash it with water, grind it in a mortar with water, filter again, wash it with a small amount of alcohol, then with a small amount of ether and allow the solid to dry in the air.

(b) Resolution of D,L-s-Octyl Hydrogen Phthalate by the Use of (−)-Brucine

Procedure. To a solution of 70 g. of D,L-*s*-octyl hydrogen phthalate in 150 ml. of warm acetone contained in a 500-ml. round-bottomed flask add 108 g. of (−)-brucine tetrahydrate. Attach a reflux condenser to the flask and heat the mixture on the steam bath until a clear solution results. Upon cooling, one of the diastereoisomers [(+)-Acid·(−)-Brucine Salt] separates in crystalline form. Collect the solid by suction filtration and wash it with about 60 ml. of cold acetone. Save the filtrate and the wash solution. 120-165

Transfer the crystalline material to an Erlenmeyer flask and cover the solid with acetone. Add slowly, with stirring, a small excess of 6 *N* hydrochloric acid (about 30 ml.). If necessary, add more acetone to keep the solution clear. Add ice water until precipitation of the dextrorotatory enantiomorph of *s*-octyl hydrogen phthalate is complete. Collect the solid by suction filtration, wash it with cold water and allow it to dry in the air.

Distill about half of the solvent from the original filtrate plus wash solution and pour the residue into 30 ml. of 6 *N* hydrochloric acid. Add about 150 ml. of cold water and collect the resulting precipitate by suction filtration. This is the somewhat crude levorotatory enantiomorph of *s*-octyl hydrogen phthalate. Wash this solid with cold water and allow it to dry in the air.

Crystallize the two crude enantiomorphs from 90 per cent acetic acid and determine the melting points of the two samples. If the melting points are not sharp and within one degree of 75°, recrystallize the samples from 90 per cent acetic acid. Repeat this procedure until both enantiomorphs melt sharply at about 75°. It will probably be necessary to complete the purification of the two enantiomorphs during the next laboratory period. The enantiomorphs have specific rotations, $[\alpha]_D$, in absolute ethanol of about 44° and −44°, respectively.

NOTES

1. Phthalic anhydride can be freed of phthalic acid by extraction with chloroform. The anhydride is soluble but the acid is insoluble.

2. Pyridine dried over anhydrous barium oxide is suitable for use in this experiment. The laboratory instructor should prepare for the experiment by drying a good grade of pyridine over several successive batches of barium oxide for several days prior to the present laboratory period.

II. Optical Properties of Some Common Carbohydrates

1. Mutarotation of Glucose

A freshly prepared aqueous solution of α-D(+)-glucose, the common crystalline form of glucose, undergoes a change in rotatory power rather slowly. However, basic substances act as catalysts for bringing about equilibration of α-D(+)-glucose with some of its tautomers. In this experiment the addition of a small amount of ammonia to a solution of α-D(+)-glucose causes the solution to change its rotatory power at a moderately rapid rate.

10-30 *Procedure.* Add sufficient water to 10 g. of α-D(+)-glucose to prepare 100 ml. of solution. Fill a 1-decimeter polarimeter tube with this solution and determine the rotation. Add 1 drop of concentrated ammonium hydroxide to 50 ml. of the original solution, fill the polarimeter tube and determine the rotation of this solution. Take several readings at intervals of a minute or two. Does the polarimeter reading remain constant? Does it increase or decrease? Write equations to show the structural changes which α-D(+)-glucose undergoes on standing in solution (Note 1).

2. Acid-Catalyzed Hydrolysis of Sucrose

Sucrose (which is dextrorotatory) undergoes acid-catalyzed hydrolysis to produce equimolar amounts of D(+)-glucose and D(−)-fructose. Inasmuch as the specific rotation of D(−)-fructose is greater than that of D(+)-glucose, the course of the hydrolysis can be followed by observation of inversion of rotation of the solution.

Procedure. Prepare 100 ml. of a 10 per cent solution of sucrose in water as accurately as possible without the use of an analytical balance. Determine its rotation in a polarimeter and calculate the specific rotation. 30-70

To 50 ml. of the solution add 5 ml. of concentrated hydrochloric acid, dilute the solution to 100 ml. and heat the solution on the steam bath for 20 minutes. Determine the rotation of this solution and calculate the approximate specific rotation. These results will be only approximations owing to the inexperience of the student taking the polarimetric measurements and also to the lack of precision in the preparation of the solutions. Write the equation for the hydrolysis of sucrose.

NOTE

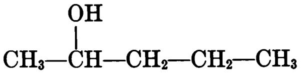
1. In order to avoid congestion in the use of the polarimeter, it might be necessary for the instructor to limit the number of students carrying out this experiment during any one laboratory period.

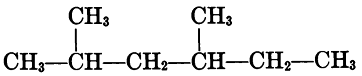
QUESTIONS

1. Give one-sentence definitions or descriptions of each of the following terms: (a) resolution, (b) racemization, (c) enantiomorphs, (d) diastereoisomers, (e) meso form, (f) specific rotation, and (g) racemic mixture or compound.

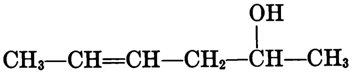
2. Why is it usually impossible to separate enantiomorphs by conventional techniques such as fractional crystallization or fractional distillation? Under what circumstances may a resolution sometimes be effected following recrystallization of certain racemates?

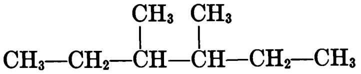
3. How many and what types of stereoisomers exist for each of the following compounds?

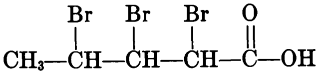
(a)

$CH_3-\overset{\overset{\displaystyle OH}{|}}{C}H-CH_2-CH_2-CH_3$

(b)

$CH_3-\overset{\overset{\displaystyle CH_3}{|}}{C}H-CH_2-\overset{\overset{\displaystyle CH_3}{|}}{C}H-CH_2-CH_3$

(c) $CH_3-CH=CH-CH_2-CH_3$

(d)

$CH_3-CH=CH-CH_2-\overset{\overset{\displaystyle OH}{|}}{C}H-CH_3$

(e)

$CH_3-CH_2-\overset{\overset{\displaystyle CH_3}{|}}{C}H-\overset{\overset{\displaystyle CH_3}{|}}{C}H-CH_2-CH_3$

(f)

$CH_3-\overset{\overset{\displaystyle Br}{|}}{C}H-\overset{\overset{\displaystyle Br}{|}}{C}H-\overset{\overset{\displaystyle Br}{|}}{C}H-\overset{\overset{\displaystyle O}{\|}}{C}-OH$

4. Will an L-alcohol undergo Fischer esterification with each of two enantiomorphic carboxylic acids at equal speeds? Explain.

5. What is the difference between conformers and optical or geometrical isomers?

EXPERIMENT 42

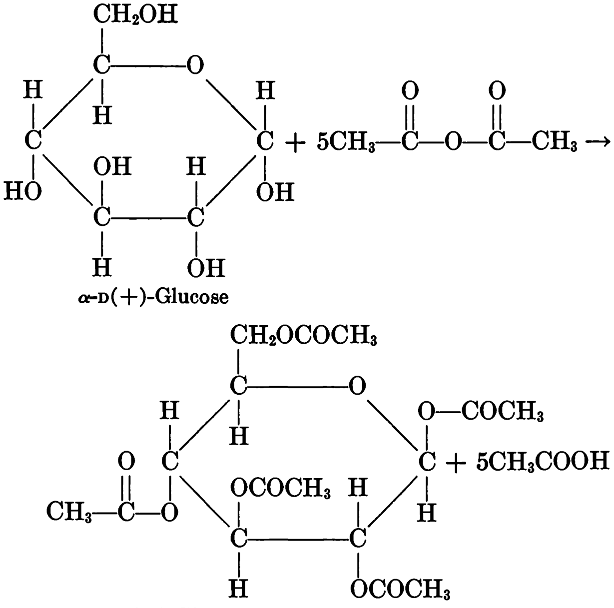
I. Preparation of β-D(+)-Glucose Pentaacetate

II. Preparation of Dextrorotatory 2-Octanol

Introduction. Esters may be prepared by reaction of alcohols with acid anhydrides. Since glucose contains five alcoholic groups per molecule, it is possible to prepare a pentaacetate by reaction with acetic anhydride. The use of a catalyst is of importance, not only in increasing the speed of the reaction, but also in influencing the stereochemical course of the reaction. For example, the use of sodium acetate to catalyze the reaction between D(+)-glucose and acetic anhydride leads to the formation of β-D(+)-glucose pentaacetate, whereas the use of zinc chloride leads to the formation of α-D(+)-glucose pentaacetate.

In today's work while the mixture of D(+)-glucose, acetic anhydride and sodium acetate is being heated, one of the enantiomorphs, the dextrorotatory 2-octyl hydrogen phthalate, prepared during the preceding laboratory period, will be saponified and the corresponding optically active alcohol isolated. If time was insufficient to complete the purification of the two hydrogen phthalate esters during the last period, begin or repeat the recrystallization step before starting with Part I of today's experiment.

I. Preparation of β-D(+)-Glucose Pentaacetate


α-D(+)-Glucose

β-D(+)-Glucose pentaacetate

0-20 *Procedure.* Place 10 g. of dry α-D(+)-glucose and 6 g. of anhydrous sodium acetate (Note 1) in a mortar and mix the two compounds thoroughly by grinding them with the pestle. Transfer the mixture to a round-bottomed flask, add 50 ml. of acetic anhydride, attach an air condenser, and heat the mixture on the steam 20-80
bath for an hour, with occasional shaking of the flask.

[While the mixture is being heated, proceed with Part II.]

To about 400 ml. of crushed ice and water contained 80-90
in a beaker slowly add the hot reaction mixture with
stirring. Stir occasionally, and allow the mixture to 90-130
stand for 40 minutes.

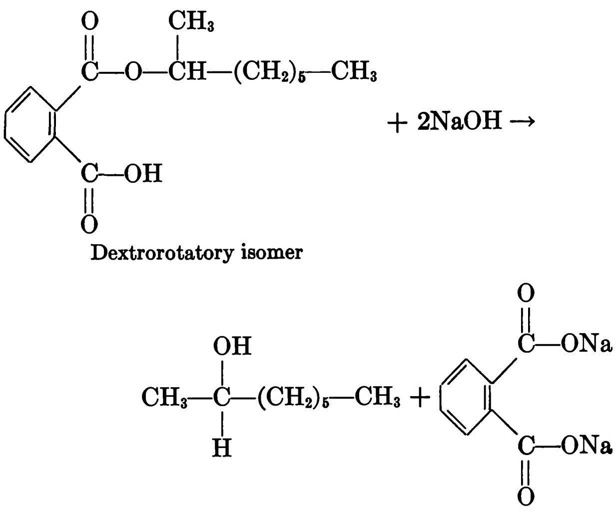
[Continue with Part II.]

Filter the solid with suction, wash it with small
amounts of cold water, alcohol, and ether, and re- 130-160
crystallize about 1 g. of the material from hot water.
Determine the melting point of the purified material
(Note 2). Weigh the air-dried solid and calculate the
per cent yield.

NOTES

1. If anhydrous sodium acetate is not available in the laboratory, prepare some according to the directions given on page 45.
2. Pure β-D(+)-glucose pentaacetate melts at 132°.

II. Preparation of Dextrorotatory 2-Octanol


Dextrorotatory isomer

Dextrorotatory isomer

Procedure. Place 20 g. of dextrorotatory *s*-octyl hy-
drogen phthalate and a solution of 8 g. of sodium 20-35
hydroxide in 20 ml. of water in a round-bottomed
flask equipped with a reflux condenser and boil the
solution for 15 minutes. Add 150 ml. of water and re- 35-50

50-80 arrange the apparatus for distillation. Collect distillate until it is no longer turbid.

Extract the distillate with two 50-ml. portions of **80-95** ether, and dry the ether extract over anhydrous magnesium sulfate for 15 minutes. Filter the solution and **95-130** remove the ether by distillation. Weigh the residue and dilute it to a volume of 30 ml. by addition of ethanol. Determine the rotation of this solution in a polarimeter. Calculate the approximate specific rotation of the solution.

Levorotatory 2-octanol could be obtained by treatment of the levorotatory hydrogen phthalate in the same manner as described previously for the dextrorotatory enantiomorph. However, there is insufficient time to carry out this experiment, and, in any event, this would represent an uninstructive repetition of work already done.

QUESTIONS

1. Write structural formulas for sucrose octaacetate and α-D(+)-glucose pentaacetate.

2. Write the Fischer projection formula for β-D(+)-glucose pentaacetate.

3. Draw the most stable conformation for β-D(+)-glucose pentaacetate. Are the acetoxyl groups axial or equatorial?

4. Write out a detailed mechanism for the saponification of *s*-octyl hydrogen phthalate. Are any of the bonds to the asymmetric carbon atom broken in the saponification step? Does the optically active alcohol obtained from one of the enantiomorphic hydrogen phthalates have the same absolute configuration as the half ester?

5. Write out the mechanism for the reaction of 2-octanol with phthalic anhydride. Would you expect to obtain an optically active hydrogen phthalate ester by reaction of dextrorotatory 2-octanol with phthalic anhydride?

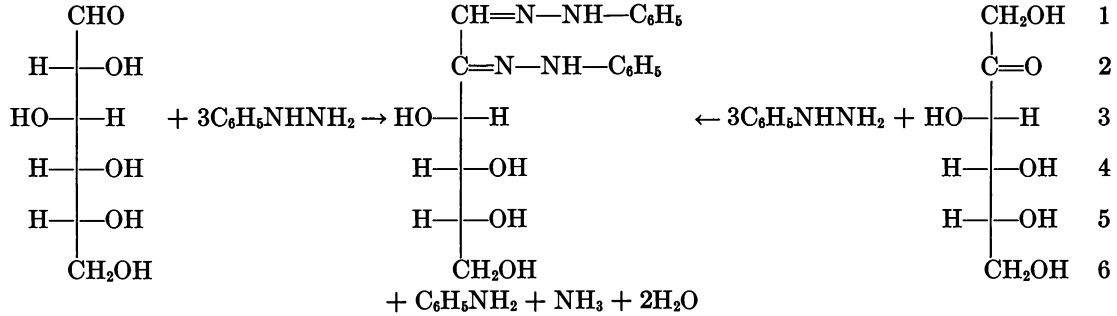
EXPERIMENT 43

Chemical Properties of Some Common Carbohydrates

Introduction. Over the years, phenylhydrazine has proved to be a very valuable reagent in the characterization of many carbohydrates and in stereochemical studies of the sugars. Both uses of the reagent are illustrated in today's major experiment, which consists of the preparation of phenylosazones of D(+)-glucose and D(−)-fructose. As supplementary experiments, the relative ease of oxidation of D(+)-glucose, sucrose, maltose, and lactose will be studied. In addition, both the acid-catalyzed and enzymatic hydrolysis of sucrose will be investigated.

Fasten melting point tubes containing the two samples of phenylosazone to the thermometer and carry out **135-160** both melting point determinations at the same time. Since phenylosazones melt with decomposition, and since the decomposition range varies markedly, depending on the rate of heating of the melting point bath, the bath should be heated at a standard rate, viz., 0.5° per second. Mix equal amounts of the two samples and determine the decomposition point of the mixture. Record your conclusions in your notebook.

I. PHENYLOSAZONES OF D(+)-GLUCOSE AND D(−)-FRUCTOSE



D(+)-Glucose

D(−)-Fructose

Procedure. Heat about 600 ml. of water to its boiling
0-20 point in a large beaker. While the water is being heated, introduce 20-ml. portions of 5 per cent solutions of D(+)-glucose and D(−)-fructose into each of two large test tubes. To each solution add either 2 ml. of phenylhydrazine, 3 g. of sodium acetate, and 3 ml. of glacial acetic acid or 3 g. of phenylhydrazine hydrochloride plus 3 g. of sodium acetate. Stir the solutions. As soon as the water in the beaker begins to boil, extinguish the burner and place the test tubes in the hot water. Allow
20-50 them to stand in the hot water for 30 minutes.

[Proceed with the next part of the assignment for today.]

During this time crystals of the phenylosazone appear and increase in amount as the mixtures cool. Col-
50-60 lect the crystals on a filter and with a low-power microscope examine the shapes of the crystals from the two reaction mixtures. Do the two batches of crystals have the same appearance?

Crystallize the two batches of phenylosazone from
60-75 hot 50 per cent ethanol. In this case it is better to sacrifice yields in order to obtain small amounts of pure product for melting point determinations. Collect the crystals by filtration and allow them to dry on a
75-135 porous clay plate for 20 to 30 minutes.

[Proceed with the short experiments given in Parts II, III and IV.]

II. EASE OF OXIDATION OF D(+)-GLUCOSE

(*a*) *With Permanganate.* Place a few ml. of a 10 per **20-30**
cent glucose solution in a test tube and add a few drops of 0.3 per cent potassium permanganate solution. Does oxidation occur at room temperature or must the mixture be warmed in order for the reaction to take place? Repeat the experiment with a 10 per cent glucose solution to which has been added 1 drop of 10 per cent sodium hydroxide solution. What is your observation?

(*b*) *With Tollens' Reagent.* Determine whether **30-40**
glucose, in dilute solution, is oxidized by Tollens' reagent. What is the relative ease of oxidation as compared with any typical aliphatic aldehyde? What complicating situation exists?

(*c*) *With Fehling's Solution.* Add a few drops of 10 **40-50**
per cent glucose solution to 6 ml. of Fehling's solution (3 ml. each of solutions A and B) and heat. Record your observations.

III. REDUCING ACTION OF DISACCHARIDES

Add a few drops of dilute solutions of sucrose, malt- **75-90**
ose, and lactose to separate test tubes each containing 5 ml. of Fehling's solution. Place the tubes in boiling water and note the results. Carry out similar tests with Tollens' reagent. Record your observations.

IV. HYDROLYSIS OF SUCROSE

(*a*) *Conditions Favoring Hydrolysis.* Place three test **90-110**
tubes, each containing 5 ml. of a 5 per cent solution of

sucrose, in a beaker of hot water and to these add equal volumes of (1) water, (2) 10 per cent hydrochloric acid, and (3) 10 per cent sodium hydroxide solution. Heat the tubes for 5 minutes, then test a portion of each reaction mixture with Fehling's solution. What are your conclusions?

110-135 (*b*) *Enzymatic Hydrolysis*. Prepare a suspension of baker's yeast by adding a few drops of water to one eighth of a small cake of compressed yeast, macerating the mixture, then adding 10 ml. of water. Add 5 ml. of the suspension to an equal volume of 5 per cent sucrose solution, and, as a control, add 5 ml. of water to the second portion of the suspension. Warm the two mixtures to about 35° in a beaker of warm water and allow them to stand at that temperature for 15 minutes.

[Begin to answer the questions at the end of this assignment.]

Test a portion of each suspension with Fehling's solution. What are your observations? The control experiment is carried out to check whether the yeast itself contains a reducing agent.

QUESTIONS

1. May D-gluconic acid be prepared by oxidation of D(+)-glucose with either Fehling's solution or Tollens' reagent? What is the reagent usually used for the preparation of D-gluconic acid?

2. Write structural formulas for sucrose, maltose, and lactose. Which of these disaccharides would be expected to exhibit mutarotation?

3. What conclusions may be drawn as to the relative configurations of carbon atoms numbered 3, 4, and 5 in both D(+)-glucose and D(−)-fructose as a result of the phenylosazone preparation?

4. What products would be obtained on treatment of maltose with methanol and a catalytic amount of hydrogen chloride? Answer the same question for lactose. Equations.

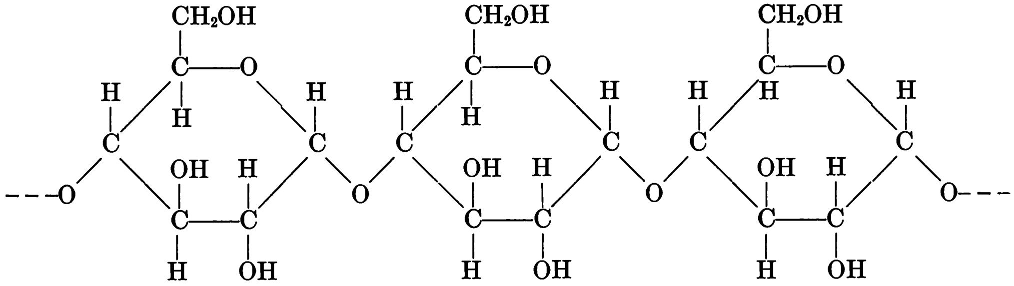
5. Write the structural formula of a typical acetal. How would this acetal behave toward (1) water, (2) dilute hydrochloric acid, and (3) dilute sodium hydroxide solution?

EXPERIMENT 44

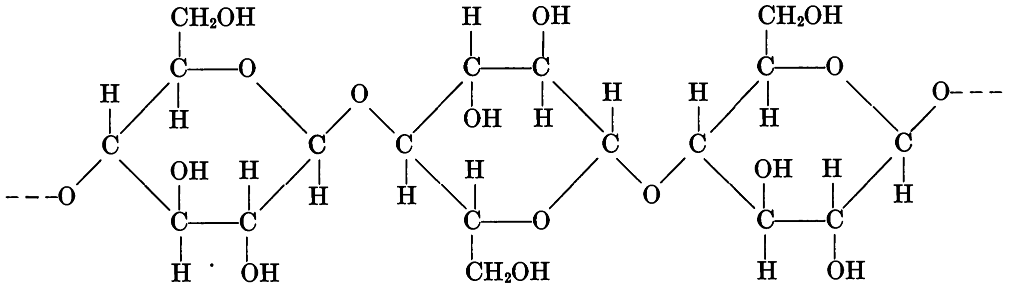
Polysaccharides

Introduction. Starch is widely distributed in plants and is stored in grains and tubers as a food supply for the germinating seed. All types of starch give a blue color with iodine, and this serves as a sensitive qualitative test either for starch or for iodine. Acid-catalyzed hydrolysis of starch converts it through several grades of dextrin to maltose and finally to D(+)-glucose. The iodine test is used to follow the extent of hydrolysis since the coloration changes progressively from blue to faint red as the molecular weight of the organic molecule decreases. In fact, the dextrins of low molecular weight, maltose, and D(+)-glucose show no coloration with iodine.

The functional groups found in starch and cellulose are hydroxyl and acetal groups. As shown in the structures, these molecules differ in configuration, starch having the α-glucoside and cellulose the β-glucoside configuration. They also differ in size, cellulose having a much larger average molecular weight than starch.



A segment of the starch molecule



A segment of the cellulose molecule

The chemical properties of starch and cellulose reflect the properties of the individual functional groups present. Acid-catalyzed hydrolysis represents a typical property of acetals. The formation of cellulose nitrate, cellulose acetate, and cellulose xanthate illustrate the ester-forming property of the alcoholic hydroxyl groups present in the polymer.

Cellulose dissolves in cupric ammonia hydroxide solution (Schweitzer's reagent) and is reprecipitated when acid is added to the solution. Probably the solution contains complex ions in which each copper ion is coordinated with several of the oxygen atoms of the hydroxyl groups of cellulose.

When paper (cellulose) is treated with 80 per cent sulfuric acid, the surface of the paper is altered and the resulting product resembles parchment. Although the exact chemistry of this process is obscure, the changes in the surface molecules probably involve both hydrolysis and dehydration.

Experimental

The following tests show some of the easily observed properties of starch and cellulose.

(a) Iodine Test for Starch

Prepare a starch solution by mixing thoroughly 2 g. of starch with 10 ml. of water and then pouring this mixture into 200 ml. of boiling water. Save part of the solution for later experiments. **0-25**

Add a drop of a very dilute aqueous solution (straw-colored) of iodine in potassium iodide to a few ml. of the starch solution. Note the color of the solution. Heat the colored solution to boiling and observe the effect. Also note the effect produced by cooling the solution. Add a few drops of sodium thiosulfate solution to the cooled solution and note the result. Explain.

(b) Starch and Fehling's Solution

Test the reducing action of Fehling's solution on 3 ml. of starch solution and record the result. **25-30**

(c) Hydrolysis of Starch

30-50 Add 1 ml. of concentrated hydrochloric acid to 25 ml. of starch solution. Boil the solution and withdraw about 1 ml. at frequent intervals for an iodine test. Record the color of the test solutions at the various intervals.

When the solution no longer gives a color with iodine, neutralize it and test a portion with Fehling's solution. Write structural formulas for the end products (a disaccharide and a monosaccharide) of the hydrolysis of starch.

50-65 Repeat the experiment, adding 5 ml. of 10 per cent sodium hydroxide solution instead of hydrochloric acid as the catalyst. Are the results the same?

(d) Enzymatic Hydrolysis of Starch

65-85 Collect about 10 ml. of saliva. Its flow may be accelerated by chewing paraffin. Filter the saliva through a previously moistened filter paper and add 5 ml. of the filtrate to 50 ml. of starch solution. Watch for changes in the appearance of the starch solution, and also test 1-ml. samples of the solution from time to time with iodine. Note the period of time required for essentially complete hydrolysis of the starch solution (negative iodine test).

Test the solution with Fehling's solution at this time. Is the principal end product the same in both the enzymatic and acid-catalyzed hydrolysis? Do different samples of saliva show equal activity in catalysis of starch hydrolysis? (Consult your neighbors about their results.)

(e) Dialysis of a Starch Solution

85-105 The purpose of this experiment is to determine whether starch in solution will pass through a parchment paper membrane. The same test will be made with a glucose solution. Select 2-3 pieces of parchment paper about 5 cm. square and allow them to soak in water several minutes. Add to a large test tube 10 ml. of starch solution and carefully cover the mouth of the tube with parchment paper, holding it fast with a number of windings of string. Dry the outside of the parchment paper with a piece of filter paper and clamp the test tube to a ring stand in the inverted position for a few minutes to test whether it leaks. If it does leak, repeat the procedure with a different piece of parchment paper.

Rinse the outside of the tube and paper with distilled water, then clamp the tube in a beaker of distilled water in the inverted position and adjust it such that the level of water in the beaker coincides with that of the solution in the test tube. Carry out exactly the same procedure with a test tube containing 10 ml. of a 5 per cent solution of D(+)-glucose.

Allow the two tubes to remain in the separate beakers of distilled water until the next period. At that time, test the contents of the beakers for starch and glucose, respectively. How might you effect separation of the components of a starch-glucose mixture?

(f) Cellulose Nitrate-Collodion

Add 10 ml. of concentrated sulfuric acid to 10 ml. of concentrated nitric acid contained in a small beaker and heat the mixed acid solution on the steam bath. Add about 0.5 g. of cotton and allow it to remain in contact with the acid solution for 3 minutes. Remove the partially nitrated cotton (cellulose) from the acid with a stirring rod and press the cotton against the wall of the beaker in order to free it of as much of the acid solution as possible. Next, wash the nitrated cotton with a large amount of water, squeeze out as much of the water as possible, and allow the material to dry. While it is drying, proceed with the remaining parts of today's assignment. 105-115

Digest the nitrated cotton with 20 ml. of a mixture of equal volumes of ether and alcohol, decant, and allow a portion of the solution to evaporate on a watch glass. Note the appearance of the residual film and test its flammability on a very small portion. Record your observations. 155-160

(g) Cellulose Acetate

To a solution of 6 ml. of acetic anhydride and 2 drops of concentrated sulfuric acid in 20 ml. of glacial acetic acid, contained in a small Erlenmeyer flask, add 0.5 g. of cotton and wet it as thoroughly as possible with the solution. Stopper the flask and allow the reaction mixture to stand until the next laboratory period. By this time the cotton will have been converted to cellulose acetate, which is soluble in the reaction medium. 115-125

Pour the solution in a thin stream into 500 ml. of water and collect the resulting precipitate by filtration. Dry the precipitate by pressing it between pieces of filter paper. Dissolve a small portion of the solid in chloroform and allow the solution to evaporate on a watch glass. Note the appearance of the film and test a small portion for its flammability. How do you account for its behavior as contrasted with that of cellulose nitrate?

(h) Cellulose Xanthate-Viscose

To 5 ml. of 20 per cent sodium hydroxide solution contained in a test tube add a small wad of cotton. Wet the cotton thoroughly and warm the solution for about 3 minutes. Remove the cotton with a stirring rod, and squeeze out as much as possible of the solution. The fingers should be protected from the alkaline solution by the use of rubber cots or gloves. Place the cotton in another test tube and add 5 ml. of carbon disulfide. Stopper the tube and allow the mixture to stand until the next laboratory period. 125-135

Remove the cotton from the orange-colored solution and squeeze out the liquid. Allow the carbon disulfide to evaporate from the cotton wad, then add it to about 10 ml. of a 10 per cent sodium hydroxide solution. Shake the mixture until a fairly homogeneous suspension is obtained. Pour the viscous liquid in a thin stream into dilute hydrochloric acid. Record your observations.

(i) Action of Schweitzer's Reagent on Cellulose

135-150 To 100 ml. of a 5 per cent copper sulfate solution add 5 ml. of 10-20 per cent ammonium chloride solution, then add sodium hydroxide solution as long as a precipitate forms. Wash the precipitate by decantation with 500 ml. of water three times. Collect the precipitate in a cotton-cloth filter and wash it until the wash water is free of sulfates.

Dissolve as much of the solid copper hydroxide as possible in 10 ml. of concentrated ammonium hydroxide solution (sp. gr. 0.90). This solution is Schweitzer's reagent. Dissolve some filter paper (cellulose) in the solution and then pour the cellulose solution into dilute hydrochloric acid. Why does acid cause the reprecipitation of the cellulose?

(j) Parchment Paper

150-155 Carefully pour 40 ml. of concentrated sulfuric acid into 20 ml. of water. Cool the solution thoroughly and place it in an evaporating dish. Immerse a piece of filter paper in the solution and allow it to remain there 10-12 seconds. Remove the paper, rinse it with running water, neutralize the remaining traces of acid by dipping the paper in dilute ammonium hydroxide solution, then wash it again with running water. The resulting material is parchment paper. How does it differ from the paper used in its preparation?

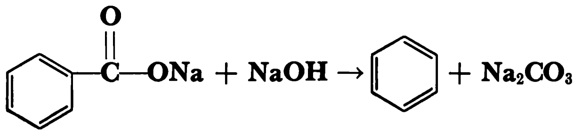
QUESTIONS

1. What are some of the lines of evidence for the structures of starch and cellulose?
2. Write a structural formula for cellobiose. How is cellobiose related to cellulose? How does cellobiose differ from maltose?
3. What is glycogen? Where is it found? It acts also as a reservoir for what inorganic group of importance in biological processes?
4. What is inulin? Where is it found?
5. Write partial equations to show the conversion of cellulose to cellulose trinitrate, cellulose triacetate and cellulose xanthate.
6. What is ethyl cellulose and how may it be prepared?
7. How may β-cellulose be differentiated from α-cellulose?
8. What is Pyroxylin? Celluloid? Collodion? Cellophane?
9. Of what use is cellulose to termites and other insects?

EXPERIMENT 45

Properties of Aromatic Hydrocarbons[1]

A. Preparation of Benzene by the Decarboxylation of Sodium Benzoate



0-40 In a 6-inch evaporating dish place 10 g. (0.25 mole) of sodium hydroxide and 20 ml. of water. Warm the dish gently over the Bunsen burner until the sodium hydroxide has dissolved and then add 12 g. (0.1 mole) of benzoic acid. While stirring the solution continuously, evaporate it to dryness by gentle application of heat from the burner. (CAUTION: Wear your goggles.)

Transfer the dry mixture of sodium benzoate and sodium hydroxide to a 25 x 200 mm. test tube which is connected to a delivery tube and condenser as shown in Figure 29. Heat the tube with the Bunsen burner until no more liquid is collected in the receiver. Separate the upper layer of benzene from the layer of water, dry it over a little calcium chloride, and determine the yield of benzene by measuring its volume in a graduated cylinder. The density of benzene at 20° is 0.879. Note the boiling point of benzene by the method described in Experiment 1 upon the calibration of a thermometer.

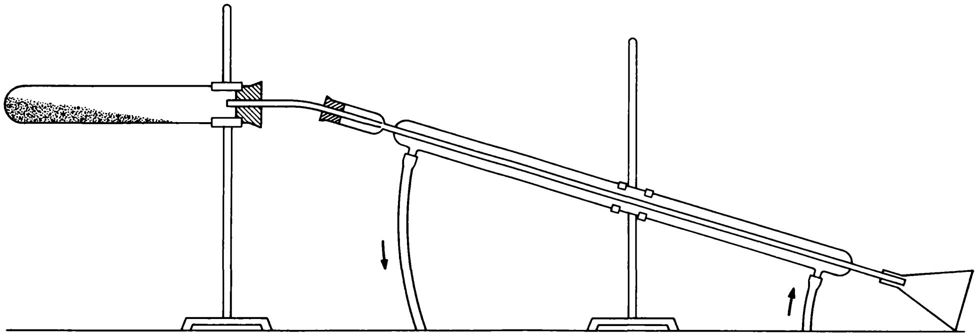


Fig. 29. Apparatus for decarboxylation of an acid.

B. Properties of Benzene

40-50 *1. Solubility.* Test the solubility of 2-ml. portions of benzene, obtained from the side shelf, in water, ethanol, gasoline, and ether.

50-55 *2. Benzene as a Solvent.* Determine the solubility of a small amount of iodine, paraffin wax, and of cottonseed oil in a few ml. of benzene.

3. Flammability. Ignite a few drops of benzene in a small evaporating dish. Note the character of the flame and the appearance of the dish when the flame dies. 55-60

4. Reaction with Bromine. Pour about 5 ml. of benzene into a test tube, take the tube to the hood and, after adding 2 or 3 drops of bromine, pour one half of the solution into another test tube. Into one of the tubes introduce 2 or 3 small iron tacks and observe the difference in the rates of reaction in the two tubes. If the reaction does not begin at once, set the tubes in the beaker of warm water. The comparative rates of reaction may be judged by blowing your breath across the mouth of each tube. What is the gas evolved? Write the equation for the reaction of benzene with bromine. 60-70

5. Permanganate Test. Shake a few drops of benzene with dilute potassium permanganate solution. Compare the behavior of benzene in this test with that of an alkene. 70-75

6. Sulfonation of Benzene. Add 1 ml. of benzene to 5 ml. of concentrated sulfuric acid contained in a test tube. Does the benzene dissolve in the cold acid? Heat the tube in a beaker of water at 70° and shake it frequently for 10 minutes or until a clear solution is obtained. 75-80

[During this heating period go on to the nitration of benzene, section 7.]

Cool the tube and pour its contents carefully into 25-30 ml. of cold water. Write the equation for the formation of the water-soluble derivative of benzene that has been produced.

---

[1] If this experiment is assigned on the opening day of a semester when the students are checking the apparatus in their desks, it will be well to omit certain portions of the experiment because sufficient time will not be available for performing all of the tests described.

80-90 *7. Nitration of Benzene.* In a large test tube cautiously add 2 ml. of concentrated sulfuric acid to 3 ml. of concentrated nitric acid. Then introduce 1 ml. of benzene dropwise. Note the exothermic character of the reaction. Shake the tube 2-3 minutes and pour the contents into about 25 ml. of cold water. What is the heavy oil that separates? Write the equation for the reaction.

C. NAPHTHALENE

90-95 *8. Sublimation.* Place about 2 g. of flake naphthalene into a test tube. Heat the lower end of the tube gently over the Bunsen burner and note the result.

95-100 *9. Bromination.* To 0.5 g. of naphthalene add, at the hood, 1-2 drops of bromine. Does a catalyst appear to be necessary? Equation. Compare this experiment with the bromination of benzene.

100-120 *10. Sulfonation.* Add about 0.2 g. of naphthalene to 5 ml. of concentrated sulfuric acid contained in a test tube and heat the mixture with frequent shaking of the tube in a beaker of boiling water for about 15 minutes.

[During this time go on to section 11.]

At the end of the heating period cool the tube and pour its contents into 25-30 ml. of cold water. Does a precipitate of unchanged naphthalene separate? What derivative of naphthalene has been obtained? What variation in the product results if the sulfonation has been conducted at a higher temperature (180°-190°)?

120-130 *11. Nitration.* To a solution of 3 ml. of concentrated nitric acid and 3 ml. of concentrated sulfuric acid (nitrating acid) contained in a large test tube, add about 0.05 g. of naphthalene. Shake the tube and note the evolution of heat. When the lower part of the tube has cooled to 50°-60° (i.e., not uncomfortably hot to the hand), add another small portion of naphthalene and continue in this manner until 0.2 g. of naphthalene has been added.

Maintain a temperature of 50°-60° for about 3 minutes and then cool the tube and pour its contents into 40-50 ml. of cold water contained in a small beaker. The α-nitronaphthalene, some of which usually separates in the nitration tube, is obtained as a pale yellow solid. Equation.

12. Naphthalene Picrate. Add about 0.1 g. of naphthalene to 5 ml. of a saturated solution of picric acid in ethanol, heat the mixture in hot water until a clear solution is obtained and then set the tube into an ice bath. A double compound of the composition $C_{10}H_8 \cdot C_6H_2(OH)(NO_2)_3$ is obtained. **130-140**

Naphthalene, anthracene, and various other aromatic hydrocarbons (but not benzene) form fairly stable addition compounds of this type. In some instances the compounds are sufficiently stable to permit their identification by their melting points and "mixed melting points" with known samples.

D. FAMILIARITY WITH OTHER HYDROCARBONS **140-150**

On the supply shelf the storekeeper will have placed specimens of other aromatic hydrocarbons, such as toluene, ethylbenzene, xylene, cumene, mesitylene, anthracene, phenanthrene, and perhaps others. Each bottle will be labeled with the name and boiling point, or melting point, of the material that it contains. Make note of these physical properties as well as the appearance and odor of each specimen. Write the formula for each of the compounds presented.

QUESTIONS

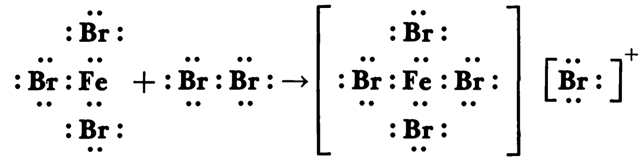
1. How does the method for the preparation of benzene used in today's experiment compare with that used for the production of methane in Experiment 9?
2. What other solvent you have used does benzene resemble in its solvent properties? For what kinds of compounds is benzene a good crystallization solvent? What are its advantages as a crystallization solvent? Its disadvantages?
3. What structural characteristic of benzene accounts for the fact that benzene burns with a luminous flame?
4. Is benzene more or less unsaturated than 1,3-hexadiene?
5. In reaction with bromine and with potassium permanganate, does benzene behave more like an alkane or like an alkene? How do you account for this fact?
6. Is naphthalene more or less reactive than benzene toward bromine and sulfuric acid? How can you explain this fact?

EXPERIMENT 46

Bromobenzene

(1) $$2Fe + 3Br_2 \rightarrow 2FeBr_3$$

(2)



$$\begin{array}{c}:\mathrm{Br}:\\ :\mathrm{Br}:\mathrm{Fe}\\ :\mathrm{Br}:\end{array} + :\mathrm{Br}:\mathrm{Br}: \rightarrow \left[\begin{array}{c}:\mathrm{Br}:\\ :\mathrm{Br}:\mathrm{Fe}:\mathrm{Br}:\\ :\mathrm{Br}:\end{array}\right] [\mathrm{Br}:]^{+}$$

(3) $$C_6H_6 + [FeBr_4]^- [Br]^+ \rightarrow C_6H_5Br + HBr + FeBr_3$$

Introduction. A substitution reaction in benzene may be described as one in which a substituting reagent makes an electrophilic attack upon the aromatic nucleus. In today's experiment the attacking agent is probably a bromine cation derived from an iron polybromide. The ferric bromide, formed on the surface of the iron wire, is an effective catalyst for the reaction. After its regeneration, as shown in the last equation, it may react again according to the second equation.

Procedure

The apparatus, consisting of a 500-ml. flask, condenser, and absorption trap, is assembled as shown in Figure 30. The hydrogen bromide evolved during the reaction must not be allowed to escape into the room and is absorbed in a suitable trap. Home-made traps such as those shown in Figure 30, are easily constructed from 38-40 mm. tubing and may be kept in the storeroom to lend to students. Such devices, as compared with absorption bottles fitted with tubes and two-holed stoppers, save a great deal of time. The instructor will indicate what type of trap is to be used. The hydrobromic acid collected may be utilized as described later in this experiment. The 500-ml. flask must be dry; if it should be wet, rinse it once with alcohol and then three times with small portions of benzene.

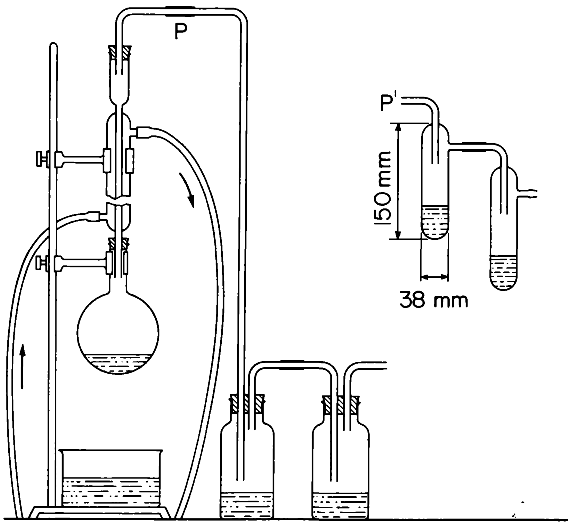


FIG. 30. Apparatus for the preparation of bromobenzene and collection of the evolved hydrogen bromide.

When the apparatus has been assembled, remove the flask to the hood and introduce into it first 35 ml. of benzene and then 40 g. (0.25 mole, 13.5 ml.) of bromine according to a procedure which the instructor will describe (Note 1). Return the flask immediately to your desk and drop into it 4 or 5 iron tacks (Note 2) and attach it at once to the condenser. Do not surround the flask, as yet, with the bath of cold water unless a vigorous reaction should begin at once. If the reaction is slow in starting, warm the bottom of the flask gently with a very small flame of the Bunsen burner. 15-50

As soon as the evolution of hydrogen bromide becomes rather brisk, bring the bath of cold water up around the flask and support the bath with an iron ring. When the rate of reaction, which at first is often fairly rapid, subsides, the bath may be heated gradually in order to maintain a satisfactory rate.

During this time the absorption trap may require some attention to see that it is operating effectively. A little bromine and benzene will usually be carried along with the hydrogen bromide into the trap. Any intense red color in the condenser, however, indicates that the reaction is going too fast and the temperature of the bath should be lowered by the addition of cold water or a few pieces of ice. Within 15-20 minutes the rate of reaction ordinarily decreases sufficiently to permit the bath to be heated to about 50°, at which temperature the completion of the reaction, evidenced by the absence of red vapors above the liquid, will be attained in about 10 minutes.

Remove the stopper and tube from the top of the condenser and pour 150 ml. of water through the condenser into the flask. The water absorbs hydrogen bromide which would otherwise escape into the room. Remove the flask from the condenser, shake it well, and separate the layer of bromobenzene which, of course, contains some benzene because an excess of 50-85

0.25 mole of benzene was used. Transfer the bromobenzene to a flask for steam distillation, add enough sodium hydroxide solution to make the well shaken liquid faintly but distinctly alkaline and purify the bromobenzene by distillation in steam (see page 32). The steam distillation should be conducted as rapidly as the capacity of the condenser will permit; often this is about 15 ml. per minute; hence, 10-15 minutes of distillation will be sufficient to distill all of the bromobenzene with 150-200 ml. of water. (During this time prepare for the final distillation of the bromobenzene.)

85-110 Separate the bromobenzene from the water and dry it for a few minutes over calcium chloride or other drying agent. Decant the liquid from the drying agent and distill it using a short fractionating column or a flask with a long neck. The fraction boiling at 150°-160° may be collected. The recorded boiling point of bromobenzene at normal barometric pressure is 156°. The yield is 25-30 g.

110-130 Some *p*-dibromobenzene is always formed in this process, although the amount is usually small. The high-boiling residue, if any, remaining in the distilling flask consists chiefly of *p*-dibromobenzene and a little more of the solid often collects in the condenser tube during the distillation with steam. Both of these portions may be combined and recrystallized from a little hot ethanol. *p*-Dibromobenzene is a white crystalline material melting at 87°.

130-140 Wash and dry your glassware and clean your desk. Leave your working space in proper order for the students in the next laboratory class.

Utilization of the Hydrobromic Acid. The by-product of hydrobromic acid obtained in this experiment may well be saved for some future time and then purified for general laboratory use. If 30-40 ml. of water is placed in each of the absorption bottles, the solution in the first bottle will attain a high concentration; that in the second bottle will, of course, be more dilute. At the end of the experiment, pour the contents of the first bottle into the large container that the storekeeper will provide labeled "Concentrated Hydrobromic Acid" and the contents of the second bottle into the container labeled "Dilute Hydrobromic Acid."

In order to purify the acid, add sodium sulfite to the more concentrated solution to reduce any free bromine to hydrogen bromide and fractionally distill the solution. The boiling point of the constant-boiling acid is 125°-125.5° at 758 mm. This acid has a specific gravity of 1.486 and contains 46.83 per cent of hydrogen bromide. The dilute solution may be saved for later repetitions of this experiment, at which time you can enrich the dilute acid in its hydrogen bromide content by placing some of it into the first absorption bottle.

NOTES

1. Details of safe procedures for dispensing bromine differ somewhat among various laboratories; hence, the instructor will prescribe the method that is to be followed.
2. A small coil of iron wire of about the same surface area as the tacks may also be used as a catalyst. Often somewhat rusty wire or tacks have better catalytic value than does iron having a bright polished surface.

QUESTIONS

1. Predict the relative rates of reaction of bromine, chlorine, and iodine with benzene. Give reasons for the predicted orders.
2. Calculate the maximum weight of bromobenzene that could be formed in today's experiment if a total of 5.0 g. of dibromobenzenes were formed in the reaction.
3. At a price of 31¢/lb. for benzene and 39¢/lb. for bromine, what was your cost for starting materials per pound of bromobenzene? Compare this with the commercial price for bromobenzene of $3.12/lb.
4. A compound of formula C_xH_yBr contains 73.4% of bromine. Can this compound be a bromine substitution product of an aromatic hydrocarbon? If so, of which hydrocarbon? Of an aliphatic hydrocarbon? If so, which one?

EXPERIMENT 47

Iodobenzene

$$2C_6H_6 + I_2 + 2HNO_3 \rightarrow 2C_6H_5I + 2NO_2 + 2H_2O$$

Introduction. Iodine, the least active of the halogens, does not replace readily one or more of the hydrogen atoms of benzene. The addition of an oxidizing agent, such as nitric acid, however, will bring about the formation of iodobenzene according to the equation. Note that all of the iodine goes into the production of iodobenzene.

0-15

Procedure

A 250-ml. standard-taper flask is connected with a reflux condenser the top of which is fitted to an absorption trap to absorb oxides of nitrogen that are evolved in this experiment. A large flask containing 100 ml. of 15 per cent sodium hydroxide solution will prove effective (see trap A, Figure 32, page 163).

15-60 Into the standard-taper flask are placed 12.7 g. (0.1 g. atomic weight) of iodine, 20 ml. of benzene (what excess over 0.1 mole?), 2 ml. of pyridine, and 20 ml. of nitric acid. The contents of the flask are then heated to boiling under reflux until the violet color of the iodine has disappeared. Additional quantities of nitric acid will be required and at intervals of 15 minutes the tube and stopper at the top of the condenser are removed momentarily for the introduction of 10 ml. of nitric acid. Ordinarily two such additions of nitric acid are sufficient and the reaction is completed in a total time of about 40 minutes.

60-90 When the color of the free iodine has disappeared, the burner is extinguished and the flask is cooled in cold water. The heavy layer containing the iodobenzene ($D = 1.824$) and the excess benzene is separated from the acid layer, washed with water and dilute alkali, dried over calcium chloride, and distilled. Yield about 15 g. B.p. 188°.

Iodobenzene-dichloride

Obtain from the side shelf 10 ml. of a saturated solution of chlorine in carbon tetrachloride. Add to this solution 2 ml. of iodobenzene and set the test tube containing the reactants in ice. Result? Equation. What product may be obtained by the reaction of iodobenzene-dichloride with sodium hydroxide solution? Equation. 90-100

QUESTIONS

1. Rate the hydrohalic acids in order of their strengths as reducing agents.
2. What reaction would occur if iodobenzene were refluxed with constant boiling hydriodic acid? How do you explain the role of nitric acid in improving the yield of iodobenzene in today's experiment?
3. Could the method used for the preparation of iodobenzene be used for the preparation of bromobenzene? Would there be the same advantage costwise? (Bromine is quoted at 39¢/lb. and resublimed iodine at $2.00/lb.)
4. Would you expect much diiodobenzene to be formed in today's experiment? Explain.
5. An unknown iodine-containing organic compound has a boiling point of 176°. Can it be an aromatic compound?
6. Which compound forms a Grignard reagent more readily, bromobenzene or iodobenzene? Which was used in Experiment 24? Why?

EXPERIMENT 48

Aromatic Nitro Compounds

$$C_6H_6 + HNO_3 \xrightarrow{H_2SO_4} C_6H_5NO_2 + H_2O$$

Introduction. Ease of nitration is a characteristic property of aromatic hydrocarbons and of many of their derivatives. In some instances, such as the reaction with phenol (Experiment 63), the nitration is accomplished readily with dilute nitric acid; other compounds, including benzene, bromobenzene, and many others, require the use of concentrated nitric acid ($D = 1.42$) mixed with approximately an equal volume of concentrated sulfuric acid. The use of this solution of the two strong acids, often called **nitrating acid,** is illustrated by the nitration of benzene in the following experiment.

I. Nitration of Benzene

0-20 Prepare the nitrating acid by adding 30 ml. of concentrated sulfuric acid to 30 ml. of concentrated nitric acid ($D = 1.42$) contained in a 500-ml. flask. Measure 22.5 ml. of benzene (19.5 g., 0.25 mole) in the graduated cylinder and add 2-3 ml. of it to the nitrating acid. Shake the flask vigorously with a rotatory motion (Note 1) in order to mix the reactants thoroughly. Note the rise in temperature by resting the flask in the palm of your hand (Note 2).

If the temperature rises above 60° the flask should be cooled in a pan of cold water. As soon as the reaction following the first addition of benzene has subsided, add another 2-3 ml. portion of benzene and shake the flask vigorously as before. Cool the flask in cold water as required to maintain a temperature of 50°-60° and continue the nitration in this manner until all of the benzene has been used.

20-45 When all of the benzene has been added to the nitrating acid, shake the flask continuously and thoroughly for 10 minutes by the clock (Note 3). If the temperature falls below the 50°-60° range, the flask should be warmed gently over a low flame of the Bunsen burner or in a pan of hot water. At the conclusion of this 10-minute period, cool the flask and pour the contents into a separatory funnel for separation of the two layers. The acid layer may be discarded (Note 4); the nitrobenzene is washed once with water, once with 5 per cent sodium hydroxide solution, and then finally with water.

45-75 Dry the nitrobenzene over 2-3 g. of calcium chloride for about 15 minutes while you prepare for its distillation. Distill the nitrobenzene using a small distilling flask and an air-cooled condenser. The first portion of the distillate, consisting of unchanged benzene and perhaps a little water, is discarded. Collect the portion boiling at 200°-215°, but do not go above this temperature nor distill to dryness because the small quantity of residue contains dinitrobenzene which may decompose violently at high temperature. The normal boiling point of nitrobenzene is 210°. Yield 15-20 g.

II. Action of Alkali upon Nitroethane and Nitrobenzene

From the bottle on the side shelf pour about 1 ml. of nitroethane into a test tube, add 10 ml. of 10 per cent sodium hydroxide solution, and shake the tube vigorously. Repeat this experiment in another test tube, replacing the nitroethane with 1 ml. of the nitrobenzene that you have prepared. In which tube does the nitro compound dissolve in the alkali? Acidify the solution with hydrochloric acid and set the tube aside for a few minutes. Does the nitro compound separate from the solution? Write the equations for the reactions involved. **75-95**

III. Solid Nitro Compounds for Purposes of Identification

Introduction. Many aromatic nitro compounds are solids which may be identified by their melting points and by "mixed melting points" with known specimens. As illustrations of such procedures, bromobenzene and nitrobenzene, liquids at ordinary temperatures, may be converted respectively into *p*-nitrobromobenzene and *m*-dinitrobenzene.

Suggestion. It is often advantageous for one student to make one of these compounds while his neighbor prepares the other. They may then compare notes and exchange data.

Option I. m-Dinitrobenzene. Add 1 ml. of nitrobenzene to a little nitrating acid made by mixing 5 ml. of concentrated sulfuric acid with 5 ml. of concentrated nitric acid contained in a 25 x 200 mm. test tube. Note that heat is evolved. Heat the tube over the burner nearly to the boiling point as indicated by the evolution of oxides of nitrogen. Keep the contents of the tube hot, but not actually boiling, for 2-3 minutes, then cool the tube and pour its contents into 75-100 ml. of cold water containing a few pieces of ice. **95-140**

Stir the mixture well, collect the *m*-dinitrobenzene on a small Hirsch funnel, and recrystallize the material from a little hot alcohol. Bring the crystals again onto the filter, press out the solvent as well as possible, and dry a portion of the purified product upon a fragment of unglazed dry plate. Observe its melting point. The recorded melting point is 90°. Equation.

Option II. p-Nitrobromobenzene. Prepare the "nitrating acid" by adding 5 ml. of concentrated sulfuric acid to 5 ml. of concentrated nitric acid contained in a 25 x 200 mm. test tube, and then add 1 ml. of bromobenzene. The reaction, when the tube is shaken, is suf- **95-140** ficiently exothermic that no heat need be applied from the Bunsen burner or steam bath. Within a few minutes, as the tube cools somewhat, crystals of *p*-nitrobromobenzene appear first upon the upper part of the tube and then throughout the reacting mixture.

Pour the contents of the tube into 75-100 ml. of cold water, collect the crystals on a small Hirsch filter, and recrystallize them from a little hot alcohol. Dry some of the recrystallized product upon a fragment of unglazed clay plate and take its melting point. The recorded melting point is 127°. Equation.

NOTES

1. A rotatory motion of the flask permits vigorous shaking and mixing of the contents of the flask and has the added advantage of avoiding spattering.

2. A thermometer may be used to measure the temperature but, in this instance, the sensitivity of the hand will serve almost equally well because the desired temperature of 50°-60° is about as hot as can be borne without discomfort.

3. Vapors of nitric acid and of nitrobenzene are irritating to the skin. Hence it is convenient to fit the mouth of the flask with a one-holed cork stopper bearing a piece of 6-mm. glass tubing 10-12 inches in length to carry such vapors away from the hand.

4. Be careful to save the layer containing the nitrobenzene. Which layer should be soluble in water?

QUESTIONS

1. Compare the boiling points (see handbook) of *n*-butylbenzene, nitrobenzene, and benzoic acid, all of which have approximately the same molecular weight. How do you account for the difference?

2. A comparison of the conditions for the nitration of bromobenzene and of nitrobenzene, as in today's experiment, clearly shows that the former compound nitrates more rapidly than the latter. How do you account for this difference?

3. What is the Victor Meyer method for the preparation of a nitroalkane? Is this method adaptable to the production of nitrobenzene? Of phenylnitromethane?

EXPERIMENT 49

Preparation of Aniline by Reduction of Nitrobenzene

$$(1)\qquad 2C_6H_5NO_2 + 3Sn + 14HCl \rightarrow 2C_6H_5NH_3^+,Cl^- + 3SnCl_4 + 4H_2O$$

$$(2)\qquad C_6H_5NH_3^+,\ Cl^- + NaOH \rightarrow C_6H_5NH_2 + NaCl + H_2O$$

Introduction. From among the various procedures that may be used for the reduction of nitro compounds to amines, the one selected for today's experiment makes use of tin and hydrochloric acid as the reducing agent. As a second step, aniline is liberated from its hydrochloride by the addition of alkali.

In commercial practice the reduction is accomplished by iron and steam. A small quantity of acid is usually employed at the start of the process.

$$C_6H_5NO_2 + 2Fe + 4H_2O \rightarrow C_6H_5NH_2 + 2Fe(OH)_3$$

Procedure

0-45 Into a 1-liter flask which later is to be used for steam distillation, introduce 20 ml. (24.6 g., 0.2 mole) of nitrobenzene and 50 g. of granulated tin. Measure 90 ml. of concentrated hydrochloric acid in the graduated cylinder and pour about 10 ml. of the acid into the flask containing the tin and nitrobenzene. An exothermic reaction soon begins, and it is necessary to cool the flask in cold water to prevent loss of material by boiling. Avoid excessive cooling as the reducing reaction proceeds more rapidly at a higher than at a lower temperature. Aim to keep the contents of the flask hot but below the boiling point.

As soon as the rate of reaction subsides, add another 5-10 ml. portion of the hydrochloric acid, shake the flask thoroughly, and cool it as required to prevent boiling. Continue the addition of the acid in this way with almost constant shaking of the flask until all of the hydrochloric acid has been used. Heat the flask on the steam bath for 20 minutes. During this interval shake the flask frequently, prepare the solution of sodium hydroxide described below, and get ready for the distillation with steam.

45-90 Liberation of the Aniline and Its Removal by Steam Distillation

Weigh 40 g. of sodium hydroxide (commercial flake) into a 400-ml. beaker and add to it 200 ml. of water. Cool this solution to about 30° in a pan of cold water. Remove the reaction flask from the steam bath and cool it in cold water until the temperature of the contents is not higher than 50°, then add a small portion of the sodium hydroxide solution, shake the flask well, and cool it so that no steam escapes. Add successive small portions of the alkali, cooling the flask as required, until all of the sodium hydroxide solution has been introduced.

Shake the flask thoroughly and remove a drop of the liquid on a glass rod for a test on litmus paper. If the contents are not alkaline, more sodium hydroxide must be added (Note 1).

Subject the contents of the flask to distillation with steam (Note 2). (See Figure 15, page 33.) At first oily drops of aniline collect in the receiver but toward the end of the distillation the small quantity of aniline coming over may be dissolved by the water (Note 3).

Collect 250-300 ml. of distillate, add 40-50 g. of sodium chloride, and stir the mixture until the salt dissolves (Note 4).

[During the steam distillation, turn to the list of questions and answer as many of them as time allows.]

90-120 Transfer the distillate to a separatory funnel and remove directly as much of the aniline as possible. Return the water solution to the funnel and extract any remaining quantity of aniline by shaking the solution with 20 ml. of benzene. Separate the benzene layer and combine it with the aniline previously obtained. Dry the benzene solution of aniline, contained in a small Erlenmeyer flask, by shaking it with about 5 g. of solid sodium hydroxide.

As soon as the apparatus for the final distillation of the aniline is ready, decant the benzene solution of aniline from the drying agent into a small distilling flask and distill it. Discard the benzene fraction (b.p. 75°-90°) and collect the aniline (b.p. 180°-186°) separately. The intermediate fraction (b.p. 90°-180°) should be refractionated and any aniline obtained from it may be combined with the first lot. Yield about 15 g.

Pure freshly distilled aniline is nearly colorless. It darkens on exposure to the light and air. A trace of nitrobenzene that escapes reduction in this experiment often imparts an orange tint to the preparation. Add 1 ml. of nitrobenzene to 1 ml. of nearly colorless aniline and note the red color produced.

NOTES

1. It is not necessary that the precipitate of stannous and stannic hydroxides be dissolved in excess alkali.

2. Conduct the steam distillation as rapidly as the capacity of the condenser will permit. Steam must not be allowed to escape into the room, however, because the aniline vapor accompanying it is highly toxic. If the condenser has a capacity of 12-15 ml. per minute, the distillation can be completed in about 20 minutes.

3. The solubility of aniline is about 3.5 g. in 100 ml. of water at room temperature or 6.3 g. of aniline in 100 ml. of water at the boiling point.

4. Aniline, like many other organic compounds, is less

soluble in saturated salt solution than in water. Aniline ($D = 1.02$) sinks in water but floats on the salt solution.

QUESTIONS

1. In the commercial method of making aniline using iron and steam as the reducing agent, would the addition of a base be needed to liberate the aniline? Explain.

2. In our laboratory procedure how many grams of tin will be required to reduce 1 mole of nitrobenzene (a) if the tin is oxidized to the tetravalent (stannic) state; (b) if the tin is oxidized only to the divalent (stannous) condition?

3. Write the formula for (a) the double salt of aniline hydrochloride and stannic chloride; (b) the double salt of aniline hydrochloride and platinic chloride.

4. What is the molecular weight of an amine whose hydrochloride and platinic chloride gave a double salt containing 31.4 per cent of platinum?

5. If nitrobenzene is reduced with hydrogen with the aid of a platinum or nickel catalyst, what volume of hydrogen, measured at 0° and 760 mm. pressure, will be required for the reduction of 0.5 mole of nitrobenzene?

6. Under what conditions of temperature and pressure may aniline be made from chlorobenzene?

EXPERIMENT 50

Aniline and Some of Its Derivatives

I. PROPERTIES OF ANILINE

0-20 A. Basic Character of Aniline

(*a*) *Action on Indicators.* Shake a few drops of aniline with 10 ml. of distilled water and test the action of the solution with litmus paper or with phenolphthalein indicator solution. How does aniline compare with ammonia in basicity?

(*b*) *Ferric Chloride Test.* Shake a few drops of aniline with 5 ml. of water and add 2 ml. of ferric chloride solution. Is aniline sufficiently basic to give a precipitate of ferric hydroxide? Equation.

(*c*) *Formation of Aniline Hydrochloride.* On a watch glass mix 1 drop of aniline with 1 drop of concentrated hydrochloric acid. Equation.

(*d*) *Formation of Aniline Acid Sulfate.* Add a drop of concentrated sulfuric acid to a drop of aniline on a watch glass. Equation.

20-35 B. Reaction of Aniline with Oxidizing Agents

(*a*) *Bleaching Powder Test.* Shake 0.5 g. of bleaching powder with 5 ml. of water to which 1 drop of aniline has been added. Note the formation of an intense purple color.

(*b*) *Dichromate Test.* Dissolve a drop of aniline in 3-4 ml. of concentrated sulfuric acid in a porcelain evaporating dish and add a few drops of a solution of sodium dichromate. Note the intense blue coloration produced upon mixing the solutions.

35-45 C. Isocyanide Test for Aniline

To 3-4 drops of aniline contained in a test tube add 5 ml. of 10 per cent sodium hydroxide solution and a few drops of chloroform. Warm the tube over the Bunsen burner and note carefully the nauseating odor of phenyl isocyanide. Cf. Chloroform, p. 77. Equation. (Flush the contents of the tube down the drain in the hood.)

45-75 II. FAMILIARITY WITH OTHER AROMATIC AMINO COMPOUNDS

On the supply shelf will be found small samples of important amino compounds, such as the toluidines (*o, m, p*), the nitroanilines (*o, m, p*), *o*-chloroaniline and other halogenated derivatives of aniline, some of the xylidines (aminodimethylbenzenes), and any others that the instructor may select. Note the appearance and odor of each of these specimens. Write the structural formula for each of them.

75-150 III. SOLID DERIVATIVES OF ANILINE

[Aniline and other liquid amino compounds may be converted readily into solid derivatives which may be identified by their melting points and mixed melting points with known samples.]

A. Acetanilide

The acetyl derivative of aniline, acetanilide, is easily obtained by the acetylation of aniline with acetyl chloride or acetic anhydride.

(*a*) *Use of Acetyl Chloride.* Place 1 ml. of aniline into a dry test tube and cautiously add 2 ml. of acetyl chloride in portions of a few drops at a time. Equation. Note the vigor of the reaction. Dissolve the crude acetanilide in 20-25 ml. of hot water, filter and allow the filtrate to cool. Collect the recrystallized product on a filter, dry some of the crystals on a piece of unglazed clay plate, and determine their melting point.

(*b*) *Use of Acetic Anhydride.* Add about 2 ml. of acetic anhydride to 1 ml. of aniline as in paragraph (a). Note that the reaction is less vigorous than that observed when acetyl chloride was used. Equation. Dissolve the crude acetanilide in about 25 ml. of boiling water and set the solution aside to crystallize. If the melting point was observed in paragraph (a), it need not be repeated here.

B. Benzanilide

The benzoyl derivative of aniline, benzanilide, is easily prepared by the time-honored Schotten-Baumann method consisting of benzoylation in alkaline medium.

To 1 ml. of aniline contained in a large test tube add 10 ml. of 10 per cent sodium hydroxide solution and 1.5 ml. of benzoyl chloride. Equation. (The benzoyl chloride is so highly irritating to the eyes and nose that it should be used in the hood.) Shake the tube vigorously, collect the benzanilide on a filter, wash it with water, and recrystallize it from a little hot alcohol. Determine its melting point. The recorded melting point is 161°.

C. Carbanilide (Diphenylurea)

Dissolve 1 ml. of aniline in 7-8 ml. of benzene and add 1 ml. of phenyl isocyanate from the small bottle of this reagent which is kept in the hood because of its strong lachrymatory property. Crystals of carbanilide separate almost immediately. Equation. When recrystallized from hot alcohol, the product melts at 240°.

D. Thiocarbanilide (Diphenylthiourea)

Dissolve 1 ml. of aniline in about 10 ml. of ethanol and add 1 ml. of phenyl isothiocyanate. Crystals of thiocarbanilide separate within a few minutes. Equation. The material may be recrystallized from hot alcohol. M.p. 154°.

E. Hinsberg Reaction

Into three separate test tubes introduce 3 or 4 drops of aniline, monomethylaniline, and dimethylaniline, respectively, and add 5 ml. of water to each tube. Take the tubes to the hood and add to each of them a few drops of benzenesulfonyl chloride. Note the reaction, or lack of it, that occurs in each tube. In the tube (or tubes) in which a solid product was formed, determine if the product is soluble in alkali. How does the use of benzenesulfonyl chloride (Hinsberg reaction) serve to distinguish among primary, secondary, and tertiary amines? Write equations for the reactions involved.

EXPERIMENT 51

Identification of an Unknown Amino Compound

Introduction. The amino compound given to you will be one of those shown in Table 7. The identification of a compound selected from such a limited list may be obvious from its appearance, odor, boiling point, or other easily observed property. Your purpose in this experiment, however, is to *prove* the identity of the unknown given to you by making solid derivatives of the compound, comparing the melting points of these derivatives with those shown in Table 6, and, finally, making mixed melting point tests with known samples.

TABLE 6. MELTING POINTS OF DERIVATIVES OF COMMON AROMATIC AMINO COMPOUNDS

Amino Compound	Boiling Point	Acetyl Deriv. $RNHCOCH_3$	Benzoyl Deriv. $RNHCOC_6H_5$	Urea (with C_6H_5NCO) $RNHCONHC_6H_5$	Thiourea (with C_6H_5NCS) $RNHCSNHC_6H_5$
Aniline	184	114	161	238	154
Methylaniline	195	102	63	104	87
Ethylaniline	204	53	60	91	89
o-Toluidine	200	110	145	196	139
m-Toluidine	203	66	125	173	92
p-Toluidine	m.p. 44	153	158	212	142
o-Chloroaniline	209	88	99	182	165
p-Chloroaniline	231	179	187	237	152
p-Bromoaniline	m.p. 66	168	202	245	158
o-Anisidine	225	88	60	144	136
p-Anisidine	244	132	154	193	157
o-Phenetidine	229	79	104	173	142
p-Phenetidine	254	137	173	187	137

Procedure

0-170 Note the boiling point, or melting point, of your *unknown*. If it is an oily liquid of dark color, distill it. Determine the presence or absence of halogen by the Beilstein (copper wire) test (page 42). Make at least two derivatives of your *unknown* by the methods given in Part III of Experiment 50. Recrystallize these derivatives at least once (twice will be better) and observe their melting points.

Compare the melting points that you have obtained with those of the corresponding derivatives of the compounds in Table 6 and decide upon the probable identity of your *unknown*. Since the melting points of various compounds are often nearly the same, it may be necessary to make a third derivative of the unknown in question.

When you have arrived at the probable identity of your *unknown*, ask the instructor for a small sample of this compound and make at least two derivatives of it for melting point tests (Note 1). If, for example the acetyl derivative of your *unknown* and the acetyl derivative of the known sample have the same melting point and if an intimate mixture of the two shows no depression of the melting point, it is highly probable that the two specimens are identical (Note 2). Clinch the argument, however, by making similar comparisons of the individual and "mixed" melting points of a second derivative.

If the melting points of two or more derivatives of your unknown and the corresponding derivatives of a known sample have the same melting points individually and show no depression of the melting point when intimately mixed, the two compounds may be considered identical and you are ready to make your report to the instructor.

NOTES

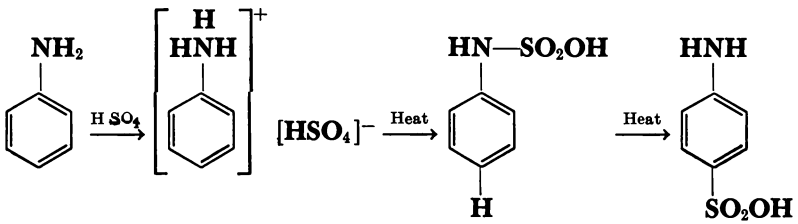
1. Your instructor may be able to supply small quantities of *known* samples of derivatives for the mixed melting point tests.
2. See page 4 for a discussion of eutectic mixtures.

QUESTIONS

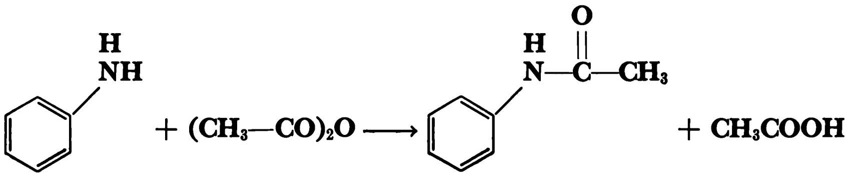
1. What structural features account for the fact that the various derivatives of the liquid amines are solids?
2. Which of the various types of amine derivatives do you find most satisfactory? Why?

EXPERIMENT 52

I. Preparation of Sulfanilic Acid



II. Preparation of Acetanilide



Introduction. The usual methods of preparation of some organic compounds specify that the reactants be heated for 6-8 hours—a requirement that is highly inconvenient for laboratory classes. The difficulty may be circumvented, however, by any of several procedures.

One method of operation that gives very good results employs a large heating bath such as is shown in Figure 31. Each student, at one laboratory period, may mix the reactants in a large tube, or small flask, and place the tube along with others in the bath where the combined lot may be heated before the next meeting of the class. A group of student volunteers can easily arrange a schedule of hours so that the temperature of the bath may be adequately controlled throughout the heating period. When the class returns to the laboratory the product of the reaction may be isolated without loss of time.

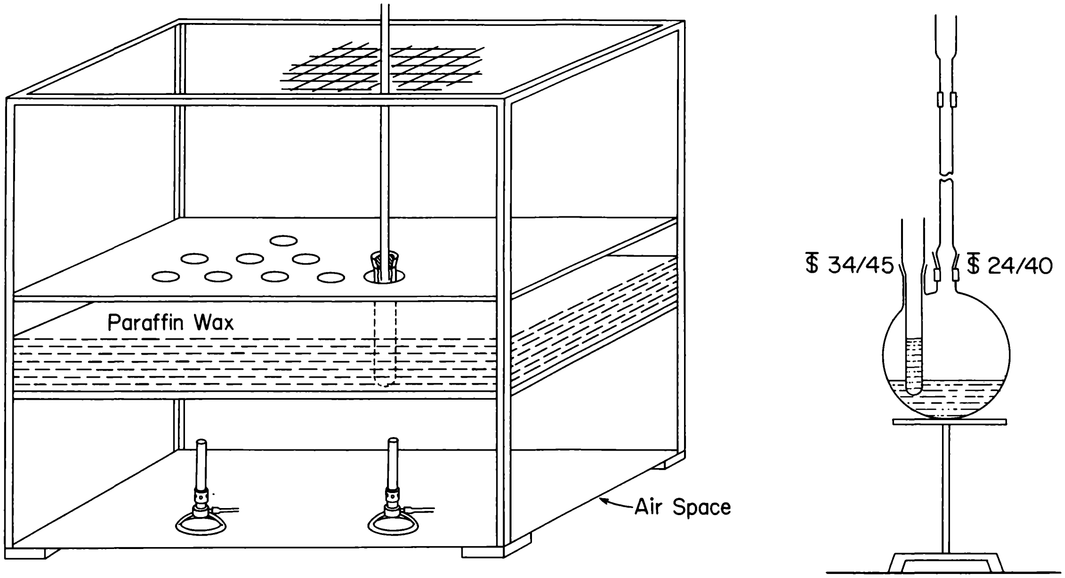


Fig. 31. Convenient devices for heating tubes at 150-190°C.

Another device, intended for individual use, is also shown in Figure 31. The reaction tube may be made by sealing a piece of glass tubing onto a standard taper joint, or an ordinary 25 x 200 mm. test tube passing through a large hole in a cork stopper will serve equally well. Such a large hole in the cork is not easily made and, as a substitute, a stopper may be improvised by wrapping the tube with a narrow strip of asbestos paper. The temperature at which the reacting materials contained in the tube are heated is controlled automatically by the boiling point of the liquid placed in the flask.

Regardless of the type of apparatus used it is often desirable to shorten the period of time during which the reactants are heated. Some sacrifice in yield may be made in order to complete an experiment in a single laboratory period. Such an exchange of yield for time is suggested in today's preparation of sulfanilic acid. In the production of acetanilide, the mixture of aniline and acetic acid may be boiled for 6-8 hours as in commercial practice but, again to save time, the addition of some acetic anhydride to the aniline-acetic acid solution is proposed as a means of acetylating the aniline rapidly.

I. Preparation of Sulfanilic Acid

0-10 The instructor will designate the type of apparatus to be used. Pour 9 ml. (9.3 g.; 0.1 mole) of aniline into the reaction tube and cautiously add 12 ml. of concentrated sulfuric acid. The solid aniline acid sulfate formed will melt when the tube is heated.

Heating the Aniline Acid Sulfate

10-120 *Option A*. If the large bath of molten paraffin wax is used, heat the tube in the bath at a temperature of 180°-190° for about 2 hours counting from the time the bath has attained a temperature of at least 170°.

[Go on to Part II.]

Option B. Place about 75 ml. of ethylene glycol into the two-necked flask (Figure 31), insert the reaction tube, and attach a reflux condenser. Heat the flask over the Bunsen burner at such a rate that the glycol boils steadily and condensate drips from the condenser. Continue the heating process for nearly 2 hours, during which time the specimen of acetanilide (Part II) may be prepared as the sulfanilic acid experiment will require little or no attention.

120-170 *Isolation of the Sulfanilic Acid*. After the preparation of acetanilide has been completed, remove the tube containing the sulfanilic acid from the hot bath and allow it to cool partially before pouring the contents of the tube into a beaker containing 50-60 g. of crushed ice and a little water. Collect the crystals of crude sulfanilic acid on a Büchner funnel and recrystallize them from boiling water using a little carbon for decolorization. Set the resulting hot solution in a pan of ice and, when crystallization appears to be complete, bring the product onto the suction filter. Press out as much water as possible. Dry the crystals by rinsing them with alcohol and ether as described for drying the specimen of acetanilide (Part II, following). Weigh the product and calculate the yield. Do not attempt to determine the melting point. Sulfanilic acid chars at 280°-300° without melting.

II. Preparation of Acetanilide

Into a 200-ml. flask introduce 9 ml. (0.1 mole) of aniline, 15 ml. of glacial acetic acid, and 15 ml. of acetic anhydride. Note that heat is evolved owing to the reaction of the acetic anhydride and aniline. Attach the flask to a reflux condenser and heat the solution to boiling for 10 minutes. At the end of this time, cool the flask somewhat under the water faucet and pour its contents into a beaker containing about 50 ml. of water and 40-50 g. of ice. Stir the mixture well and collect the crystals of acetanilide upon a Büchner funnel. 15-90

Rinse the crystals on the filter with a little cold water and transfer them to a 600-ml. beaker for recrystallization. Add 200 ml. of water and heat the mixture until the water is boiling. If all of the acetanilide does not dissolve, add another 50 ml. of water and again heat to boiling (Note 1). Remove the beaker from the flame, allow the contents to cool for a moment, and add 1-2 grams of decolorizing carbon (Note 2). Again heat the solution to boiling, stir well, and filter through a funnel fitted with a hot-water, or steam, jacket (see page 21).

Chill the filtrate in ice, collect the crystals on a Büchner funnel, and press out as much water as possible. Shut off the suction pump and stir the crystals on the filter with 5 ml. of cold ethanol. Suck the alcohol through the filter, again shut off the pump, and stir the crystals gently with 10 ml. of ether. Draw the ether through the filter and spread the crystals on a sheet of paper to dry in the air. As an alternative procedure to the rinsing with alcohol and ether, the moist acetanilide may be dried in an oven at 50°-60°. Yield 8-10 g. M.p. 115°.

Use this intervening period of time for answering some of the questions at the end of this experiment. 90-120

NOTES

1. The solubility of acetanilide is 5.55 per cent at 100°; 3.45 per cent at 80°; 0.84 per cent at 50°; 0.46 per cent at 20°.

2. The addition of finely divided carbon (or other substance, for that matter) to the solution at the boiling point often causes the solution to boil over.

QUESTIONS

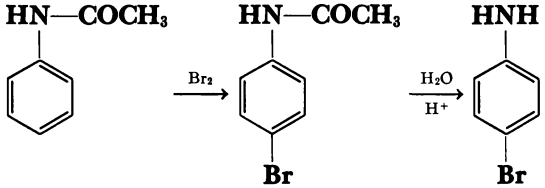
1. May acetanilide be considered *N*-phenylacetamide? May acetamide be made by heating ammonium acetate? May acetanilide be made by heating phenylammonium acetate? What is the commercial method for the manufacture of acetanilide?

2. How do you account for the extremely high melting point of sulfanilic acid? Write the formula for the acid as it largely exists.

3. How does the structural formula of sulfanilic acid compare with that of sulfanilamide?

EXPERIMENT 53

I. *p*-Bromoacetanilide and Its Hydrolysis to *p*-Bromoaniline



II. Separation of a Mixture of Benzene, Nitrobenzene, and Aniline

0-30 *Procedure.* In a 250-ml. flask add 13.5 g. (0.1 mole) of acetanilide (Experiment 52) to 50 ml. of glacial acetic acid. Note that the heat of solution is negative. Warm the flask slightly, if necessary, to bring the last of the acetanilide into solution and then, at a temperature not above 40°, add slowly with constant shaking of the flask a solution of 16 g. (0.1 mole, 5.5 ml.) of bromine dissolved in 20 ml. of glacial acetic acid. (Handle the bromine in the hood.) Note that the solution becomes warm, that hydrogen bromide is evolved, and that the red color of the free bromine gradually fades.

Within 7 or 8 minutes the bromination is complete and the solution (along with any *p*-bromoacetanilide which may have separated) is poured into about 300 ml. of cold water containing a little ice. If any yellow or orange color persists, because of excess bromine, discharge it by adding sodium bisulfite solution until the precipitate is white. Equation. Collect the *p*-bromoacetanilide on a Büchner funnel. Remove a small part of the material (a few tenths of a gram) for recrystallization from alcohol and determination of its melting point. Use the main portion for hydrolysis to *p*-bromoaniline.

30-80 *Hydrolysis.* Transfer the *p*-bromoacetanilide from the Büchner funnel to a 500-ml. flask and add 150 ml. of water and 50 ml. of concentrated hydrochloric acid. Fit the flask with a reflux condenser and boil the liquid for 30 minutes. At the conclusion of this time, cool the flask, make the contents alkaline by the addition of a 20 per cent solution of sodium hydroxide, and remove the *p*-bromoaniline by distillation in steam.

[Begin Part II.]

If the *p*-bromoaniline solidifies in the tube of the condenser, shut off the water temporarily until the solid melts. The solidified *p*-bromoaniline in the receiver is collected on the Büchner funnel and dried between folded pieces of paper towel. Weigh the product, determine its melting point, and calculate the percentage yield.

II. SEPARATION OF A MIXTURE OF BENZENE, NITROBENZENE, AND ANILINE

60-140 Into the separatory funnel pour 20 ml. of benzene, 15 ml. of nitrobenzene, and 15 ml. of aniline. The solution now contains one basic compound (aniline) and two neutral compounds of widely different boiling points; hence, their separation may be accomplished easily.

Devise a method for the separation of the mixture into its three components and submit your method in diagrammatic form to the instructor. If he approves the method, proceed with the separation.

QUESTIONS

1. Write equations to show:

(a) how *p*-bromoaniline may be made from bromobenzene
(b) how *m*-*b*romoaniline may be made from nitrobenzene
(c) how *p*-chloroaniline may be made from acetanilide.

2. Write equations showing the reaction of *p*-bromoaniline with each of the following reagents and name the chief product formed in each reaction:

(a) acetyl chloride
(b) acetic anhydride
(c) benzoyl chloride
(d) ethyl chlorocarbonate
(e) phenyl isocyanate
(f) phenyl isothiocyanate
(g) benzenesulfonyl chloride
(h) bromine water

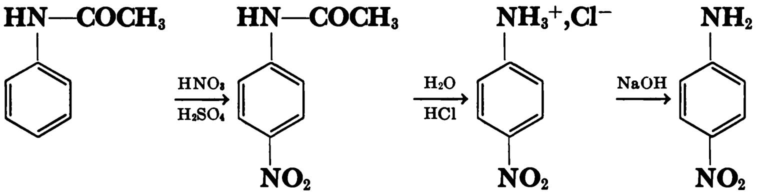
3. Write the formula and name of the compound that may be hydrolyzed to:

(a) formic acid (1 mole) and *p*-bromoaniline (1 mole)
(b) *n*-butyric acid (1 mole) and aniline (1 mole)
(c) benzoic acid (1 mole) and aniline (1 mole)
(d) acetic acid (1 mole) and *p*-chloroaniline (1 mole)
(e) aniline (1 mole), CO_2 (1 mole), and ethanol (1 mole)

4. List the following compounds in order of decreasing basicity: aniline, *p*-chloroaniline, *p*-toluidine, *p*-methoxyaniline, *p*-nitroaniline, picramide, diphenylamine, and triphenylamine. Could each of these amines be separated from benzene and nitrobenzene by the method you used for aniline? Explain.

EXPERIMENT 54

p-Nitroacetanilide and *p*-Nitroaniline



I. Nitration of Acetanilide

Introduction. The direct nitration of aniline and most other aromatic amino compounds usually produces a tarry mixture of nitrated and oxidized substances from which the desired product can be isolated only with difficulty and in poor yield. The nitration of the acyl derivatives of the amino compounds, however, proceeds smoothly and the subsequent removal of the acyl group by hydrolysis gives the nitrated product both in good yield and in a satisfactory state of purity.

0-30 *Procedure*. Pour 30 ml. of concentrated sulfuric acid into a small beaker and add 13.5 g. (0.1 mole) of acetanilide in small portions with constant stirring. As soon as all, or nearly all, of the acetanilide has dissolved, set the beaker in a pan of crushed ice and add from a dropping funnel a solution of 12 ml. of nitric acid in 12 ml. of concentrated sulfuric acid in portions of but a few drops at a time. Stir the reacting mixture gently with a thermometer and add the nitrating acid so slowly that the temperature does not exceed 35°. When all of the nitrating acid has been added, remove the beaker from the ice bath and let it stand at room temperature for 15 minutes.

45-70 Pour the solution of nitrated acetanilide into a 600-ml. beaker containing 200 ml. of water and about 50 g. of ice. Stir the mixture well and collect the precipitated *p*-nitroaniline on the Büchner funnel. Wash it on the funnel twice with 100-ml. portions of cold water, press out as much water as possible, and remove about 0.5 g. of the *p*-nitroacetanilide for recrystallization from hot alcohol and determination of the melting point.

70-125

II. Hydrolysis of *p*-Nitroacetanilide to *p*-Nitroaniline

Transfer the moist cake of *p*-nitroacetanilide from the Büchner funnel to a 600-ml. beaker and stir it into a thin paste with 200 ml. of water. Pour the mixture into a 500-ml. flask, using a little water for rinsing purposes, add 75 ml. of concentrated hydrochloric acid, and fit the flask with a reflux condenser. Heat the flask over the Bunsen burner to maintain active boiling of the contents for 30-40 minutes.

[During this interval give your attention to the questions at the end of this experiment.]

At the end of this 30-minute period of hydrolysis, **125-160** cool the flask and contents somewhat under the water faucet and pour the contents into an 800-ml. beaker. Add 75-100 g. of crushed ice and precipitate the *p*-nitroaniline by making the solution alkaline through the addition of ammonium hydroxide solution. (Because of the low basicity of *p*-nitroaniline some of it usually separates from the diluted acidic solution before any ammonium hydroxide is added.)

Bring the precipitate of *p*-nitroaniline onto the Büchner funnel, wash it with water, press out as much water as possible, and dry the material in an oven at 60°-70°. Recrystallize about 0.5 g. of the moist *p*-nitroaniline by dissolving it in 40-50 ml. of boiling water. Add a little decolorizing carbon and filter the hot solution through a fluted filter paper in a heated funnel. If the solution is allowed to cool slowly, the *p*-nitroaniline separates in long needle-shaped crystals melting at 146°.

Stains on Hands and Clothing. Avoid getting any of the *p*-nitroaniline solution on your clothing because the yellow stains cannot easily be removed without bleaching the original dye in the cloth. Colored spots on your hands may be removed by application of a thin paste of bleaching powder in water. Follow this treatment by an alcohol rub to get rid of the odor of chlorine.

QUESTIONS

1. How do you explain the observation that:

(a) Direct nitration of aniline ordinarily is an unsatisfactory procedure.

(b) In the direct nitration of aniline some *m*-nitroaniline is obtained.

(c) In the nitration of phenyltrimethylammonium sulfate the nitro group enters the *meta* position almost exclusively.

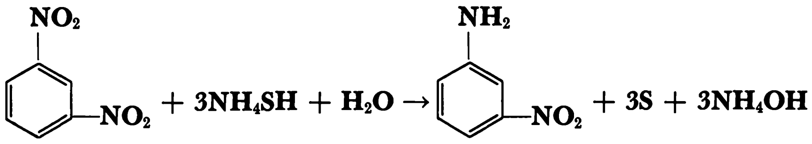
2. May *p*-nitroacetanilide be considered *N*-*p*-nitrophenylacetamide?

3. As a rule are amides easily hydrolyzed? Is the hydrolysis of *p*-nitroacetanilide comparable to the hydrolysis of acetamide?

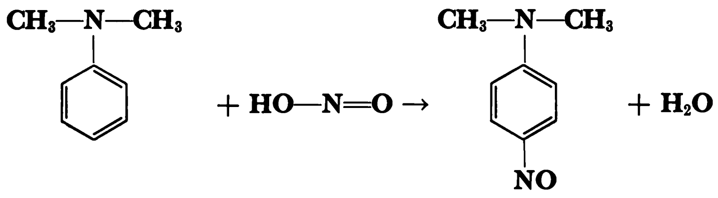
4. How do you account for the low basicity of *p*-nitroaniline?

EXPERIMENT 55

I. *m*-Nitroaniline



II. *p*-Nitrosodimethylaniline



I. Reduction of *m*-Dinitrobenzene to *m*-Nitroaniline

Introduction. Strong reducing agents, such as metals with acids, reduce both nitro groups in *m*-dinitrobenzene producing *m*-phenylenediamine. Milder reducing agents, of which ammonium hydrosulfide is an example, attack but one of the nitro groups yielding *m*-nitroaniline. The preparation of the ammonium hydrosulfide reagent by passing hydrogen sulfide gas into ammonium hydroxide solution is inconvenient; hence, in this experiment, a solution of ammonium chloride and sodium sulfide is employed.

0-60 *Procedure.* Place 8.4 g. (0.05 mole) of *m*-dinitrobenzene into a 500-ml. flask, add 50-60 ml. of 95 per cent ethanol, and warm the flask on the steam bath until the solid dissolves. Meanwhile prepare a solution of 10 g. of ammonium chloride in 25 ml. of hot water and another solution of 10 g. of sodium sulfide (anhydrous commercial flake, or the equivalent quantity of the crystalline material, $Na_2S \cdot 9H_2O$) in 25 ml. of hot water. At a temperature of 50°-60°, slowly add the ammonium chloride solution to the alcoholic solution of *m*-dinitrobenzene. This will cause some precipitation, but all of the precipitated *m*-dinitrobenzene may be redissolved by heating the flask on the steam bath. Add a little more alcohol if necessary to obtain complete solution.

Remove the hot alcoholic solution from the steam bath and introduce the sodium sulfide solution in portions of not more than 1 or 2 ml. at a time at intervals of 10-15 seconds. Hold the hot flask with a towel and shake it continuously during the addition of the sodium sulfide solution, which requires 2-3 minutes. The reaction is exothermic and no heat need be applied during this time. After all of the sodium sulfide solution has been added, return the flask to the steam bath for another 5 minutes.

Reduction of the nitro group is now complete, or nearly so. Cool the flask under the water faucet and add about 250 ml. of cold water. The precipitate consists of *m*-nitroaniline, sulfur, and any remaining unreduced *m*-dinitrobenzene. Bring the precipitate onto the Büchner funnel and wash it 2-3 times with small amounts of water to remove the red alkaline solution. Transfer the yellow precipitate to a 600-ml. beaker, add 250 ml. of water with 50 ml. of concentrated hydrochloric acid, and heat the mixture to boiling in order to dissolve the *m*-nitroaniline.

Separate the solution from the undissolved sulfur and any *m*-dinitrobenzene that may have escaped reduction by filtration through a funnel equipped with a hot-water jacket (page 21, Figure 11c). Cool the filtrate thoroughly in ice, and precipitate the *m*-nitroaniline by the addition of a 10 per cent solution of sodium hydroxide (Note 1). The *m*-nitroaniline is precipitated as a bright yellow solid. Recrystallize about 0.5 g. of the material from a little boiling water and dry the main portion in the oven at 60°. Yield 6-7 g. M.p. 114°.

Stains on Hands and Clothing. Avoid getting *m*-nitroaniline on your clothing as the stains cannot easily be removed without bleaching the original color of the cloth. Remove spots from your hands by application of bleaching powder and water followed by an alcohol rub.

NOTE

1. *m*-Nitroaniline is such a weak base that some of it separates as the solution cools, even before any sodium hydroxide is added.

II. *p*-Nitrosodimethylaniline

Introduction. From the study of aliphatic compounds it will be recalled that (1) aliphatic primary amines react with nitrous acid to give alcohols with evolution of nitrogen, (2) secondary amines and nitrous acid yield oily nitroso compounds, and (3) tertiary amines merely form salts, the trialkylammonium nitrites. In a tertiary amine, such as dimethylaniline, however, substitution on the benzene ring occurs so easily that *p*-nitrosodimethylaniline is obtained rapidly. Hence, it is obvious that the common statement that "tertiary amines do not have any visible reaction with nitrous acid" needs to be reconsidered in the light of the group, aliphatic or aromatic, that may be attached to the amino nitrogen atom.

60-120 *Procedure.* In a small beaker dissolve 3 ml. of dimethylaniline in 10 ml. of concentrated hydrochloric acid and 10 ml. of water. Add a small quantity of crushed ice to cool the solution to 0° and then, with constant stirring of the solution, add 2 g. of sodium nitrite dissolved in a little water. Keep the temperature of the solution at 0°-10°. The orange-colored crystals that separate are *p*-nitrosodimethylaniline hydrochloride. Collect the crystals on the Büchner or Hirsch funnel, remove as much of the liquid as possible, and return the hydrochloride to a small beaker for liberation of the free base by the addition of ammonium hydroxide.

Bring the green crystals of *p*-nitrosodimethylaniline onto the suction funnel and rinse them with a little water. After pressing out as much of the water as possible, dissolve the product in ether and set the beaker containing the ethereal solution aside to evaporate slowly. The recorded melting point of the green foliated crystals is 85°.

QUESTIONS

1. If a 90 per cent yield is obtained in each step of the following sequence of operations, what weight of *m*-nitroaniline will be obtained from 78 g. (1 mole) of benzene?

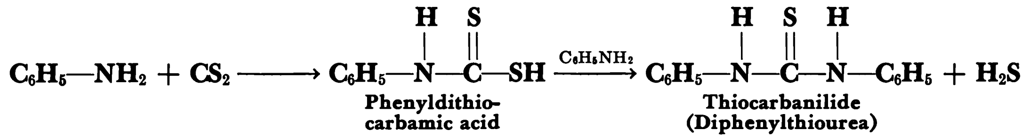
$$C_6H_6 \rightarrow C_6H_5NO_2 \rightarrow m\text{-}C_6H_4(NO_2)_2 \rightarrow m\text{-}O_2N\text{—}C_6H_4\text{—}NH_2$$

2. Write equations to show how *m*-nitroaniline will react with (a) acetic anhydride, (b) benzoyl chloride, (c) Sn + HCl.

3. Upon bromination of *m*-nitroaniline, the bromine atoms would be expected to enter what positions?

EXPERIMENT 56

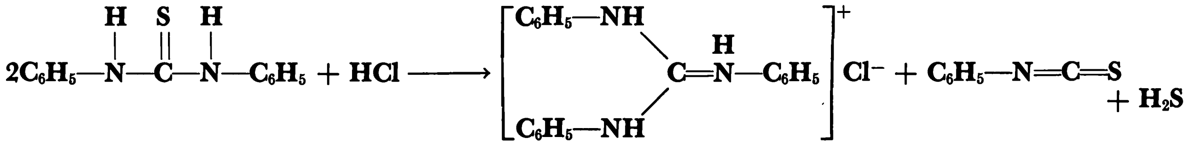
I. Thiocarbanilides



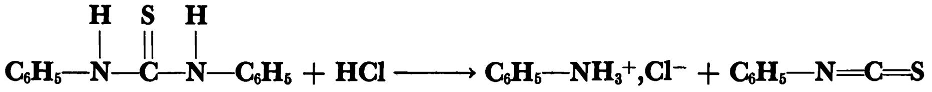
$$C_6H_5{-}NH_2 + CS_2 \longrightarrow \underset{\text{Phenyldithiocarbamic acid}}{C_6H_5{-}\overset{H}{N}{-}\overset{S}{\overset{\|}{C}}{-}SH} \xrightarrow{C_6H_5NH_2} \underset{\text{Thiocarbanilide (Diphenylthiourea)}}{C_6H_5{-}\overset{H}{N}{-}\overset{S}{\overset{\|}{C}}{-}\overset{H}{N}{-}C_6H_5} + H_2S$$

II. Phenyl Isothiocyanate

(1)



(2)



$$C_6H_5{-}\overset{H}{N}{-}\overset{S}{\overset{\|}{C}}{-}\overset{H}{N}{-}C_6H_5 + HCl \longrightarrow C_6H_5{-}NH_3^+,Cl^- + C_6H_5{-}N{=}C{=}S$$

I. Thiocarbanilide

Introduction. The reaction between aniline and carbon disulfide at room temperature is slow and must be allowed to proceed for several days in order to afford a reasonable yield of thiocarbanilide. When the reactants are boiled under reflux, a yield, satisfactory for laboratory purposes, can be obtained in a few hours. The reaction apparently proceeds in stages. In alkaline solution, however, as used in the following experiment, the reaction is so rapid that a specimen of thiocarbanilide may be obtained quickly.

0-40 *Procedure.* In a 500-ml. flask place 28 g. (0.3 mole, 27.5 ml.) of aniline and 20 ml. of carbon disulfide. Then gradually add in small portions a cooled solution of 15 g. of sodium hydroxide in 40 ml. of water. Shake the flask continuously and cool it in cold water if the contents should begin to boil. Continue the vigorous shaking of the flask for about 10 minutes after all of the alkaline solution has been added. By this time the contents will have become almost solid with the separation of thiocarbanilide.

Add 200 ml. of cold water to the orange-colored mixture and collect the crystals on a Büchner funnel. To wash the product on the filter shut off the suction, fill the funnel nearly full of water, stir the mixture well, but gently to avoid tearing the filter paper, suck the wash water through the funnel, and repeat the process two or three times until the press cake is nearly free of alkali. Transfer the product into a 600-ml. beaker, stir it into a slurry with 100-150 ml. of water, and add hydrochloric acid until the mixture is acidic to litmus.

Put the thiocarbanilide, now in the form of nearly white flakes, onto the Büchner funnel and wash the product with water to remove excess acid and a little aniline hydrochloride. Press out as much water as possible, shut off the pump, and wet the crystals with 10 ml. of cold alcohol. Stir the material on the filter gently with a glass rod and suck out the alcohol. Repeat this rinsing process using 10 ml. of ether.

Spread the crystals on a sheet of paper to dry in the air. This method of drying is convenient but involves some loss because of the solubility of the thiocarbanilide. As an alternative procedure, the material, after washing with water, may be dried in an oven at 60°-70°. Yield 28-30 g. Recrystallize a small portion from hot ethanol for observation of the melting point. The recorded melting point is 154°.

II. Phenyl Isothiocyanate

Introduction. The reaction of thiocarbanilide (diphenylthiourea) with boiling hydrochloric acid proceeds partially according to both of the above equations. Usually reaction (1) leading to the formation of phenyl isothiocyanate and triphenylguanidine hydrochloride predominates.

Procedure. In a 500-ml. flask place 22.8 (0.1 mole) of thiocarbanilide, 100 ml. of concentrated hydrochloric acid, and 50 ml. of water. Fit the flask with a reflux condenser and boil the mixture until the solid thiocarbanilide has been replaced by the oily phenyl isothiocyanate (about 45 minutes). Disconnect the flask from the condenser and add 125 ml. of water. Introduce a few boiling chips and join the flask to the condenser by a bent piece of glass tubing for downward distillation. 40-140

Heat the flask over the Bunsen burner and distill about 175 ml. of water which carries with it the phenyl isothiocyanate and some hydrogen chloride. Add to the distillate about 20 ml. of carbon tetrachloride to aid in collecting the oily phenyl isothiocyanate, separate the lower layer, dry it over a little calcium chloride and distill it. The carbon tetrachloride boils at 77° and the phenyl isothiocyanate at 220°. Yield 6-7 g.

Isolation of the Triphenylguanidine. The triphenylguanidine, as its hydrochloride salt remains in the distillation flask partly in solution and partly in the solid state. Some of the solid matter is unchanged starting material (thiocarbanilide). To isolate the triphenylguanidine, pour the contents of the flask into a 600-ml. beaker and dilute the acidic solution with water until the beaker is half full (about 300 ml. total volume of liquid).

Heat the water to boiling in order to dissolve the triphenylguanidine hydrochloride and filter, while still hot, through a large fluted filter paper in order to remove the undissolved thiocarbanilide (see Figure 11b, page 21). Cool the filtrate to about 50° and make the solution alkaline by the addition of 10 per cent sodium hydroxide solution. The triphenylguanidine is precipitated as a white solid. Note that the hot mixture has an odor of aniline. How is the presence of aniline to be explained?

Add a little ice to the beaker to lower the temperature of its contents to 30°-40° and collect the triphenylguanidine on a Büchner funnel. After recrystallization from hot 60 per cent ethanol, it melts at 143°.

Use of Phenyl Isothiocyanate as a Reagent for Amines. If the usefulness of phenyl isothiocyanate in the identification of amines has not been studied previously (Section D, Part III, Experiment 50), that short test should be made now.

QUESTIONS

1. Write the structural formulas for the following compounds, all of which are related to urea:

(a) monophenylurea
(b) *N,N′*-diphenylurea (symmetrical diphenylurea)
(c) *N,N*-diphenylurea (unsymmetrical diphenylurea)
(d) urethane (ethyl carbamate)
(e) thiourea
(f) *N,N′*-diphenylthiourea
(g) carbodiphenylimide
(h) *N*-phenylurethane (ethyl phenylcarbamate)
(i) guanidine
(j) *N,N,N*-triphenylguanidine
(k) ethyl phenyldithiocarbamate

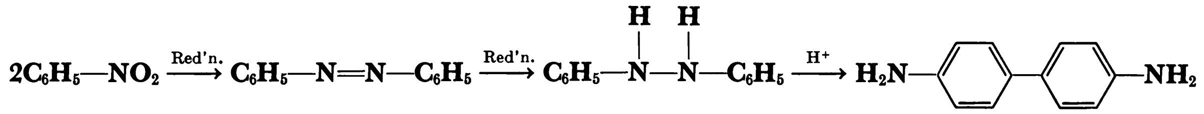
Which of the above is thiocarbanilide? Which of the above is carbanilide? Which of the above are isomers?

2. What three compounds may be made from aniline and phosgene by suitable control of concentrations and temperature?

3. Ethyl phenylthiocarbamate can be prepared by refluxing of a solution of phenyl isothiocyanate in ethanol for several hours. Write the equation for the reaction.

EXPERIMENT 57

Azobenzene, Hydrazobenzene,[1] and Benzidine



Introduction. You will probably recall that azobenzene and hydrazobenzene are among the reduction products of nitrobenzene and that the rearrangement of hydrazobenzene yields benzidine. The reduction process is conducted commercially by warming nitrobenzene with zinc dust and sodium hydroxide solution, although the rate of reaction is so slow that 15-20 hours may be required for conversion of the nitrobenzene to hydrazobenzene. For laboratory purposes magnesium turnings and absolute methanol may be used to prepare either azobenzene or hydrazobenzene in much less time. The product obtained depends upon the quantity of magnesium used and also upon the length of time during which the reduction is continued.

After the hydrazobenzene has been obtained, you can convert it into benzidine hydrochloride by warming it with a dilute solution of hydrochloric acid. The free benzidine is then liberated from its salt by the addition of alkali.

I. Preparation of Azobenzene

0-10 [The preparations of azobenzene and of hydrazobenzene may be conducted almost concurrently. As soon as Part I is well started, begin Part II.]

In a dry 250-ml. flask place 6.15 g. (5.1 ml., 0.05 mole) of nitrobenzene, 125 ml. of commercial absolute methanol, and a small crystal of iodine. Weigh 6.0 g. of magnesium turnings on a piece of paper, add one half of the magnesium to the solution of nitrobenzene, and attach the flask to a water-cooled reflux condenser. The exothermic reaction, which begins at once, causes the solution to boil.

[Begin Part II.]

15-60 In 7-8 minutes the rate of ebullition will have subsided somewhat and the remainder of the magnesium turnings may be introduced into the flask. Again attach the flask to the reflux condenser and allow the spontaneous reaction to proceed until boiling nearly ceases (about 15 minutes). Thereafter heat the flask in a pan of hot water at 70°-80° for an additional 30 minutes. (At a higher temperature, excessive bumping occurs.)

60-100 Pour the orange-colored contents of the flask into a beaker containing 100 g. of ice and 100 ml. of water and add hydrochloric acid until the mixture is acidic to litmus. Set the beaker in an ice bath and stir the mixture well to facilitate the separation of the azobenzene. Collect the red precipitate of azobenzene on a Büchner funnel and recrystallize the material from a little ethyl alcohol. The yield of azobenzene, m.p. 68°, is 2.5-3.0 g.

II. Preparation of Hydrazobenzene

15-40 Pour 3 g. (2.6 ml., 0.025 mole) of nitrobenzene into a dry 250-ml. flask and add 50 ml. of commercial absolute methanol along with a small crystal of iodine. Then add 3 g. of clean magnesium turnings and connect the flask to a reflux condenser. A vigorous exothermic reaction begins quickly and is allowed to proceed unchecked unless the boiling solution reaches nearly to the neck of the flask, in which event the flask is momentarily surrounded by cold water.

In about 10 minutes the separation of magnesium
methoxide becomes so extensive that the contents of the
flask tend to set to a thick paste. Add, through the top
of the condenser, an additional 25 ml. of absolute meth- 40-55
anol, shake the flask, and allow the reaction to proceed
as before.

Within another 10-15 minutes the rate of reaction
becomes slow and the flask is heated in a pan of hot
water at 75°-85°. A bath temperature of 80°-85° pro-
duces gentle bumping which is advantageous as it helps
to stir the thick suspension. Above 85° the bumping
usually becomes excessive. Add another 2-g. portion of 55-75
magnesium turnings (usually these will drop through
the condenser) and continue heating the flask and shak-
ing it occasionally during the next 20 minutes or a little
longer if you are busy with the production of the speci-
men of azobenzene.

75-100 Disconnect the flask from the condenser and stir the hot contents into a slurry so that the thick suspension may be poured into a 400-ml. beaker. Add 100 ml. of water, part of which is used in rinsing the flask, and slowly acidify the suspension by the addition of glacial acetic acid. About 25-30 ml. of the acid will be required.

As the magnesium methoxide dissolves, a white (or pale yellow) residue of hydrazobenzene remains which, for the most part, floats on the surface of the liquid. A small quantity of excess magnesium settles to the bottom of the beaker. Pour the water solution and suspended hydrazobenzene onto the suction filter, leaving the magnesium granules, in so far as is possible, in the beaker.

Wash the product on the Büchner funnel well with water to remove magnesium salts and avoid drawing much air through the filter cake in order to minimize

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[1] The preparation of azobenzene and of hydrazobenzene given here is modeled after that described by A. I. Vogel, A. Watling, and J. Watling, *J. Chem. Educ.*, **35**, 40 (1958).

atmospheric oxidation of the hydrazobenzene (colorless when pure) to red azobenzene. We shall not recrystallize the hydrazobenzene for determination of its melting point nor make a direct measurement of the yield. The latter may be derived from the weight of benzidine sulfate obtained in Part III.

III. BENZIDINE

100-125 Transfer the moist hydrazobenzene to a 250-ml. beaker and add 100 ml. of water plus 15 ml. of concentrated hydrochloric acid. Warm the mixture to 40°-50° and stir it for a few minutes. The hydrazobenzene rearranges rather rapidly to benzidine and passes into solution as benzidine hydrochloride. Usually a small quantity of orange-red azobenzene remains undissolved. This is removed by filtration and the filtrate containing benzidine hydrochloride is used in sections (a), (b), and (c) of this experiment.

Dilute the solution with distilled water to a volume of 150 ml. and stir the solution well to assure its uniform concentration. Reserve 25 ml. of this solution for tests (b) and (c).

(*a*) *Benzidine Sulfate.* To 125 ml. of the solution of benzidine hydrochloride add 5 ml. of concentrated sulfuric acid and set the solution in an ice bath for a few minutes. Collect the white, slightly soluble benzidine sulfate on a small Büchner or Hirsch funnel, rinse it on the filter with two 5-ml. portions of ethyl alcohol, then with a little ether, and spread the material on a sheet of filter paper to dry in the air.

Weigh the benzidine sulfate and calculate the yield, assuming the salt obtained to be the double acid sulfate, $[H_3N—C_6H_4—C_6H_4—NH_3]^{++}$, $2HSO_4^-$. Remember that this weight of salt is from 5/6 of your benzidine hydrochloride; hence, in calculating the yield the weight of salt obtained should be multiplied by 6/5.

(*b*) *Benzidine as a Reagent for Free Chlorine.* To 50 ml. of water contained in a 25 x 200 mm. test tube add 2 or 3 drops of your solution of benzidine hydrochloride. Shake the tube to mix the solutions well and then add 1 or 2 drops of chlorine water. A green coloration is produced. If the color is orange or red, the solutions are too concentrated. Dilute them and repeat the test. **125-135**

o-Tolidine, which is commonly used as a colorimetric reagent for free chlorine in municipal water supplies, is structurally similar to benzidine and gives a yellow color the intensity of which is a measure of the concentration of chlorine in the water.

(*c*) *Precipitation of Benzidine.* Add a 5 per cent solution of sodium hydroxide to the remainder of your solution of benzidine hydrochloride until the solution is alkaline to litmus. Collect the gray precipitate of benzidine upon a filter, recrystallize it from a small amount of ethyl alcohol, and observe its melting point. The recorded melting point of benzidine is 128°. **135-160**

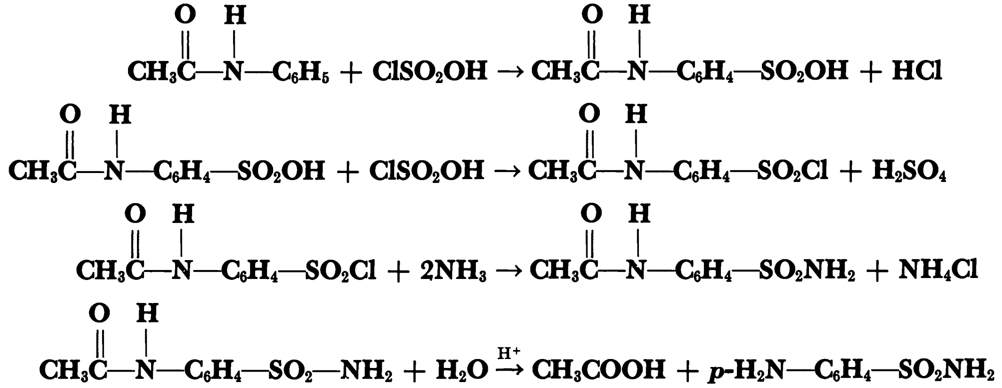
QUESTIONS

1. (a) What is the formula for *o*-tolidine? (b) How would you make it?

2. What is the importance of benzidine and related compounds to the manufacture of dyes for cotton cloth?

EXPERIMENT 58

Sulfanilamide



(1a) $$CH_3\overset{O}{\overset{\|}{C}}-\overset{H}{\overset{|}{N}}-C_6H_5 + ClSO_2OH \rightarrow CH_3\overset{O}{\overset{\|}{C}}-\overset{H}{\overset{|}{N}}-C_6H_4-SO_2OH + HCl$$

(1b) $$CH_3\overset{O}{\overset{\|}{C}}-\overset{H}{\overset{|}{N}}-C_6H_4-SO_2OH + ClSO_2OH \rightarrow CH_3\overset{O}{\overset{\|}{C}}-\overset{H}{\overset{|}{N}}-C_6H_4-SO_2Cl + H_2SO_4$$

(2) $$CH_3\overset{O}{\overset{\|}{C}}-\overset{H}{\overset{|}{N}}-C_6H_4-SO_2Cl + 2NH_3 \rightarrow CH_3\overset{O}{\overset{\|}{C}}-\overset{H}{\overset{|}{N}}-C_6H_4-SO_2NH_2 + NH_4Cl$$

(3) $$CH_3\overset{O}{\overset{\|}{C}}-\overset{H}{\overset{|}{N}}-C_6H_4-SO_2-NH_2 + H_2O \xrightarrow{H^+} CH_3COOH + p\text{-}H_2N-C_6H_4-SO_2NH_2$$

Introduction. The preparation of sulfanilamide involves three successive steps: (1) The sulfonation of acetanilide and subsequent formation of *p*-acetaminobenzenesulfonyl chloride, (2) the conversion of the sulfonyl chloride to *p*-acetaminobenzenesulfonamide, and (3) the removal of the acetyl group by hydrolysis.

0-70 Step I. *p*-Acetaminobenzenesulfonyl Chloride

In a 100-ml. flask place 20 ml. of chlorosulfonic acid and cool it to 15° in cold water. (CAUTION: chlorosulfonic acid causes bad burns on the skin. Handle it with care.) Add to the acid in the flask 7 g. (approximately 0.05 mole) of dry acetanilide in small portions. Stir the mixture with a stirring rod and add the acetanilide slowly so that the temperature does not rise above 25°.

When all, or nearly all, of the acetanilide has dissolved, fit the flask with a stopper, through which is inserted a piece of glass tubing about 2 feet long to exclude moisture, and heat the flask on a steam bath for 45 minutes. At the end of this time pour the contents of the flask slowly and cautiously into a 400-ml. beaker which is half filled with ice and water. The *p*-acetaminobenzenesulfonyl chloride separates as a gummy mass which soon solidifies. It is broken into lumps, collected on a Büchner funnel, dried as much as possible by suction, and used immediately in the next step.

70-120 Step II. *p*-Acetaminobenzenesulfonamide

Place the acid chloride obtained in step I into a 100-ml. flask and add 25 ml. of concentrated ammonium hydroxide solution. The reaction begins at once and is exothermic. Stir the mixture to produce a thin paste and heat the flask on the steam bath or in a pan of boiling water for 10 minutes. (At this point the preparation may be set aside until the next laboratory period if necessary.)

Chill the flask in an ice bath and slowly add dilute sulfuric acid (15-20 per cent) until the solution is acidic to Congo red paper. Allow the flask to stand in the ice bath for 5 minutes and collect the crystals of the amide upon a Büchner funnel. Wash the crystals with a little water, dry them as much as possible by suction, and proceed to step III.

In order to verify the identity of the product, recrystallize a small portion of it from alcohol and determine its melting point. *p*-Acetaminobenzenesulfonamide melts at 219°.

Step III. *p*-Aminobenzenesulfonamide 120-170

Weigh the *p*-acetaminobenzenesulfonamide and place it in a small flask. Add to the amide twice its weight of dilute hydrochloric acid (one volume of acid to one volume of water) and boil the mixture gently under a reflux condenser for 20 minutes. At the end of this time dilute the solution with an equal quantity of water and transfer it to a beaker. Add solid sodium carbonate in small quantities at a time until the solution, after thorough stirring, is barely alkaline to litmus.

A precipitate of sulfanilamide forms during the neutralization and grows when the beaker is chilled in ice. Collect the product on a suction filter, wash it with a little water, and dry it on paper or on a piece of porous clay plate. The yield is about 4 g. Dissolve the sulfanilamide in about fifteen times its weight of boiling water, decolorize the solution with a little charcoal, filter, and chill the filtrate in ice. The sulfanilamide separates in needle-shaped crystals which melt at 163°.

Note that sulfanilamide will dissolve in either dilute acid or dilute alkali.

QUESTIONS

1. Why must sulfanilic acid be acetylated before the sulfonic acid group is converted into the sulfonyl chloride?
2. What explanation would you offer for the observa-

tion that sulfanilic acid undergoes acetylation with acetic anhydride slowly, whereas the acetylation of sodium sulfanilate proceeds rapidly?

3. How do you account for the amphoteric nature of sulfanilamide?

4. In consideration of the fact that *p*-acetaminobenzenesulfonamide contains the amide of a carboxylic acid as well as the amide of a sulfonic acid, how do you explain the observation that the former is hydrolyzed far more rapidly than the latter?

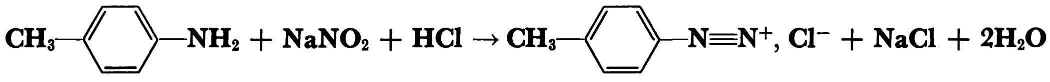
EXPERIMENT 59

I. Chlorobenzene by the Sandmeyer Reaction

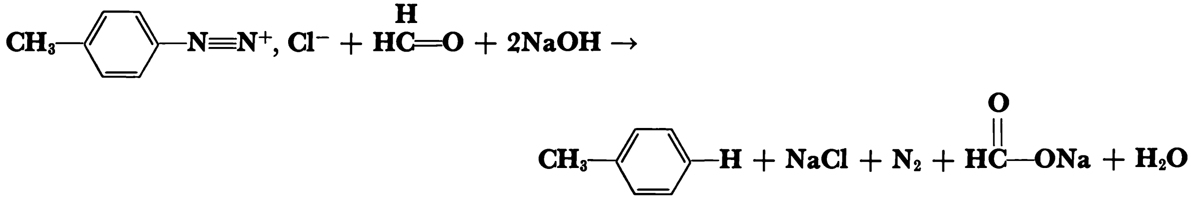
$$C_6H_5—N{\equiv}N^+, Cl^- \xrightarrow{CuCl} C_6H_5—Cl + N_2$$

II. Toluene by the Deamination of *p*-Toluidine

(1)



(2)



I. CHLOROBENZENE

0-15 The Cuprous Chloride Solution

Prepare a solution of cuprous chloride by one of the following methods as directed by the instructor.

(*a*) *From Copper Sulfate.* In a 1-liter flask dissolve 80 g. of pulverized copper sulfate ($CuSO_4 \cdot 5H_2O$) in about 300 ml. of hot water and add 30 g. of sodium chloride. In a 400-ml. beaker prepare a solution of 18 g. of sodium bisulfite and 12 g. of sodium hydroxide in 150 ml. of water and add this solution (reducing agent) in small portions to the hot solution of copper sulfate during the course of 2 or 3 minutes. Throughout this time shake the flask containing the copper sulfate continuously. Close the mouth of the flask loosely with a stopper to minimize oxidation and set the flask aside while you diazotize the aniline.

(*b*) *From Copper Carbonate.* In a 500-ml. flask place 20 g. of copper carbonate with 100 ml. of water and dissolve the copper carbonate by the gradual addition of 75 ml. of concentrated hydrochloric acid. Then add 20 g. of copper turnings (Note 1), cover the mouth of the flask with a watch glass, and heat the solution to the boiling point for 15 minutes while you diazotize the aniline (Note 2).

(*c*) *From Cupric Chloride.* Dissolve 28 g. of cupric chloride ($CuCl_2 \cdot 2H_2O$) in 100 ml. of water and 75 ml. of concentrated hydrochloric acid and heat the solution with 20 g. of copper turnings as in section (b) above.

15-40 Diazotization of the Aniline

Pour 22.5 ml. (23.2 g., 0.25 mole) of aniline into a 400-ml. beaker and dissolve it by the addition of 50 ml. of water and 75 ml. of concentrated hydrochloric acid. Cool the solution to about 5° by setting the beaker in a pan of ice and by adding about 50 g. of ice to the solution. Diazotize the aniline by adding, in small portions, a solution of 18 g. of sodium nitrite in a little water during the course of 2 or 3 minutes. Let the solution stand in the ice bath for about 10 minutes while you prepare for the steam distillation.

When the apparatus for steam distillation has been assembled, give your attention to the cuprous chloride solution. If procedure (a) has been followed, carefully pour off and discard the supernatant solution and wash the white precipitate of cuprous chloride by decantation with water. Then dissolve the cuprous chloride in 100-125 ml. of concentrated hydrochloric acid and 30-40 ml. of water. Cool the solution, contained in a 1-liter (or 2-liter) flask, to 0°-10° in an ice bath. If method (b) or (c) was used, add a sufficient quantity of concentrated hydrochloric acid to dissolve any precipitate of cuprous chloride that may have formed, pour the solution into a 1-liter (or 2-liter) flask and cool it in ice.

40-130 *The Main Reaction.* With almost continuous shaking and cooling of the flask containing the cuprous chloride, slowly add the solution of benzenediazonium chloride. A voluminous precipitate of a double salt of cuprous chloride–benzenediazonium chloride is formed which loses nitrogen as the temperature rises. When all of the diazo solution has been added, warm the flask gently to aid in the decomposition of the double salt. The heat should be applied slowly in order to avoid excessive foaming in connection with the loss of nitrogen. When the temperature has risen to approximately 50°, all of the solid will have been replaced by an oily layer of chlorobenzene which is then removed by distillation with steam.

Chlorobenzene has a high vapor pressure at temperatures near the boiling point of water and is carried over so rapidly that the collection of 125-150 ml. of distillate is sufficient. Add a little sodium hydroxide solution to the distillate to dissolve any phenol that may have been formed, separate the chlorobenzene, wash it once with water, dry it over a little calcium chloride, and distill it. The yield is 16-18 g.; b.p. 132°.

NOTES

1. If copper turnings are not available, copper shot or pieces of copper foil may be used. In any event the metal should be in such form that it is well covered by the solution. Avoid pouring residual copper shot into the sinks because it clogs the drain pipes.

2. The solution should simmer only. Vigorous boiling results in the loss of acid from the flask where it is needed and in the acidification of the atmosphere which cannot be tolerated.

II. TOLUENE BY DEAMINATION OF *p*-TOLUIDINE

60-75 *Diazotization of the p-Toluidine.* As soon as the steam distillation in Part I is well started, diazotize 27 g. (0.25 mole) of *p*-toluidine in the following manner: Dissolve the *p*-toluidine, contained in a beaker, in 75 ml. of concentrated hydrochloric acid and 200 ml. of water. Cool the solution to 0°-5° in an ice bath and add about 100 g. of ice to the solution. Slowly add a solution of 18 g. of sodium nitrite in a little water and set the solution aside while you prepare the alkaline solution of formaldehyde.

75-100 *Reduction of p-Toluenediazonium Chloride with Alkaline Formaldehyde Solution.* In a 2-liter flask fitted with a mechanical stirrer dissolve 50 g. of commercial sodium hydroxide in 300 ml. of water and add 300 g. of crushed ice. Start the stirrer (or, if mechanical stirrers are not available, shake the flask) and add 50 ml. of formalin (37 per cent formaldehyde). Then introduce the *p*-toluenediazonium chloride in a slow stream into the stirred alkaline solution of formaldehyde. The rapid escape of nitrogen causes considerable frothing.

The toluene, produced by the reaction, quickly separates from the solution as an upper layer. Remove the stirring motor, add a few boiling chips and, by means of stoppers and a bent tube, connect the flask to a condenser for distillation of the toluene. The introduction of steam is unnecessary; simply boil the mixture over the Bunsen burner and collect about 150 ml. of the toluene-water distillate.

[While the toluene is being distilled from the reaction mixture, complete the preparation of the chlorobenzene.] **100-130**

Separate the upper layer of toluene, wash it once with water, dry it over a little calcium chloride and distill it. Yield 15-18 g.; b.p. 110°. **130-170**

QUESTIONS

1. How do you account for the presence of small amounts of phenol in the chlorobenzene prepared in Part I?

2. What products other than hydrocarbons may be obtained by reduction of diazonium salts under various conditions?

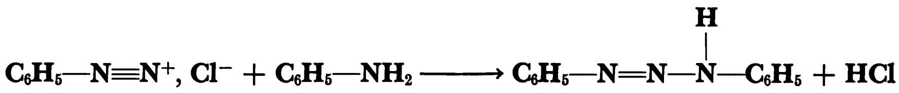
3. Write equations showing how reactions of diazonium salts may be used in the preparation of *p*-bromotoluene, iodobenzene, benzoic acid, *p*-toluic acid, *o*-iodotoluene, and phenylhydrazine.

EXPERIMENT 60

I. Preparation of Diazoaminobenzene

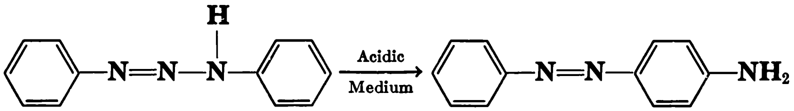
(1) $$C_6H_5{-}NH_2 + NaNO_2 + 2HCl \longrightarrow C_6H_5{-}N{\equiv}N^+, Cl^- + NaCl + 2H_2O$$

(2)



$$C_6H_5{-}N{\equiv}N^+, Cl^- + C_6H_5{-}NH_2 \longrightarrow C_6H_5{-}N{=}N{-}\overset{\displaystyle H}{\overset{|}{N}}{-}C_6H_5 + HCl$$

II. Rearrangement of Diazoaminobenzene to Aminoazobenzene



I. Diazoaminobenzene

Diazotization of Aniline. In a 400-ml. beaker dissolve 9.3 g. (9 ml., 0.1 mole) of aniline in 10 ml. of concentrated hydrochloric acid and 50 ml. of water. Cool the solution to 0°-5° by the introduction of 50-75 g. of ice and diazotize half of the aniline by the addition of 3.5 g. (0.05 mole) of sodium nitrite dissolved in a little water. Set the solution aside for about 15 minutes while you prepare some aniline hydrochloride that will be needed in Part II (Note 1).

15-30 [Prepare the aniline hydrochloride as described in Part II.]

30-60 *Coupling of Benzenediazonium Chloride with Aniline.* Return to the original experiment and add to the solution, now containing approximately 0.5 mole of aniline and 0.5 mole of benzenediazonium chloride, a solution of 25 g. of sodium acetate in 100 ml. of water. A voluminous precipitate of diazoaminobenzene is formed. Stir the mixture until the precipitate is well coagulated and then collect the precipitate on a Büchner filter. Remove as much liquid as possible by suction and wash the solid twice on the filter with small quantities of water.

Again remove the water by suction and press the crystals with the flat top of a large glass stopper in order to obtain a compact cake of diazoaminobenzene that is fairly dry. Remove about 0.5 g. of the diazoaminobenzene for recrystallization from ethanol and observation of the melting point. The recorded melting point is 98°.

Silver Salt. Dissolve about 0.1 g. of diazoaminobenzene in ethanol and add 1 ml. of an alcoholic solution of silver nitrate. The orange-colored precipitate has the composition $C_6H_5{-}N{=}N{-}N(Ag){-}C_6H_5$.

II. Aminoazobenzene

Introduction. For the conversion of diazoaminobenzene to aminoazobenzene, the former compound is dissolved in aniline and warmed with aniline hydrochloride, which is the acidic agent.

15-30 *Preparation of Aniline Hydrochloride.* In a 100-ml. beaker stir 10 ml. of aniline with 25 ml. of concentrated hydrochloric acid. Cool the mixture in ice until a thick paste is obtained. Thin the paste by addition of 10-15 ml. of ether and collect the crystals of aniline hydrochloride on a small Büchner funnel. Suck the crystals as dry as possible, rinse them on the filter with about 10 ml. of ether and spread them out on a sheet of paper to dry in the air.

Conversion of Diazoaminobenzene to Aminoazobenzene. Transfer the moist solid cake containing the major portion of the diazoaminobenzene to a 250-ml. beaker, add the crystals of aniline hydrochloride prepared above, and 10-15 ml. of aniline. Stir the mixture well and heat the beaker in boiling water or on the steam bath for 30 minutes to bring about the molecular rearrangement. At the end of this time remove the beaker from the steam bath, cool the contents to 40°-50°, add 25 ml. of glacial acetic acid, and pour the well stirred solution into 200 ml. of cold water for precipitation of the aminoazobenzene (Note 2).

Stir the mixture well until the aminoazobenzene settles readily leaving a clear supernatant liquid. Bring the solid material onto the Büchner funnel and wash it twice with water. After removing as much water as possible by suction, press the crystals well with the flat top of a glass stopper.

Recrystallize the crude brown product by transferring it from the Büchner funnel to a 250-ml. flask that is fitted with a stopper bearing a piece of glass tubing about 18 inches long and proceeding in the following manner:

Introduce 100 ml. of ligroin (b.p. 90°-100°) into the flask, replace the stopper and tube, and heat the flask on the steam bath to dissolve as much of the solid material as possible. (CAUTION: Keep clear of lighted Bunsen burners; do not give mishap a chance!) Remove the flask from the steam bath, allow the dark solid material to settle for a moment and decant the clear solution into a 250-ml. beaker, being careful to retain all dark material in the flask. The clear solution in the beaker quickly deposits small aggregates of orange-colored needle-shaped crystals of aminoazobenzene when cooled in ice.

As soon as crystallization appears to be complete (about 3 minutes), the crystals are collected on the suction filter and the filtrate returned to the flask for a second extraction of the crude material by heating on the steam bath, decanting, and cooling as before. Repeat this extraction process as long as a worthwhile yield of crystals is obtained. Combine the various crops of crystals, dry them, and observe the melting point. The recorded melting point is 127°. Yield 5-6 g.

NOTES

1. Aniline and benzenediazonium chloride do not combine in strongly acidic solution. In order to bring about the combination with the formation of diazoaminobenzene, the acidity of the solution is diminished by the addition of sodium acetate. In the present experiment the concentration of hydrochloric acid is so low that some diazoaminobenzene may separate even before the sodium acetate is added. This, of course, does no harm.

2. Both aniline and aminoazobenzene are basic and, consequently, form salts with acids. The aminoazobenzene is a weaker base than aniline, however, and its acetate is so nearly completely hydrolyzed in dilute water solution that the free base precipitates. Aniline, a stronger base, remains in solution as its salt with acetic acid.

QUESTIONS

1. Which of the following amines may be diazotized?

(a) ethylamine
(b) ethylenediamine
(c) trimethylamine
(d) aniline
(e) *p*-toluidine
(f) benzylamine
(g) diphenylamine
(h) dimethylaniline
(i) *p*-nitroaniline
(j) 2,4-dichloroaniline

2. Write equations to show the diazoamino compound formed when (a) benzenediazonium chloride reacts with *p*-bromoaniline and (b) when *p*-bromobenzenediazonium chloride reacts with aniline. How do you account for the fact that the two products are indistinguishable?

3. How would you separate a mixture of aniline and aminoazobenzene?

4. What products will be formed by strong reduction of aminoazobenzene (as with metal and acid)?

EXPERIMENT 61

Preparation and Properties of Phenol

(1) $$C_6H_5\text{—}NH_2 + NaNO_2 + 2H_2SO_4 \longrightarrow C_6H_5\text{—}N{\equiv}N^+, HSO_4^- + NaHSO_4 + 2H_2O$$

(2) $$C_6H_5\text{—}N{\equiv}N^+, HSO_4^- + H_2O \xrightarrow{50\text{-}60^\circ} C_6H_5\text{—}OH + N_2 + H_2SO_4$$

I. PREPARATION OF PHENOL

Introduction. Today's experiment for the production of phenol involves (1) the diazotization of aniline and (2) the hydrolysis of the benzenediazonium salt.

[CAUTION: Phenol, except in dilute solution, causes burns on the skin. Should any concentrated phenol come in contact with the hands wash them at once with alcohol and with water.]

0-90 *Procedure.* Into a 1-liter flask pour 300 ml. of water and 30 ml. of concentrated sulfuric acid. Then, with continuous shaking of the flask, add 28 g. (27.5 ml., 0.3 mole) of aniline in small portions so that the precipitate of aniline acid sulfate, $(C_6H_5NH_3)^+HSO_4^-$, will be finely divided.

Cool the solution to 25°-30° by rotating the flask in a bath of ice and water and then introduce into the flask 200-250 g. of crushed ice to bring the temperature of the solution below 10°. Diazotize the aniline by the portion-wise addition of 22 g. of sodium nitrite dissolved in 100 ml. of water. Shake the flask well during the addition of the sodium nitrite, which will require about 3 minutes.

Let the solution stand for 10 minutes to allow time for the diazotization reaction to proceed, then warm the flask over the Bunsen burner until a thermometer immersed in the liquid records a temperature of 45°-50°. At this point the burner is removed, as the exothermic hydrolysis of the diazonium salt during the next 10-12 minutes will cause a slow rise in the temperature of the liquid to about 70°. During this process, stir the contents of the flask gently with a stirring rod to facilitate a smooth and continuous evolution of nitrogen.

After most of the nitrogen has escaped, allow the liquid to attain a temperature of 70°, either automatically or with a little help from the Bunsen burner, add a few boiling chips, connect the flask with a condenser for distillation and collect 350 ml. of distillate (30-35 minutes of distillation).

55-90 [During this half hour perform the short experiments given in Part II.]

90-140 *Extraction of the Phenol from the Distillate.* To the phenolic distillate add 100 g. of clean salt (NaCl) and stir the mixture until the salt dissolves. Note that some phenol is "salted out" as it is less soluble in brine than in pure water. Pour the liquid into a separatory funnel and separate directly as much of the phenolic layer as possible.

Return the aqueous solution to the separatory funnel and extract the dissolved phenol by shaking the solution vigorously with 20 ml. of carbon tetrachloride. Ten ml. of concentrated hydrochloric acid added to the contents of the funnel at this point will break the emulsion and aid in the rapid settling of the carbon tetrachloride.

Remove the lower layer of carbon tetrachloride which contains some phenol, extract the aqueous solution with a second 20-ml. portion of carbon tetrachloride, and combine the two extracts with the phenol that was separated directly. Should there be a small upper layer of water on the carbon tetrachloride solution, remove it with a separatory funnel and dry the lower layer over a little anhydrous magnesium sulfate.

Distill the solution collecting three fractions: (1) up to 100°, consisting chiefly of carbon tetrachloride, (2) 100°-170°, a small fraction containing both phenol and carbon tetrachloride, and (3) 170°-182°, phenol. Redistillation of the second fraction will give a little more phenol which is added to the main portion. The product should solidify when placed in a bath of cold water. Yield 16-18 g.

The tarry material remaining in the flask in which the main reaction was conducted may be removed by washing with warm sodium hydroxide solution.

II. PROPERTIES OF PHENOL AND OTHER PHENOLIC COMPOUNDS

1. Solubility in Water. Pour about 5 ml. of molten phenol, obtained from the side shelf, into a large test tube and add an equal volume of water. Insert a thermometer and warm the contents of the tube to about 70°, at which temperature the water and phenol are completely miscible. Stir the solution gently with the thermometer and allow it to cool slowly, noting the temperature at which clouding occurs.

[Note: At room temperature phenol is soluble in water to the extent of about 10 per cent and water in phenol to about 27 per cent. The solubilities increase as the temperature rises; the recorded temperature for complete miscibility is 65.3°, or higher.]

2. Solubility in Alkali. Add a little phenol to dilute (5 per cent) sodium hydroxide solution and note the ready solubility of sodium phenoxide. Equation.

3. Color Reaction with Ferric Chloride. Add a drop of phenol to 25 ml. of water. To a portion of this solution add a few drops of ferric chloride solution and note the purple coloration produced. Dilute the original solution of phenol and make repeated trials to show the delicacy of this test for phenol. Many other phenolic compounds show similar color reactions.

4. Reaction with Bromine Water. Dissolve 1 or 2 drops of phenol in a little water and add bromine water until a yellow coloration in the well-shaken mixture indicates that a slight excess of bromine is present. Remove the excess bromine by the addition of a little sodium bisulfite. The white precipitate of 2,4,6-tribromophenol (m.p. 96°) has such low solubility that it is often used not only as a qualitative test for phenol but also as a quantitative measure of the amount of phenol present. Equation.

5. Comparative Reducing Power of Phenol, Resorcinol, Hydroquinone, and Pyrogallol. Dissolve 0.2 g. of phenol in 10 ml. of water and test the reducing power of this solution upon Tollens' reagent. Repeat the experiment replacing the phenol, in turn, by resorcinol, hydroquinone, and pyrogallol. Results? How do the increased number of hydroxyl groups and their relative positions influence the reducing power of the phenolic compounds? Do the polyhydric phenols have greater solubility in water than does phenol?

QUESTIONS

1. Write equations to show the preparation of:

(a) phenol from chlorobenzene
(b) phenol from benzenesulfonic acid
(c) *p*-cresol from *p*-toluidine
(d) guaiacol (monomethylether of catechol) from *o*-anisidine.

2. Write the formula and name for the chief product formed by the reaction of phenol with each of the following reagents:

(a) NaOH solution
(b) CH_3COCl
(c) $(CH_3CO)_2O$
(d) C_6H_5COCl
(e) $(C_3H_7CO)_2O$
(f) dil. HNO_3
(g) bromine water
(h) $C_6H_5N_2^+$, Cl^-
(i) NaOH + C_2H_5I

3. To what approximate dilution does the ferric chloride test for phenol appear to be sensitive? Propose a structure for the colored product.

4. (For Specially Interested Students) Is phenol a stronger or a weaker acid than carbonic acid? Propose and carry out an experiment designed to prove your answer.

EXPERIMENT 62

I. Preparation of Phenetole

$$C_6H_5—OH + (C_2H_5)_2SO_4 + 2NaOH \rightarrow C_6H_5—O—C_2H_5 + C_2H_5—OH + Na_2SO_4 + H_2O$$

II. Solid Derivatives of Phenol

Introduction. Aromatic ethers such as diphenyl ether or phenyl ethyl ether (phenetole) are not easily obtained in good yield by heating a phenolic compound, or a mixture of a phenol and an alcohol, with sulfuric acid or other dehydrating agent. The laboratory procedure usually followed for the preparation of such an ether is a variation of the method devised by Williamson for the production of aliphatic ethers.

In today's experiment we shall use the Williamson method for the preparation of phenetole by heating a solution of sodium phenoxide with diethyl sulfate. In the Ullmann variation of the Williamson reaction, the alkaline salt of a phenol is heated with an aromatic halide in which the halogen is activated by the presence of one or more nitro groups in the molecule. Thus, when potassium phenoxide is heated with *p*-nitrochlorobenzene, usually in the presence of copper powder as a catalyst, phenyl 4-nitrophenyl ether is obtained.

Further modifications of the Ullmann process employ, as the active halogen compound, 4-nitrofluorobenzene or 2,4-dinitrochlorobenzene. The use of the latter of these nitrated aromatic halides is illustrated in section (d) of Part II in today's assignment.

I. PREPARATION OF PHENETOLE

0-25 *Procedure.* In a 200-ml. flask dissolve 16 g. of sodium hydroxide in 50 ml. of water and add 18.8 g. (0.2 mole, about 18 ml.) of molten phenol or the equivalent quantity of the 90 per cent liquid phenol. To this solution add 30.8 g. (0.2 mole, 27 ml.) of diethyl sulfate in portions of 2 or 3 ml. at a time and shake the flask well after each addition. If the mixed liquids should begin to boil, cool the flask in cold water. Note that the reaction is rapid and that a layer of pleasant-smelling phenetole (phenyl ethyl ether) quickly rises to the surface of the liquid. In order to bring the reaction nearly to completion, connect the flask with a reflux condenser and boil the liquid for 10 minutes.

25-60 At the conclusion of this period cool the flask and pour the contents into a separatory funnel for removal of the upper layer of phenetole. Extract any small amount of phenetole remaining in the alkaline solution by shaking the solution with 15-20 ml. of carbon tetrachloride and combine this extract with the phenetole previously separated. Dry the combined lot with a few grams of magnesium sulfate, decant from the drying agent, and distill the liquid, collecting the portion boiling from 165°-172°. The yield is usually about 18-20 g.

II. SOLID DERIVATIVES OF PHENOLIC COMPOUNDS

Introduction. For the identification of an unknown phenolic compound it is advantageous to prepare several of its solid derivatives so that the identity of the phenolic compound in question may be established (1) by the melting points of these crystalline compounds, and (2) by their "mixed melting points" with known samples. Four derivatives of phenolic compounds which, in most instances, are well crystallized solids that may be prepared easily are (a) the bromine substitution product, (b) the benzoyl derivative, (c) the substituted ester of carbamic acid (urethane type) made by reaction of the phenol with phenyl isocyanate, and (d) the substituted diphenyl ether obtained from the phenol and 2,4-dinitrochlorobenzene.

(*a*) *The Bromine Derivative.* Reaction of a phenolic compound with bromine water, or bromine in acetic acid solution, results in substitution of bromine atoms at positions *ortho* and *para* to the hydroxyl group unless those positions are firmly held by other substituents. For example, trisubstitution readily occurs in phenol yielding 2,4,6-tribromophenol, whereas but two bromine atoms are substituted in *p*-cresol. In the latter instance, the bromine atoms occupy the two positions *ortho* to the hydroxyl group. No reaction occurs elsewhere in the *p*-cresol molecule because the positions *meta* to the hydroxyl group are not activated and the methyl group is securely attached to the benzene ring at the *para* position.

A feebly held substituent, such as the carboxyl group in salicylic acid, is replaced by bromine; thus salicylic acid and bromine water give a precipitate of 2,4,6-tribromophenol with elimination of carbon dioxide.

Tribromophenol. Dissolve 0.5 g. of phenol in 10 ml. of water and add bromine water to the solution until the color of the solution indicates that a slight excess of bromine is present. Add a little sodium bisulfite solution to remove the excess bromine. Remove the precipitate of 2,4,6-tribromophenol by filtration, wash it with water, and recrystallize it from a little hot ethyl alcohol. The purified crystals should melt at 96°. 60-85

(*b*) *The Benzoyl Derivative* (*Production of Phenyl Benzoate by the Schotten-Baumann Reaction*). Dissolve approximately 1 g. of phenol in 10 ml. of water with the addition of 10 ml. of a 10 per cent solution of sodium hydroxide. Add 10-12 drops of benzoyl chloride and shake the tube for a few minutes. The odor of benzoyl chloride soon disappears and a pre- 85-110 cipitate of phenyl benzoate forms. Equation. Remove the precipitate by filtration. After recrystallization from a little hot ethyl alcohol the product melts at 70°.

(*c*) *The Substituted Ester of Carbamic Acid* (*A compound of the Urethane Type*). Phenyl isocyanate reacts with a phenol more slowly than does an amino compound, and usually a little anhydrous aluminum chloride must be added as a catalyst. The following procedure for the combination of phenyl isocyanate with *p*-cresol is a typical illustration of the method to be used.

110-140 Dissolve 5 g. of *p*-cresol in 40 ml. of dry benzene and, at the hood, add 4 g. of phenyl isocyanate (a powerful lachrymator) and 5 g. of anhydrous aluminum chloride. Heat is evolved and it may be necessary to cool the flask somewhat. Let the reaction proceed for 10 minutes and then pour the mixture cautiously into 100 ml. of ice water. Separate the benzene layer, cool it in ice, and precipitate the ester by the addition of ligroin. Collect the solid ester on a filter and recrystallize it from ligroin, m.p. 114°.

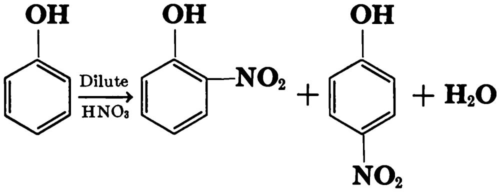
140-160 (*d*) *The Ether of 2,4-Dinitrophenol.* Dissolve 0.3 g. of phenol in 10 ml. of ethanol and add 10 drops of 10 per cent sodium hydroxide solution and 0.5 g. of 2,4-dinitrochlorobenzene. Heat the solution to boiling for a few minutes. If the phenyl 2,4-dinitrophenyl ether separates as an oil, add a little more alcohol to bring it into solution in the boiling solvent and set the tube aside until the product crystallizes. After recrystallization from a small amount of ethanol, the ether melts at 71°. Many other phenols react in a similar manner though sometimes at a slower rate; consequently the period of heating the reactants may vary from 2 to 20 minutes.

QUESTIONS

1. Write the formula for the following ethers and esters of phenolic compounds:
    (a) anisole (phenyl methyl ether)
    (b) phenetole (phenyl ethyl ether)
    (c) hydroquinone dimethyl ether
    (d) resorcinol diethyl ether
    (e) hydroquinone dibenzoate
    (f) 4-chlorophenyl 4-nitrophenyl ether
    (g) benzyl phenyl ether
    (h) 2,4-dichlorophenyl 2,4-dinitrophenyl ether
2. Suggest convenient means for preparing each of the above ethers.
3. May alkyl halides be used in place of alkyl sulfates in the production of ethers of phenolic compounds?
4. Write the equation for the reaction of phenol with phenyl isocyanate. Why does phenol react more slowly than an amine? Name the product. Does it exist to any appreciable extent in tautomeric forms? Can you suggest why, or why not?

EXPERIMENT 63

Preparation of *o*- and *p*-Nitrophenol



Introduction. The nitration of phenol with concentrated nitric and sulfuric acids leads to the formation of 2,4,6-trinitrophenol (picric acid). Nitration of the phenol with dilute nitric acid, alone, introduces but one nitro group and gives a satisfactory method for the laboratory preparation of *ortho*- and *para*-nitrophenol. The *o*-nitrophenol is separated from its *para* isomer by distillation in steam.

Procedure. In a 100-ml. graduated cylinder measure 25 ml. of concentrated nitric acid and fill the cylinder to the 100-ml. mark with water. In a small beaker weigh 18.6 g. (0.2 mole) of molten phenol and add 2-3 ml. of water to keep the phenol liquid or, as an alternative, if the storekeeper supplies the 90 per cent "liquid phenol," use 20 ml. of it. Pour the diluted nitric acid into a 500-ml. flask and add about 2 ml. of the liquid phenol.

The immediate nitration reaction is marked by the appearance of a dark coloration in the solution and by the evolution of heat. Cool the solution if necessary to keep the temperature below 60° and so regulate the addition of small portions of the phenol and the cooling of the flask that the temperature of the solution is maintained as nearly as possible in the 45°-55° range.

After the introduction of the phenol, which requires about 5 minutes, the flask is shaken well (or stirred mechanically) for an additional 10 minutes. Cool the flask until the temperature of the mixture is 25°-30° and pour the contents of the flask into a small separatory funnel where the lower oily layer is withdrawn into another flask for steam distillation. The upper aqueous layer may be discarded.

The heavy oily layer, consisting chiefly of *o*-nitrophenol, *p*-nitrophenol, and some tarry oxidation products of indefinite composition, is subjected to distillation in steam until all of the *o*-nitrophenol has been carried over into the receiver. This will require the collection of about 400 ml. of distillate. If the *o*-nitrophenol (m.p. 45°) does not solidify at once in the receiver, it will do so upon the addition of a little ice.

p-Nitrophenol. The *p*-nitrophenol, almost nonvolatile in steam, remains in the distillation flask partly in solution in the hot water and partly as a dark-colored oil. Add sufficient water to the flask to bring the total volume of liquid to 200-250 ml. or, if the volume of liquid is greater than 250 ml., heat the flask with the Bunsen burner to remove water by distillation until the contents of the flask do not exceed 250 ml. in volume. Heat the liquid to the boiling point and filter it through a fluted filter paper. To the hot filtrate add 2 g. of decolorizing carbon, again heat to boiling, and filter to remove the carbon.

Place an empty 400-ml. beaker into an ice bath and add to it a few ml. of the hot solution. Stir the chilled solution with a glass rod to induce crystallization of the *p*-nitrophenol. Such rapid cooling brings about crystallization of the *p*-nitrophenol and thus avoids the separation of the material as a dark oil which usually occurs if the solution is allowed to cool slowly.

When crystallization of the first small portion of the *p*-nitrophenol has been attained, add another 2-5 ml. portion of the hot solution and stir briskly as before. Continue adding small amounts of the hot solution to the chilled beaker in this manner until the entire quantity of solution has been used. Collect the crystals of *p*-nitrophenol on the Büchner funnel and dry them in an oven at about 60°. If further purification is desired, recrystallize the product from hot benzene. (CAUTION! Use a steam bath. Guard against fire.) The recorded melting point of *p*-nitrophenol is 114°.

Weigh the *o*-nitrophenol and *p*-nitrophenol separately and calculate the yield of each isomer.

COMPARATIVE ACIDITY OF PHENOL AND NITROPHENOLS

Prepare aqueous solutions of phenol, *o*-nitrophenol, *p*-nitrophenol, 2,4-dinitrophenol, and 2,4,6-trinitrophenol (picric acid) by shaking about 0.5 g. of each phenolic compound with 10 ml. of water. Test each water solution with litmus paper. Result? Add a little solid sodium bicarbonate to each solution. In which tubes is carbon dioxide evolved? Rate these phenolic compounds in the order of their acidity.

QUESTIONS

1. How do you account for the observation that *o*-nitrophenol distills with steam far more rapidly than does *p*-nitrophenol?
2. Starting from *o*-nitrophenol or *p*-nitrophenol and such inorganic reagents as may be needed, show by outline equations how it would be possible to obtain:

(a) *o*-nitroanisole
(b) *o*-anisidine
(c) guaiacol
(d) *p*-nitrophenetole
(e) *p*-phenetidine
(f) hydroquinone mono-ethyl ether

3. How may 2,4,6-trinitrophenol (picric acid) be made (a) from phenol, (b) from chlorobenzene? What is picryl chloride?

EXPERIMENT 64

IDENTIFICATION OF AN UNKNOWN PHENOLIC COMPOUND

Obtain from the instructor an unknown phenolic compound (which will be one of those in the following table) and make two derivatives of it by the procedures given in Experiment 60. Also, determine whether a halogen is present by application of the Beilstein test (page 42). The unknown may be in the form of a pure substance or as a dilute water solution. In the later case, prepare only the benzoyl and bromine derivatives.

No attempt should be made to use phenyl isocyanate with a water solution since it reacts almost instantly with water to give diphenyl urea. (Remember that phenyl isocyanate is a powerful lachrymator. Keep it in the hood.)

The most probable identity of your unknown may be deduced from the melting points of its derivatives. Then obtain from the storeroom a known sample of this phenol and make its derivatives. The mixed melting point test applied to your known and unknown derivatives will prove the identity of your sample and you may make your report to the instructor.

UNKNOWN REPORT

	M.p. or B.p.	Presence of Halogen
Unknown		
Possibility 1		
Possibility 2		
Possibility 3		
Possibility 4		

MELTING POINTS OF DERIVATIVES

	Bromine	Benzoyl	Urethane	Ether
Unknown				
Possibility 1				
Possibility 2				
Possibility 3				
Possibility 4				

Conclusion:

TABLE 3. MELTING POINTS OF DERIVATIVES OF PHENOLIC COMPOUNDS

Phenol	Benzoyl Derivative	Ester with C_6H_5NCO	Bromine Derivative	2,4-Dinitrophenyl Ether
Phenol	70	126	96	71
o-Chlorophenol	b.p. 315	121	76	99
p-Chlorophenol	86	138	92	126
p-Bromophenol	102	144	96	137
2,4-Dichlorophenol	97	112	68	119
o-Cresol	b.p. 307	145	57	90
m-Cresol	54	122	82	74
p-Cresol	71	114	49	93
Guaiacol	56	136	94	128
p-Nitrophenol	142	123	141	114

[Begin Section 8 of Experiment 65.]

EXPERIMENT 65

Properties of Benzaldehyde

Introduction. Benzaldehyde has many properties that are analogous to those of aliphatic aldehydes, such as acetaldehyde, but it also has other properties in which it differs from most of its aliphatic counterparts. This latter type of behavior, in large part, centers around the fact that benzaldehyde—like formaldehyde, trimethylacetaldehyde, and other tertiary aldehydes—has no hydrogen atom on the *alpha* carbon. The following experiments illustrate several of these properties.

[Note: Section 8 of this experiment should have been started at the previous laboratory period.]

0-10 *1. Solubility.* Test the solubility of benzaldehyde in water, alcohol, and ether.

10-15 *2. Atmospheric Oxidation.* By means of a glass rod spread a drop of benzaldehyde into a thin film on a glass plate or watch glass. Examine the material at the end of the laboratory period or at the time of the next laboratory session. Result?

15-30 *3. Addition Product with Sodium Bisulfite.* Shake 1 ml. of benzaldehyde with 5 ml. of a saturated solution of sodium bisulfite for a few minutes and then cool the mixture in an ice bath. What is the crystalline product? Equation.

30-40 *4. Reaction with Phenylhydrazine.* Dissolve a few drops of benzaldehyde in 5 ml. of ethanol and add a few drops of phenylhydrazine. Result? Equation.

40-50 *5. Reaction with Ammonia.* Shake a few drops of benzaldehyde with 10 ml. of concentrated ammonium hydroxide solution, close the mouth of the test tube with a stopper, and examine the material an hour or two later. If no crystals of hydrobenzamide have formed, let the tube stand until the next laboratory period. Equation. Compare this behavior with the analogous reactions of ammonia with formaldehyde; with acetaldehyde.

50-70 *6. Condensation with Acetone.* To 20 ml. of ethanol contained in a small flask, add 2 ml. of acetone, 4 ml. of benzaldehyde, and 10 ml. of a 5 per cent solution of sodium hydroxide. Fit the flask with a reflux condenser (an air-condenser will serve) and boil the solution gently for 5 minutes. Cool the flask and collect the dibenzalacetone ($C_6H_5CH{=}CH{-}CO{-}CH{=}CHC_6H_5$) on a filter. When purified by recrystallization from ethanol, the crystals melt at 111°. The production of dibenzalacetone is often used for the identification of either acetone or benzaldehyde. Equation.

7. Reducing Action. Test the reducing power of benzaldehyde upon Tollens' reagent and Fehling's solution. Results? Compare with acetaldehyde. **70-80**

8. Auto-oxidation and Reduction (Cannizzaro Reaction). In a 100-ml. bottle, fitted with a cork stopper, shake 15 g. of benzaldehyde with a solution of 15 g. of sodium hydroxide in 12 ml. of water until a permanent emulsion is produced. Set the bottle aside until the next laboratory period. **80-110**

Add a sufficient quantity of water to dissolve the crystals of sodium benzoate which have separated and extract the benzyl alcohol by shaking the liquid twice with ether. About 25 ml. of ether should be used for each extraction.

Separate the ether layer from the alkaline solution (which is saved for isolation of the benzoic acid) and dry it over anhydrous sodium sulfate. Distill the ether from the water bath and then distill the residual benzyl alcohol with the direct flame of a Bunsen burner. Benzyl alcohol boils at 206°.

Obtain the benzoic acid by carefully acidifying the alkaline solution with hydrochloric acid. Remove the benzoic acid by filtration and purify it by recrystallization from hot water. Write the equation for the reaction involved in this experiment and calculate the percentage yield of each product.

QUESTIONS

1. Write equations to show how benzaldehyde may be prepared from

(a) benzyl chloride
(b) benzal chloride
(c) benzoic acid
(d) by a Friedel and Crafts reaction

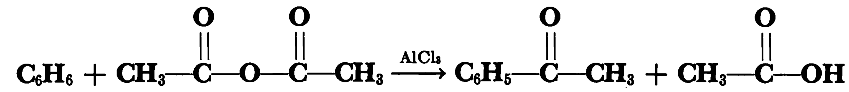
2. Show how sodium bisulfite may be used to purify benzaldehyde.

3. Write equations to show how benzaldehyde will react with the following reagents:

(a) hydroxylamine
(b) semicarbazide
(c) phosphorus pentachloride
(d) acetaldehyde (basic cat.)
(e) ethyl acetate (basic cat.)
(f) ethyl butyrate (basic cat.)
(g) phenylmagnesium bromide
(h) aniline

EXPERIMENT 66

Preparation of Acetophenone by a Friedel and Crafts Reaction



$$C_6H_6 + CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3 \xrightarrow{AlCl_3} C_6H_5-\overset{O}{\overset{\|}{C}}-CH_3 + CH_3-\overset{O}{\overset{\|}{C}}-OH$$

Introduction. A typical example of the Friedel and Crafts reaction, employing anhydrous aluminum chloride as the catalyst, ordinarily involves the reaction between an aromatic hydrocarbon and an active halogen compound. For the production of a ketone such as acetophenone, benzene may be allowed to react with acetyl chloride or, since acetyl chloride is rather too vigorous in its reactivity, the acid chloride may be replaced with the less active acetic anhydride.

The benzene used must be well dried over calcium chloride. The acetic anhydride should have a boiling range of 137°-140° to insure freedom from significant quantities of acetic acid. The anhydrous aluminum chloride should be in small lumps or in the form of a coarse powder, should fume in moist air, and should make a hissing sound upon the addition of a little water.

0-25

Procedure

Connect a 500-ml. flask to a reflux condenser, dropping funnel and one of the traps for absorption of escaping hydrogen chloride as shown in Figure 32. In the use of a trap such as types B or C in which water from the line is employed, care must be exercised in regulating the rate of flow to a small gentle stream. The pressure on the water line can easily force water into the trap faster than it will flow through the exit tube causing the water, if the flow is not properly regulated, to fill the trap and back up into the reaction flask where the presence of water may cause a vigorous (or even violent) reaction. Remember that all laboratory work requires care and thoughtfulness.

When the apparatus is assembled, disconnect the flask and put into it 40 g. of anhydrous aluminum 25-70 chloride and 65 ml. of dry benzene. (Weigh the aluminum chloride rapidly to avoid absorption of atmospheric moisture and be sure to replace the cap on the stock bottle.) Join the flask to the condenser and, during a period of about 10 minutes, add through the dropping funnel 20.4 g. (about 19.6 ml., 0.2 mole) of acetic anhydride. From time to time, loosen the clamp on the flask and shake the flask in order to mix the reactants thoroughly. If the heat of the reaction causes the benzene to boil, decrease the rate of addition of the acetic anhydride and, if necessary, bring a cooling bath up around the flask.

After all of the acetic anhydride has been added and the vigor of the reaction has diminished, heat the flask on the steam bath for 20 minutes. Then remove the steam bath, cool the flask in cold water, and pour its contents slowly into a 600-ml. beaker which contains 75 ml. of concentrated hydrochloric acid and about 150 g. of crushed ice.

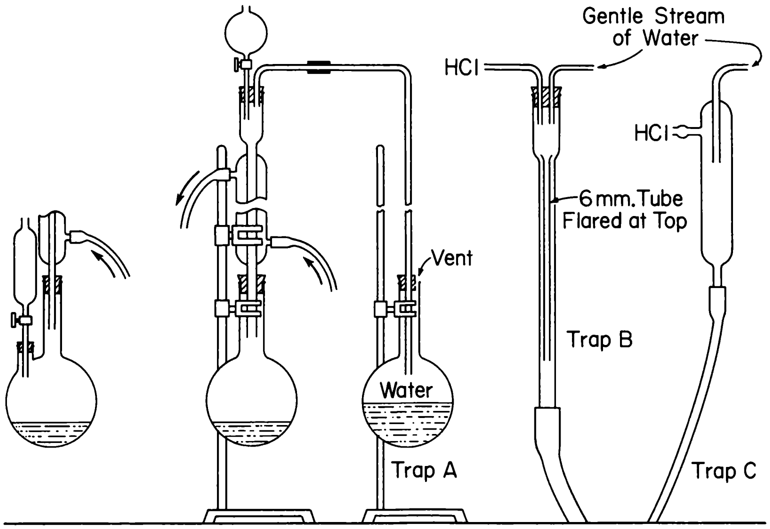


FIG. 32. Apparatus for a Friedel and Crafts reaction with absorption of escaping hydrogen chloride.

If any precipitate of basic aluminum salt remains after the mixture is well stirred, add enough hydrochloric acid to bring it into solution. The beaker now contains an acidic aqueous solution of aluminum chloride and an upper layer consisting of benzene and acetophenone.

70-140 By means of the separatory funnel remove the upper layer and extract the aqueous layer with 30-40 ml. of benzene. Combine the two benzene solutions and wash them once with dilute sodium hydroxide solution and then with water. Dry the solution of benzene and acetophenone over magnesium sulfate, decant from the drying agent and distill the liquid.

Benzene (b.p. 80°) does not distill rapidly from the steam bath but, with reasonable care, may be distilled with the aid of the burner. (Some laboratories have special arrangements for the distillation of benzene. If so, the instructor will give the necessary directions.) The acetophenone boils at 202°. Yield 16-20 g.

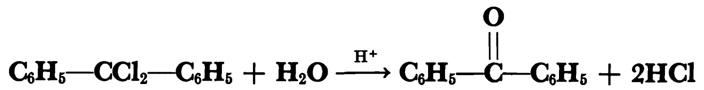
QUESTIONS

See questions following Experiment 67.

EXPERIMENT 67

Preparation of Benzophenone by a Friedel and Crafts Reaction

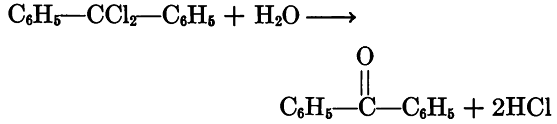
(1) $$2C_6H_6 + CCl_4 \xrightarrow{AlCl_3} C_6H_5\text{—}CCl_2\text{—}C_6H_5 + 2HCl$$

(2)

$$C_6H_5\text{—}CCl_2\text{—}C_6H_5 + H_2O \xrightarrow{H^+} C_6H_5\text{—}\overset{\overset{\displaystyle O}{\|}}{C}\text{—}C_6H_5 + 2HCl$$

Introduction. The reaction between benzene and carbon tetrachloride, in the presence of anhydrous aluminum chloride, may proceed in three stages as shown in equations I, II, and III.

I. $C_6H_6 + CCl_4 \xrightarrow{AlCl_3} C_6H_5CCl_3 + HCl$

II. $C_6H_5CCl_3 + C_6H_6 \xrightarrow{AlCl_3} C_6H_5\text{—}CCl_2\text{—}C_6H_5 + HCl$

IIA.

$$C_6H_5\text{—}CCl_2\text{—}C_6H_5 + H_2O \longrightarrow C_6H_5\text{—}\overset{\overset{\displaystyle O}{\|}}{C}\text{—}C_6H_5 + 2HCl$$

III. $(C_6H_5)_2CCl_2 + C_6H_6 \xrightarrow{AlCl_3} (C_6H_5)_3CCl + HCl$

Under ordinary conditions it is difficult to stop the reaction at the completion of the first stage (equation I) but the process may be terminated conveniently at the end of the second or third stage by control of the quantity of benzene used. If an excess of benzene is avoided, as is true in today's experiment, the production of diphenyldichloromethane, commonly called benzophenone dichloride (equation II), may be easily achieved. Hydrolysis of the dichloride (equation II A) provides a convenient method for the preparation of benzophenone.

[Note: Both the carbon tetrachloride and benzene used for this experiment must have been dried previously over calcium chloride for several hours.]

Procedure

0-25 A dry 500-ml. flask is fitted with a dry reflux condenser, dropping funnel, and trap for the absorption of escaping hydrogen chloride as shown in Figure 32. The trap may be any of those illustrated. (CAUTION: If trap B or C is used, be sure that the flow of water is regulated so that water cannot be sucked back into the reaction flask, because water will react with the anhydrous aluminum chloride in a violent manner.)

Into the flask place 35 g. of anhydrous aluminum chloride and 50 ml. of dry carbon tetrachloride. Pour a solution of 30 ml. of dry carbon tetrachloride and
25-65 30 ml. of dry benzene into the dropping funnel. Allow 5-10 ml. of the benzene–carbon tetrachloride solution to run into the reaction flask and shake the flask gently (loosen the clamp momentarily, if necessary) in order to mix the reactants.

If the reaction does not begin with evolution of hydrogen chloride within 2 minutes, warm the flask gently with the Bunsen burner. Once the reaction has started, add more of the benzene–carbon tetrachloride solution at intervals of a few minutes in order to maintain a gentle and continuous evolution of hydrogen chloride.

The temperature of the reaction flask should be at 30°-40°; i.e., just perceptibly warm to the hand. If the temperature rises above this point, cool the flask by bringing a pan of cold water up around it. About 15 minutes will be required for the addition of all of the reactants. Thereafter heat the flask on the steam bath, or in a pan of hot water, for 20 minutes in order to bring the formation of benzophenone dichloride nearly to completion.

The next step is the removal of the anhydrous aluminum chloride by addition of water. **65-85** Anhydrous aluminum chloride reacts with water so vigorously that the water must be added to the cooled reaction mixture in small portions. Therefore, replace the steam bath by a bath of ice and water and pour 50 ml. of water into the dropping funnel. Allow the water to drop slowly into the flask and shake the flask frequently by removing the cooling bath momentarily and also loosening the clamp.

The heat of hydration of the aluminum chloride may cause the carbon tetrachloride to boil gently. When all of the water has been added and the exothermic hydrolysis process has been completed, transfer all the material to a larger flask for steam distillation (Note 1).

Distillation with steam not only removes the excess **85-130** carbon tetrachloride and any remaining benzene but also accomplishes the hydrolysis of benzophenone dichloride to benzophenone as shown in equation IIA. Although the benzene and carbon tetrachloride are removed rapidly, the steam distillation should extend over a period of 45-50 minutes for completion of the hydrolysis of the dichloride to the ketone (Note 1).

The flask is then cooled and the contents poured **130-170** into a large separatory funnel where the upper layer of benzophenone is separated. The aqueous layer is returned to the separatory funnel for the extraction of any remaining benzophenone with 25-30 ml. of benzene. The benzene extract is combined with the main portion of benzophenone and the resulting solution dried over magnesium sulfate, separated from the drying agent, and distilled.

After removal of the benzene, the residual benzophenone may be distilled at atmospheric pressure, although distillation under diminished pressure is to be preferred (see Figure 28, page 102). Its boiling point is 305.9° at 760 mm., and 185° at 15 mm. Yield 20-25 g.

On cooling, the benzophenone usually solidifies to the stable rhombic crystalline form (called the α form) melting at 48.1°. There are two other modifications, known as β and γ, which melt at 26.5° and 45.8°, respectively. If your specimen does not solidify on cooling, add a crystal of the stable rhombic form and allow the material to stand.

NOTE

1. If the preparation cannot be completed in one laboratory period, the mouth of the flask may be closed tightly with a stopper and set aside at either of these points.

QUESTIONS

1. What ketone will be produced in reactions of the Friedel-Crafts type by the following pairs of reactants?
   (a) benzene and benzoyl chloride
   (b) benzene and *p*-bromobenzoyl chloride
   (c) bromobenzene and acetic anhydride
   (d) toluene and *p*-nitrobenzoyl chloride

2. Which of the following alcohols or ketones will give the haloform reaction?

(a) $C_6H_5—CO—C_6H_5$ (b) *p*-$CH_3C_6H_4—CO—C_6H_5$

(c) $C_6H_5—CO—CH_3$ (d) $CH_3O—C_6H_4—CO—CH_3$

(e) $C_6H_5—CH_2—CH_2OH$ (f) $C_6H_5—CHOH—CH_3$

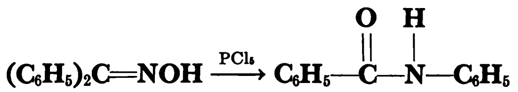
3. Is benzophenone dichloride hydrolyzed relatively easily or difficultly? How can you account for its behavior on the basis of its structure?

EXPERIMENT 68

Benzophenone Oxime and Its Rearrangement to Benzanilide

(1) $(C_6H_5)_2C{=}O + H_2NOH \longrightarrow (C_6H_5)_2C{=}NOH + H_2O$

(2)



$$(C_6H_5)_2C{=}NOH \xrightarrow{PCl_5} C_6H_5{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}\overset{\overset{\displaystyle H}{|}}{N}{-}C_6H_5$$

I. Preparation of the Oxime

0-70 To a solution of 5.4 g. (0.03 mole) of benzophenone and 6 g. of hydroxylamine hydrochloride in 75 ml. of ethanol contained in a 500-ml. flask, add a solution of 10 g. of sodium hydroxide in 50 ml. of water. Attach the flask to a reflux condenser and boil the solution gently for 40 minutes. Remove the flask from the condenser, add 300 ml. of cold water, and remove any unchanged benzophenone by filtration. Add a few lumps of ice to the filtrate and acidify it with dilute sulfuric acid to precipitate the benzophenone oxime.

Collect the oxime on a Büchner filter, press it as dry as possible, spread it into a thin layer so that it will dry quickly, and place it in an oven at 70°-80°. The dry oxime, of which the yield is about 5 g., will be needed in Part II of this experiment. Recrystallize a small portion of the product from ethanol and determine its melting point. The recorded melting point is 141°.

70-75 Test the solubility of benzophenone oxime in dilute sodium hydroxide solution. If it dissolves, acidify the solution with hydrochloric acid. Is there a precipitate?

II. Beckmann Rearrangement of a Ketoxime

75-150 The phosphorus pentachloride used in this experiment should be weighed as rapidly as possible because of the irritating odor and also because of its reaction with moisture of the air. Weigh 5 g. of the phosphorus pentachloride from the bottle in the hood and enclose the 5-g. portion in a glass-stoppered weighing bottle such as is used in quantitative analysis.

In a small flask dissolve 4.0 g. of benzophenone oxime in 50 ml. of absolute ethyl ether (previously dried over sodium). Cool the flask in an ice bath and add about 1 g. of the phosphorus pentachloride. When the heat of reaction subsides add another small portion of the phosphorus pentachloride and continue in this manner until all of the material has been added.

Mix the reactants well with a glass rod, remove most of the ether by heating the flask on the steam bath, and pour the residue onto a little crushed ice contained in a mortar. Grind the lumps to a powder under water and collect the solid benzanilide on a filter. Wash it with water and recrystallize it from alcohol. Yield about 3 g. M.p. 161°.

QUESTIONS

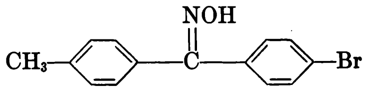
1. Are oximes soluble in dilute alkali? Cf. acetoxime, page 72, and dimethylglyoxime, page 75.

2. Write formulas to represent the *syn* and *anti* forms of benzaldoxime. Show how one may be distinguished from the other.

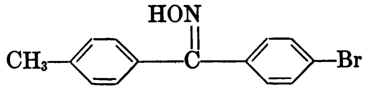
3. May benzophenone oxime exist as *syn* and *anti* isomers?

4. Name and show the structures of the substituted amides obtained by the Beckmann rearrangement of the following oximes:

a.

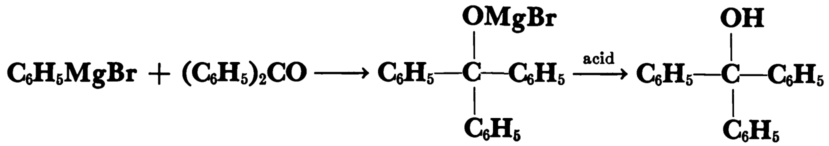


b.



EXPERIMENT 69

Preparation of Triphenylcarbinol by a Grignard Reaction



$$C_6H_5MgBr + (C_6H_5)_2CO \longrightarrow C_6H_5-\overset{OMgBr}{\underset{C_6H_5}{C}}-C_6H_5 \xrightarrow{acid} C_6H_5-\overset{OH}{\underset{C_6H_5}{C}}-C_6H_5$$

Introduction. Grignard reagents react with ketones to form tertiary alcohols. In the present experiment phenylmagnesium bromide and benzophenone (diphenyl ketone) are used for the preparation of triphenylcarbinol. The absolute ether used in the process is prepared as described on page 46.

0-60 *Preparation of the Grignard Reagent.* Attach a 500-ml. flask to a water-jacketed reflux condenser and fit the top of the condenser with a stopper and dropping funnel. Also file a rather deep groove in the stopper at the top of the condenser to serve as an air vent.

Into the distilling flask put 2.4 g. (0.1 g. atomic wt.) of clean magnesium turnings and add 50 ml. of absolute ether. Pour 15.7 g. (0.1 mole) of dry bromobenzene (or 0.1 mole of iodobenzene) and 50 ml. of dry ether into the dropping funnel. Allow about 10 ml. of the solution in the dropping funnel to run into the flask and wait for the reaction to begin.

If the reaction does not begin within a few minutes, add a crystal of iodine. If this fails, warm the flask gently in warm water.

When the reaction has begun, the remainder of the solution in the dropping funnel is added at such a rate that the heat of reaction causes vigorous refluxing of the ether. After all of the bromobenzene solution has been added, heat the flask in a bath of warm water at 40°-50° for 20-30 minutes, during which time practically all of the magnesium dissolves. The ether should boil steadily but not so rapidly that ether vapor escapes from the top of the condenser.

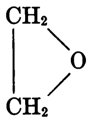
60-110 *Condensation of the Grignard Reagent with Benzophenone.* Remove the flask from the bath of warm water and cool it to 10°-15° in cold water. Through the dropping funnel at the top of the condenser slowly add, with constant shaking of the reaction flask, a solution of 18.2 g. (0.1 mole) of benzophenone in 50 ml. of dry benzene. Allow the mixture to stand at room temperature for 5 minutes and then heat it on the water bath for 20 minutes to bring the reaction nearly to completion. After cooling, pour the contents of the flask onto 100 g. of ice, stirring well during the addition, and add 15 ml. of concentrated hydrochloric acid to dissolve the basic magnesium bromide.

110-170 Return the material to the round-bottomed flask and distill as much of the ether and benzene as is possible on the steam bath. Then subject the residue to distillation with steam in order to remove the biphenyl and unchanged bromobenzene. (Write the equation for the side reaction by which biphenyl might be formed.) During the steam distillation the triphenylcarbinol usually solidifies. Cool the distillation flask and collect the triphenylcarbinol on a filter. For purification, dissolve the crude product in hot alcohol (see page 94) and cool the solution in ice until crystallization is complete. The yield is 12-15 g. M.p. 164°.

QUESTIONS

1. Write equations to show the products that are obtainable by the reaction of phenylmagnesium bromide with each of the following reagents. (Note: It is to be understood that at the end of the main reaction dilute acid may be added for liberation of the final product.)

(a) H_2O
(b) C_2H_5OH
(c) NH_3
(d) $(C_2H_5)_2NH$
(e) $HCHO$
(f) CH_3CHO
(g) C_6H_5CHO
(h) CH_3COCH_3
(i) $HCOOC_2H_5$
(j) $CH_3COOC_2H_5$
(k) $C_6H_5COOC_2H_5$
(l)



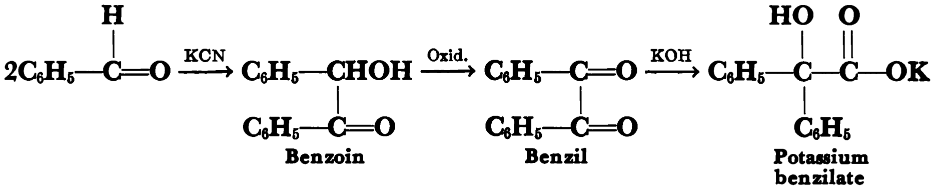
2. From the list of reagents given in question 1, select the one (or more than one) that converts a Grignard reagent, RMgX, into

(a) the hydrocarbon, RH
(b) the primary alcohol, RCH_2OH
(c) the secondary alcohol, $RCHOHR'$
(d) the tertiary alcohol, $RC(OH)(R')R''$
(e) the aldehyde, RCHO
(f) the ketone, RCOR
(g) the primary alcohol, RCH_2CH_2OH

3. Explain the role of ether in the formation of the Grignard reagent.

EXPERIMENT 70

Benzoin, Benzil, and Benzilic Acid



$$2C_6H_5-\overset{H}{\overset{|}{C}}{=}O \xrightarrow{KCN} \underset{C_6H_5-C=O}{\underset{|}{C_6H_5-CHOH}} \xrightarrow{Oxid.} \underset{C_6H_5-C=O}{\underset{|}{C_6H_5-C=O}} \xrightarrow{KOH} C_6H_5-\overset{HO}{\overset{|}{\underset{|}{\underset{C_6H_5}{C}}}}-\overset{O}{\overset{\|}{C}}-OK$$

Introduction. When benzaldehyde is boiled in alcoholic solution with a little potassium cyanide as catalyst, two molecules of benzaldehyde condense to give one molecule of benzoin. Oxidation of benzoin yields benzil (one of the most common α-diketones) which, in turn, undergoes molecular rearrangement in alkaline solution to give a salt of benzilic acid.

0-55 I. The Preparation of Benzoin

In a 250-ml. flask place 10.6 g. (0.1 mole, 10.1 ml.) of benzaldehyde, 35 ml. of ethanol and 1.5 g. of potassium cyanide. (Handle the cyanide with care.) Attach the flask to a water-cooled reflux condenser the top of which is fitted with an absorption trap to prevent the possibility of any hydrogen cyanide escaping into the room. (The reaction liberates no hydrocyanic acid but it is wise to make certain that none can escape.)

A trap such as type B shown in Figure 32 is convenient, or as an alternative effective measure, any escaping gas may be led over the surface of 10 per cent sodium hydroxide solution contained in an absorption bottle. Boil the solution of reactants gently for 40 minutes and then set the flask in a bath of ice and water for crystallization of the benzoin.

[During this 40-minute interval give your attention to the questions at the end of this experiment.]

The nearly solid mass of crystals of benzoin in the flask is transferred onto a Büchner funnel and any material remaining in the flask washed into the funnel with 100-150 ml. of water. Remove as much water as possible from the crystals by suction and rinse the crystals of benzoin, first, with a little cold alcohol and then with 10 ml. of ether. When spread on a clean sheet of paper the benzoin will dry quickly in the air. For oxidation to benzil the product need not be recrystallized. Yield 7-8 g.

[After Part II is underway, perform the following tests with a small portion of benzoin that has been reserved for this purpose.]

Recrystallization. Recrystallize a small portion of the benzoin from hot alcohol for observation of its melting point.

Reaction with Fehling's Solution. Dissolve 0.5 g. of benzoin in a little ethanol and warm the solution with 10 ml. of Fehling's solution (5 ml. each of Solutions A and B). Result? The benzoin is oxidized to benzil. Note that benzoin and fructose are related in molecular structure since each contains the —CO—CHOH— grouping.

II. Oxidation of Benzoin to Benzil 55-85

Place 6 g. benzoin in a small flask and add 20 ml. of concentrated nitric acid (D = 1.42). Connect the flask to a trap to absorb oxides of nitrogen (Figure 33) and heat the flask in boiling water, or on the steam bath, for 10-12 minutes. The evolution of brown fumes, very rapid at first, becomes much slower after the first five minutes of heating. After the flask has been in the boiling water for 10-12 minutes, disconnect the delivery tube, cool the flask in a bath of ice and water, and pour the contents into 150 ml. of water containing a few small pieces of ice. Stir the mixture well and break up with a spatula any lumps of benzil in order to wash out the nitric acid.

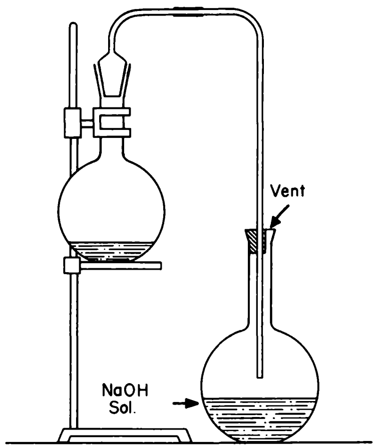


Fig. 33. An assembly suitable for the oxidation of benzoin to benzil.

Bring the yellow crystalline benzil onto the Büchner funnel and wash it with a little water. Shut off the suction pump and stir the benzil gently on the filter with a little cold alcohol. Suck the alcohol through the filter and spread the benzil onto a sheet of paper to dry for a few minutes in the air. (CAUTION: Do not attempt to obtain rapid drying of the benzil by washing the product with ether because much benzil will be lost due to its ready solubility in ether.) Yield 5 g.

85-120 III. Rearrangement of Benzil to Benzilic Acid

In a small flask place 4 g. of benzil, 5 g. of potassium hydroxide, 10 ml. of ethanol, and 10 ml. of water. Attach a reflux condenser and heat the contents of the flask to boiling for 15 minutes. Pour the hot liquid into a 250-ml. beaker and add 100 ml. of water. A little unchanged benzil usually separates at this point in the form of a colloidal suspension. As an aid in removing the residual benzil, add 1 g. of decolorizing carbon, stir well, and filter the liquid to remove the carbon.

Precipitate the benzilic acid from the filtrate in the following manner: place 50-75 g. of crushed ice into a 400-ml. beaker and add 15 ml. of concentrated hydrochloric acid. Now add to the ice and acid 10-15 ml. of the solution of potassium benzilate and stir the mixture until the benzilic acid which sometimes separates in colloidal form becomes crystalline. Then gradually, with continuous stirring, add the remainder of the potassium benzilate solution. Finally collect the benzilic acid on the Büchner filter. Yield about 3 g. After recrystallization from boiling water, it melts at 150°.

QUESTIONS

1. Write formulas for the following compounds:

(a) hydrobenzoin (b) desoxybenzoin
(c) benzilmonoxime (d) benzildioxime

2. Does hydrobenzoin have a structural relationship to ethylene glycol?

3. May desoxybenzoin be named easily as a ketone?

4. Write formulas for the geometrical isomers that you would consider possible for (a) benzilmonoxime, (b) benzildioxime.

5. Write a balanced equation for the oxidation of benzoin to benzil with concentrated nitric acid.

6. If benzoin is produced from benzaldehyde in 92 per cent yield, and if benzil is produced from benzoin in 96 per cent yield, what weight of benzaldehyde would be needed to prepare one mole of benzil?

7. What is the mechanism of the benzoin condensation? Why is the cyanide ion a specific catalyst for the reaction?

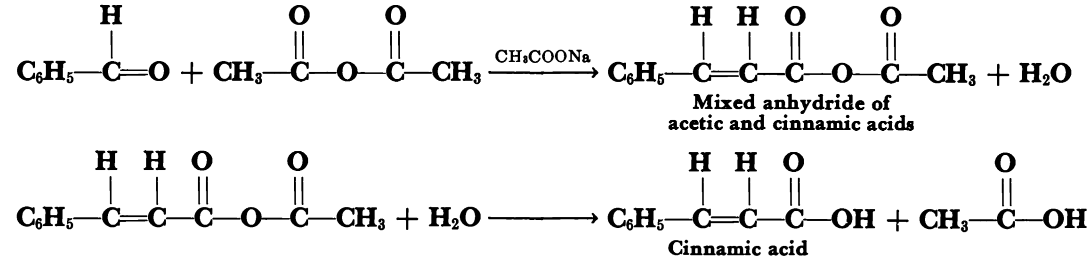
8. How may benzoin be degraded to a mixture of benzaldehyde and benzonitrile? Would this degradation reaction be of any use in establishing the structures of mixed benzoins?

9. How may p'-methylbenzoin be prepared? How may it be isomerized to p-methylbenzoin?

10. Write structural formulas for furoin and furil. How may these compounds be prepared?

EXPERIMENT 71

Preparation of Cinnamic Acid—the Perkin Reaction



(1) $$C_6H_5-\overset{H}{\overset{|}{C}}=O + CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3 \xrightarrow{CH_3COONa} C_6H_5-\overset{H}{\overset{|}{C}}=\overset{H}{\overset{|}{C}}-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3 + H_2O$$

Mixed anhydride of acetic and cinnamic acids

(2) $$C_6H_5-\overset{H}{\overset{|}{C}}=\overset{H}{\overset{|}{C}}-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3 + H_2O \longrightarrow C_6H_5-\overset{H}{\overset{|}{C}}=\overset{H}{\overset{|}{C}}-\overset{O}{\overset{\|}{C}}-OH + CH_3-\overset{O}{\overset{\|}{C}}-OH$$

Cinnamic acid

Introduction. The Perkin reaction is one of the many base-catalyzed condensation reactions which are encountered in the study of organic chemistry. The present experiment, in which benzaldehyde is condensed with acetic anhydride under the influence of sodium acetate (actually the acetate ion) as the basic catalyst, is a typical example of this reaction.

The reacting materials must be heated in a bath at 170°-180° for 6-8 hours. Such a long period of heating, though necessary, is inconvenient for laboratory classes. The authors recommend that the reaction be conducted in a large tube fitted with a stopper and an air-condenser and that the collected lot of tubes from all members of the class be heated at one time in a large paraffin bath such as that illustrated in Figure 31, page 139. If the tubes are placed in the bath at one laboratory session, the bath may then be heated by volunteers working in relays so that the reaction is complete and the product ready for isolation at the next laboratory session.

Procedure

In a large test tube, or small flask, place 10.6 g. (0.1 mole, 10.1 ml.) of benzaldehyde, 11 ml. (slight excess of 0.1 mole) of acetic anhydride, 12 g. of fused powdered sodium acetate, and 1 ml. of pyridine which has been shown to be a catalyst for this reaction. After mixing the reactants well with a glass rod, attach an air-cooled reflux condenser and heat the tube in a bath of molten paraffin wax at 140°-150° for 2 hours. Thereafter raise the temperature of the bath to 170°-180° and maintain this temperature for 4-5 hours.

At the end of the heating period allow the tube to cool and, with the aid of 200-250 ml. of water, transfer the contents of the tube to a 1000-ml. flask for removal of unchanged benzaldehyde by steam distillation. After the excess benzaldehyde has been eliminated (125-150 ml. of distillate), make the contents of the distilling flask alkaline with sodium hydroxide solution and shake the flask well to dissolve any cinnamic acid that may be present as an oil.

Filter the hot solution from any tarry matter, cool the filtrate in ice, and precipitate the cinnamic acid by addition of hydrochloric acid. Collect the cinnamic acid on the Büchner filter and recrystallize it from 800-1000 ml. of boiling water. Yield 9 g. M.p. 133°.

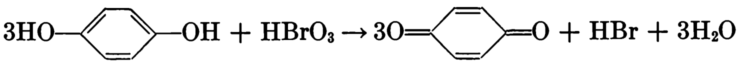
QUESTIONS

1. Write formulas for the following substances: (a) *cis*-cinnamic acid, (b) *trans*-cinnamic acid, (c) ethyl cinnamate.
2. Write equations to show the base-catalyzed condensation of benzaldehyde with the following reagents: (a) *n*-butyric anhydride (with sodium butyrate), (b) acetophenone, (c) ethyl *n*-butyrate.
3. Starting from phenol show how one may prepare salicylaldehyde and how, by a reaction of the Perkin type, this aldehyde may be used for the production of coumarin.
4. From cinnamic acid, show how one may prepare: (a) styrene, (b) dihydrocinnamic acid, (c) cinnamoyl chloride.
5. Ten grams of cinnamic acid will add what weight of bromine?
6. Write equations to show how ethyl malonate may be used for the preparation of dihydrocinnamic acid.

EXPERIMENT 72

Quinones

I. PREPARATION OF *p*-BENZOQUINONE



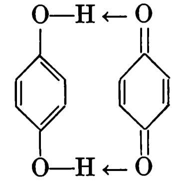
Introduction. One of the most convenient methods for the preparation of a small sample of *p*-benzoquinone consists of the oxidation of hydroquinone. Various oxidizing agents may be employed; the one selected for today's experiment is bromic acid.

0-40 *Procedure.* A mixture of 10 g. of hydroquinone, 5.5 g. of potassium bromate, 100 ml. of water, and 5 ml. of normal sulfuric acid (Note 1) is warmed to 60° in a 200-ml. flask. The solids dissolve and the reaction starts promptly giving first nearly black, crystalline quinhydrone as an intermediate product. Without further heating, the temperature rises slowly to about 75°. After 10-15 minutes the oxidation is complete, the dark color giving way to the clear bright yellow of quinone (Note 2).

The mixture is then heated to 80° to dissolve the quinone completely, next cooled to 0°, filtered, and washed free of potassium bromide with a little ice water and dried. The yield is nearly quantitative and the quinone is crystalline and exceptionally pure. M.p. 115°. Quinone has a quite noticeable vapor pressure at room temperature, hence it should be dried as quickly as possible, to avoid loss by volatilization, and transferred to a stoppered bottle.

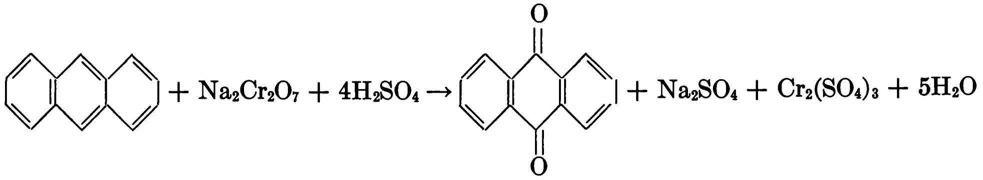
II. QUINHYDRONE 40-50

Shake about 0.5 g. of quinone with 10 ml. of water and add a solution of 0.5 g. of hydroquinone in 10-15 ml. of water. The greenish-black crystals of quinhydrone are formed by an addition reaction between the two original compounds, supposedly by hydrogen bonding.



In electrochemistry the quinhydrone electrode is used in the measurement of hydrogen ion concentration.

III. ANTHRAQUINONE



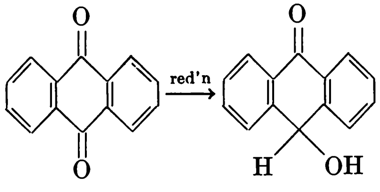
9,10-Anthraquinone

In striking contrast to benzene or naphthalene, anthracene may be directly oxidized to a quinone. Into 50-120 a 500-ml. flask fitted with a short reflux condenser place 5 g. of a good grade of anthracene and 50 ml. of glacial acetic acid. Heat the solution to the boiling point with the Bunsen burner and, during the course of 10-12 minutes, add dropwise from a dropping funnel mounted on a ring at the top of the condenser, a solution of 13 g. of sodium dichromate, 15 ml. of water, 5 ml. of concentrated sulfuric acid, and 35 ml. of glacial acetic acid. Keep the solution at the boiling point during the addition of the dichromate solution and maintain this temperature for 10 minutes after all of the oxidizing agent has been added. Extinguish the burner and allow the flask to stand without the external application of heat for 20 minutes.

At the end of this period cool the flask in cold water to bring about crystallization of the anthraquinone. Collect the crystals on a small Büchner or Hirsch funnel and wash them twice with 20 ml. of a 30 per cent solution of acetic acid. Finally, wash the crystals with a little water and spread them upon a sheet of paper to dry in the air. The yield is about 5 g.

Recrystallize a small portion of the anthraquinone from alcohol and determine its melting point. The recorded melting point is 273°. Anthraquinone may also be purified readily by sublimation.

Reduction to Oxanthranol. Boil a trace of anthra- 120-135
quinone for 1 minute with a little zinc dust and 10 ml. of 3 per cent sodium hydroxide solution. Filter the solution and blow air through it. Anthraquinone is reduced by the zinc to oxanthranol which forms a red solution in alkali and which is easily reoxidized to anthraqui-



none. The preceding test is frequently used for the identification of anthraquinone.

NOTES

1. A normal solution of sulfuric acid of sufficient accuracy for this purpose may be made by adding 3 ml. of concentrated sulfuric acid ($D = 1.84$) to 100 ml. of water.

2. If too much sulfuric acid is used the temperature of the reacting mixture rises to 80° or 85°, the oxidation is complete in 1 or 2 minutes, and the sample of quinone has an orange color due to the liberation of free bromine ($HBrO_3 + 5HBr \rightarrow 3Br_2 + 3H_2O$).

QUESTIONS

1. What advantage does bromic acid possess as an oxidizing agent?
2. Compare the melting point and volatility of quinone with the corresponding properties of hydroquinone. How do you account for the differences?
3. Write the formula for vitamin K_1.

EXPERIMENT 73

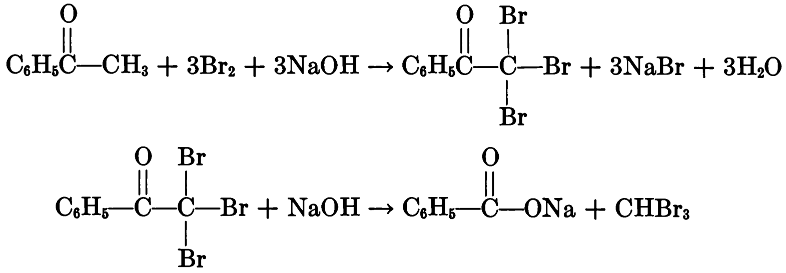
Benzoic Acid

I. Preparation of Benzoic Acid from Benzyl Chloride

$$C_6H_5CH_2Cl + Na_2CO_3 + H_2O \rightarrow C_6H_5CH_2OH + NaHCO_3 + NaCl$$

$$3C_6H_5CH_2OH + 4KMnO_4 + \rightarrow 3C_6H_5COOK + 4MnO_2 + KOH + 4H_2O$$

II. Preparation of Benzoic Acid and Bromoform by the Haloform Reaction



$$C_6H_5\overset{\overset{\displaystyle O}{\|}}{C}—CH_3 + 3Br_2 + 3NaOH \rightarrow C_6H_5\overset{\overset{\displaystyle O}{\|}}{C}—\overset{\overset{\displaystyle Br}{|}}{\underset{\underset{\displaystyle Br}{|}}{C}}—Br + 3NaBr + 3H_2O$$

$$C_6H_5—\overset{\overset{\displaystyle O}{\|}}{C}—\overset{\overset{\displaystyle Br}{|}}{\underset{\underset{\displaystyle Br}{|}}{C}}—Br + NaOH \rightarrow C_6H_5—\overset{\overset{\displaystyle O}{\|}}{C}—ONa + CHBr_3$$

I. Benzoic Acid from Benzyl Chloride

0-20 *Introduction.* The direct oxidation of toluene to benzoic acid is slow by most laboratory procedures; hence, benzyl chloride is a more convenient starting material as it is hydrolyzable to benzyl alcohol which undergoes oxidation rapidly.

Procedure. In a 500-ml. flask place 8 g. of anhydrous sodium carbonate and 12 g. of potassium permanganate with 200 ml. of water. Add 6.3 g. (5.8 ml., 0.05 mole) of benzyl chloride, fit the flask with a reflux condenser, and boil the mixture for 1 hour. (Note: Benzyl chloride is irritating to the eyes. Measure the needed quantity with a small graduated cylinder from the supply bottle which is kept in the hood.)

The brown precipitate of manganese dioxide, which gradually accumulates in the flask, sometimes settles to the bottom where it causes excessive bumping. Usually this trouble can be overcome by shaking the flask frequently. Continue boiling the mixture for 50-60 minutes while you prepare another specimen of benzoic acid from acetophenone by the haloform reaction as outlined in Part II.

80-130 Disconnect the flask from the condenser and remove it to the hood where the precipitate of manganese dioxide is removed by filtration through a large sheet of fluted filter paper. Rinse the precipitate with 50 ml. of hot water and combine the washings with the main portion. Chill the filtrate, containing the potassium benzoate, to 20° or lower in a bath of ice and water and acidify the solution with dilute sulfuric acid. Collect the precipitate of benzoic acid, which may be colored somewhat by unchanged permanganate, on a Büchner funnel and recrystallize it from hot water. The solubility of benzoic acid in water: At 0° = 1.7 g./liter; at 20° = 2.9 g./liter; at 50° = 9.5 g./liter; at 95° = 68.9 g./liter. Weigh your product and calculate the yield. Pure benzoic acid melts at 122°.

II. The Haloform Reaction

Introduction. It will be recalled that ketones in which one group is methyl show the haloform reaction (cf. acetone, page 77). In the present experiment acetophenone (phenyl methyl ketone) yields bromoform and benzoic acid as shown in the equations:

Procedure. Prepare a solution of bromine in sodium hydroxide as follows: In a 250-ml. flask dissolve 4 g. of sodium hydroxide in 50 ml. of water, add about 50 g. of crushed ice, then introduce 2 ml. of bromine and shake the flask until the bromine dissolves. (Bromine is always handled in the hood. Ask the instructor about local laboratory provisions for dispensing this reagent.) Add 2 ml. of acetophenone and shake the flask well for 6-8 minutes. Note that heat is evolved and that about 1 ml. of liquid bromoform settles to the bottom of the flask. **20-80**

Transfer the contents of the flask to a separatory funnel, withdraw the small lower layer of bromoform and give it to the instructor—the combined lot from all members of the class may be worth saving. The solution of sodium benzoate in the separatory funnel is turbid due to the presence of suspended droplets of bromoform. Pour the liquid into a beaker, stir it with 1 g. of decolorizing carbon which collects the particles of bromoform, and then remove the carbon by filtration. Add a little ice to the filtrate and acidify it with dilute sulfuric acid.

Usually the solution acquires a yellow or orange color at this point due to the presence of a slight excess of bromine. This is removed by the addition of a little sodium bisulfite and the white precipitate of benzoic acid is collected on a filter. Yield about 1 g. After recrystallization from 15-20 ml. of boiling water, benzoic acid melts at 122°.

QUESTIONS

1. The concentration of a saturated solution of benzoic acid at 25° is approximately 0.03 *M*. The ionization constant (K_A) of benzoic acid at 25° is 6.4×10^{-5}. Calculate (a) the hydrogen ion concentration in the solution, (b) the *p*H of the solution and (c) the pK_A value for benzoic acid.

2. Write equations showing how benzoic acid may be converted into the following derivatives:

(a) calcium benzoate
(b) ethyl benzoate
(c) benzoyl chloride
(d) benzanilide
(e) benzamide
(f) benzoyl peroxide
(g) *m*-nitrobenzoic acid
(h) *m*-bromobenzoic acid

3. What products may be obtained by the strong oxidation (as with $Na_2Cr_2O_7$ and H_2SO_4) of the following compounds?

(a) $C_6H_5CH_3$
(b) $C_6H_5CH_2CH_3$
(c) $C_6H_5CH(CH_3)_2$
(d) $C_6H_5CH{=}CH_2$
(e) $C_6H_5CH{=}CHC_6H_5$
(f) $C_6H_5CHClCH_3$
(g) $C_6H_5COCH_3$
(h) $C_6H_5COC_2H_5$
(i) $C_6H_5CHOHCOOH$

4. Which of the following compounds will give the haloform reaction?

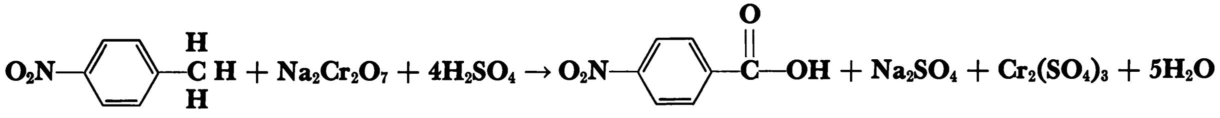
(a) $C_6H_5CCl_3$
(b) $C_6H_5CHOHCH_3$
(c) $C_6H_5COCH_3$
(d) $C_6H_5CH_2COCH_3$
(e) $C_6H_5CH_2CHOHCH_3$
(f) $C_6H_5CHOHCH_2CH_3$

5. (a) What volume (in ml.) of normal base solution will be required for the neutralization of 1 g. of benzoic acid? (b) Calculate the neutralization equivalent (its equivalent weight as determined by neutralization with a standardized solution of base) of benzoic acid.

6. What is the neutralization equivalent of an acid (a) if 1 g. requires 16.67 ml. of normal base; (b) if 1 g. of acid requires 12.05 ml. of normal base?

EXPERIMENT 74

Oxidation of *p*-Nitrotoluene to *p*-Nitrobenzoic Acid



Introduction. The direct oxidation of toluene to benzoic acid occurs so slowly with the usual laboratory reagents that the experiment is not easily adaptable to use in laboratory classes where time is limited. The introduction of a *para* nitro group, however, causes the oxidation of the methyl group to proceed readily; hence, *p*-nitrotoluene is easily oxidized to *p*-nitrobenzoic acid.

At this juncture a review of the chemistry of several series of aromatic compounds will be helpful. Such a review is provided by the *Questions* at the end of the experiment.

0-60 *Procedure*. In a 2-liter flask, fitted with a mechanical stirrer, are placed 60 g. of sodium dichromate, 150 ml. of water, and 20.5 g. (0.15 mole) of *p*-nitrotoluene. The stirrer is started and 95 ml. of concentrated sulfuric acid is added dropwise from a dropping funnel during the course of 10 minutes. The heat of dilution of the sulfuric acid causes the *p*-nitrotoluene to melt and a highly exothermic reaction soon begins. It will be necessary to cool the flask at this point if the contents begin to boil.

When the spontaneous reaction has subsided the flask is heated on the steam bath for 30 minutes or in a pan of boiling water for 1 hour with continuous stirring. The mixture is then cooled in ice to 20° and 400 ml. of water is added. The cooled solution is filtered with suction and the crude *p*-nitrobenzoic acid washed on the filter with two 50-ml. portions of water.

60-120 The crude acid is then transferred from the funnel to a beaker and warmed with 100 ml. of 10 per cent sulfuric acid solution for removal of the chromium salts. After cooling, the *p*-nitrobenzoic acid is again collected on a filter. It is then returned to the beaker, dissolved in 5 per cent sodium hydroxide solution, and filtered from any chromium hydroxide and unchanged *p*-nitrotoluene. The filtrate, which should have only a pale greenish-yellow color, is acidified with 10 per cent sulfuric acid solution. Better results are usually obtained by running the alkaline solution into the dilute sulfuric acid rather than by the use of the reverse procedure. The precipitated acid is brought onto the Büchner filter, washed, and dried. Yield about 18 g. M.p. 235°-238°.

QUESTIONS

1. Write equations to show how you would obtain:
(a) *m*-nitrobenzoic acid from toluene
(b) *m*-aminobenzoic acid from toluene
(c) *p*-aminobenzoic acid from toluene
(d) Procaine (novocaine)
(e) anthranilic acid from phthalimide

2. Substances which show the Cannizzaro reaction (auto-oxidation and reduction in alkaline solution) include:
(a) formaldehyde (b) acetaldehyde
(c) isobutyraldehyde (d) trimethylacetaldehyde
(e) acetone (f) benzaldehyde
(g) anisaldehyde (h) benzophenone
(i) phenyl *p*-bromophenyl ketone (j) benzyl phenyl ketone

3. Which of the ketones listed in question 2 will form oximes capable of existing as *syn* and *anti* isomers?

4. Which of the following substances will show the haloform reaction?
(a) benzaldehyde (b) acetaldehyde
(c) phenylacetaldehyde (d) acetone
(e) *sec.*-butyl alcohol (f) methyl ethyl ketone
(g) acetophenone (h) benzyl methyl ketone
(i) phenyl ethyl ketone (j) α-phenylethyl alcohol

5. Which of the compounds listed in Group II may be made by a base catalyzed condensation of benzaldehyde with one of the reactants shown in Group I?

Group I
(a) acetaldehyde
(b) acetophenone
(c) acetone
(d) ethyl acetate
(e) ethyl *n*-butyrate

Group II
(f) $C_6H_5CH{=}CHCOCH{=}CH{-}C_6H_5$
(g) $C_6H_5CH{=}CH{-}CH_2CH_2COOC_2H_5$
(h) $C_6H_5CH{=}CHCOOC_2H_5$
(i) $C_6H_5CH_2COOC_2H_5$
(j) $C_6H_5CH{=}CHCOC_6H_5$

6. In which of the following compounds will the action of phosphorus pentachloride replace one oxygen atom by two chlorine atoms; in which is the oxygen atom replaced by but one chlorine atom?
(a) acetophenone (b) benzophenone
(c) *p*-benzoquinone (d) phenyl *p*-tolyl ketone

7. What compounds are obtained by the condensation of benzaldehyde with:
(a) nitromethane (b) nitroethane
(c) 1-nitropropane

8. Mark the following statements true or false.

(a) Hydrolysis of a compound such as $RCHCl_2$ yields an aldehyde.

(b) Metallic sodium is similar to a free radical in that it has an "odd" or "unpaired" electron.

(c) A specimen of mandelic acid prepared from benzaldehyde by the addition of HCN and hydrolysis of the nitrile is optically active.

(d) The reduction of a Schiff base yields a primary amine.

(e) Cinnamic acid may be made from benzaldehyde by use of the Perkin reaction.

(f) Condensation of benzaldehyde with nitromethane yields a product which upon reduction may give β-phenylethylamine.

(g) The molecule of benzoin has a structural resemblance to that of fructose and, like fructose, reduces Fehling's solution.

(h) Cinnamic acid can exist in both a *cis* and a *trans* modification.

(i) *o*-Hydroxycinnamic acid easily forms a lactone known as "coumarin."

(j) Phenylacetaldehyde is an isomer of acetophenone.

(k) Aromatic ketones are often made by use of the Friedel and Crafts reaction.

(l) Acetophenone shows the haloform reaction.

(m) The Beckmann rearrangement of *syn*-phenyl-*p*-tolylketoxime gives a product which yields *p*-toluidine and benzoic acid upon hydrolysis.

(n) Vitamin K_1 is related to 1,4-naphthoquinone.

(o) Quinhydrone is a reduction product of hydroquinone.

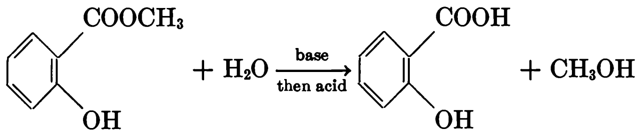
(p) Quinone shows reactions of the Diels-Alder type.

(q) Oxidation of benzoin gives first benzil and then benzoic acid.

EXPERIMENT 75

Aromatic Hydroxy Acids (Salicylic Acid, Aspirin, and Tannic Acid)

0-35 I. Preparation of Salicylic Acid from Oil of Wintergreen



In a 250-ml. flask mix 5 g. of oil of wintergreen (methyl salicylate) with a solution of 10 g. of sodium hydroxide in 50 ml. of water. The sodium salt of the phenolic group in the methyl salicylate, which usually separates at this point, dissolves when the mixture is warmed. Attach the flask to a reflux condenser and heat the contents of the flask to boiling for 15 minutes for hydrolysis of the ester.

Pour the solution into a beaker, cool it well in an ice bath and acidify it with dilute sulfuric acid. Collect the precipitated salicylic acid on a Büchner funnel and dry it in the oven or spread it out on a sheet of paper to dry in the air. After recrystallization from hot water, salicylic acid melts at 157°.

35-60 II. Properties of Salicylic Acid

A. Properties of the Carboxyl Group

1. Decarboxylation. In a test tube heat salicylic acid with an equal weight of soda lime. Note the odor evolved. Equation.

2. Esterification. Formation of Methyl Salicylate. Mix 1 g. of salicylic acid with 2 ml. of methyl alcohol and 2 ml. of concentrated sulfuric acid. Warm the mixture gently and note the odor. The odor is sometimes more apparent if the liquid is poured into 25 ml. of cold water. Equation.

60-130 B. Properties Due to the Phenolic Group

1. Ferric Chloride Test. To a dilute solution of salicylic acid in water add a few drops of ferric chloride solution. Result. Does phenol give a similar coloration?

2. Reaction with Bromine. Dissolve 0.2 g. of salicylic acid in a little warm water and add bromine water until the liquid has a faint yellow color. The precipitate is 2,4,6-tribromophenol. Explain this reaction. Does salicylic acid resemble a phenol or a carboxylic acid in this reaction?

3. Preparation of Acetylsalicylic Acid (Aspirin). Into a small flask introduce in the order named 5 g. of salicylic acid, 10 ml. of acetic anhydride, and 1-2 ml. of concentrated sulfuric acid. Stir the mixture and note the rise in temperature. All of the salicylic acid dissolves rapidly and crystals of aspirin soon begin to form.

Continue stirring the contents of the flask for a few minutes until the temperature falls somewhat and the separation of aspirin appears to be nearly complete. Dilute the crystalline paste with 10 ml. of cold glacial acetic acid, cool the mixture in cold water, and collect the crystals on a Büchner funnel. Wash the product on the filter with a little cold water and transfer it to a small beaker for recrystallization from boiling water. Determine the melting point of the recrystallized sample. Pure aspirin melts at 135°.

Suspend about 0.1 g. of your preparation in water and add 1-2 ml. of ferric chloride solution. Would you expect aspirin to give any coloration with ferric chloride? If any coloration develops with ferric chloride, to what is it due?

III. Properties of Tannic Acid 130-150

1. Fehling's Solution. Warm 5 ml. of a solution of tannic acid with 10 ml. of Fehling's solution (5 ml. each of solutions A and B). Result. Repeat the test using Tollens' reagent in place of Fehling's solution. Does the reducing power of a phenolic compound increase or decrease with increasing number of hydroxyl groups? Compare with phenol, hydroquinone, and pyrogallol.

2. Ferric Chloride. Add a few drops of ferric chloride solution to 5 ml. of a dilute solution of tannic acid. Does the coloration produced have any connection with the colors produced by phenols and ferric chloride (page 155)?

3. Ferrous Sulfate. To a dilute solution of tannic acid add a few drops of a freshly prepared solution of ferrous sulfate. Is any color produced? Dip a strip of filter paper into the solution and expose it to the oxidizing action of the air. Does a color develop? How is this principle used in the iron inks?

QUESTIONS

1. Write equations showing how:

(a) Salicylic acid may be made from phenol by the Kolbe method and by the Reimer-Tiemann process.

(b) *p*-Anisic acid (*p*-methoxybenzoic acid) may be made from *p*-nitrophenol.

(c) Salol (phenyl salicylate) may be prepared from salicylic acid.

2. Would you expect salicylic acid to be steam-distillable? Explain.

EXPERIMENT 76

Qualitative Organic Analysis

Introduction. Although the subject of the identification of organic compounds by application of a systematic scheme of qualitative organic analysis is covered in a full course at the senior or graduate student level in most schools, there is much to be gained by making a preliminary study of this phase of organic chemistry in the first course in the subject. Of course, the approach must be simplified greatly in order to be applicable to one or two laboratory periods.

The laboratory instructor will furnish each student with a 10-15 g. sample of an unknown compound, either liquid or solid, which is to be identified during the course of one or two periods. In order to limit the scope of the problem, the unknown will belong to one of the following classes of monofunctional compounds: aliphatic or aromatic aldehydes, ketones, carboxylic acids, esters, amines, amides of the type $RCONH_2$, nitriles, salts of carboxylic acids, and salts of amines; aliphatic alcohols including simple glycols; aromatic hydrocarbons, halides, nitro compounds and phenols.

The unknowns will be given to the student in the form in which they are received from the chemical supply companies; i.e., they will be of good quality but not necessarily 100 per cent pure compounds. The steps given below for the identification of each unknown should be followed in the order given, and notes should be taken after each experiment.

Purification. If the unknown is a solid, determine its melting point, then recrystallize it according to the directions given in Experiment 4, and again determine its melting point. Repeat this procedure until the melting point reaches a constant value. If the unknown is a liquid, purify it by distillation, and, at the same time, determine its boiling point. (CAUTION: Some organic liquids decompose when heated at too high a temperature. Never heat an unknown compound to dryness.)

Elemental Analysis. Test the unknown to determine whether it contains nitrogen, halogen, or a metal. Use the procedure given in Experiment 8.

Solubility Classification. Place 0.2 ml. of a liquid unknown or 0.1 g. of a solid unknown in a small test tube and add, in portions, with shaking, 3 ml. of water. If the compound proves to be soluble, repeat the test with ether as the solvent.

If the compound is insoluble in water, test its solubility in 5 per cent sodium hydroxide solution. Any compound that is found to be soluble in sodium hydroxide solution should next be tested for its solubility in 5 per cent sodium bicarbonate solution. Carry out these tests in the same manner as described for the test with water.

If the compound is insoluble in sodium hydroxide solution, test its solubility in 5 per cent hydrochloric acid.

Finally, for any unknown that is insoluble in water, 5 per cent sodium hydroxide, and 5 per cent hydrochloric acid, and that contains no nitrogen, test its solubility in concentrated sulfuric acid.

In the following chart are given the various types of compounds that belong to the different solubility classes:

I. Water-soluble Compounds
  A. Soluble in Ether.—Aliphatic alcohols, aldehydes, ketones, carboxylic acids, esters, amines, amides and nitriles of low molecular weight, and a few phenols
  B. Insoluble in Ether.—Glycols, amine salts, salts of carboxylic acids
II. Water-insoluble Compounds
  A. Soluble in 5 per cent Sodium Hydroxide
    1. Soluble in 5 per cent Sodium Bicarbonate.—Carboxylic acids, nitrophenols
    2. Insoluble in 5 per cent Sodium Bicarbonate.—Phenols
  B. Soluble in 5 per cent Hydrochloric Acid.—Amines
  C. Insoluble in Dilute Hydrochloric Acid or Sodium Hydroxide
    1. Contains Nitrogen.—Amides, nitriles, nitro compounds
    2. Contains No Nitrogen
      a. Soluble in Cold, Concentrated Sulfuric Acid.—Alcohols, aldehydes, ketones, and esters of relatively high molecular weight
      b. Insoluble in Cold, Concentrated Sulfuric Acid.—Aromatic halides, hydrocarbons

Tests for Functional Groups. Depending on the information gathered in the previous tests, carry out one or more of the following tests for detecting the presence of functional groups.

A. Aldehydes and Ketones. To 3 ml. of 2,4-dinitrophenylhydrazine reagent (Note 1) add a few mg. of the compound to be tested and shake vigorously. The 2,4-dinitrophenylhydrazones of all aldehydes and ketones are relatively insoluble and usually give an immediate precipitate. If the test with this reagent is positive, carry out tests with Tollens' reagent (Experiment 20) and Fehling's solution (Experiment 20). Also try the iodoform reaction (Experiment 23). The 2,4-dinitrophenylhydrazone can be used, also, as a derivative.

B. Alcohols. Carry out tests with acetyl chloride (Experiment 27), benzoyl chloride plus sodium hydroxide solution (Experiment 31), and metallic sodium (Experiment 31). Apply the Lucas test (Experiment 16) and the iodoform test (Experiment 23) if the above tests are positive.

C. Esters. Saponify the compound with sodium hydroxide solution and identify the carboxylic acid and alcohol produced (Experiment 26).

D. Nitriles and Amides. Add about 0.2 g. of the compound to be tested to 5 ml. of 10 per cent sodium hydroxide solution contained in a test tube, and heat the mixture to boiling. Note the odor of the vapor. Test the vapor with litmus paper. Both nitriles and amides of the type $RCONH_2$ evolve ammonia in this test.

E. Aromatic Nitro Compounds. Dissolve about 0.5 g. of the compound in 10 ml. of 50 per cent ethanol, then add 0.5 g. of ammonium chloride and 0.5 g. of zinc dust. Mix the reagents by shaking, then heat the mixture to boiling. Cool the mixture for 5 minutes, filter it, and test the filtrate with Tollens' reagent. The unknown is reduced by zinc dust and ammonium chloride to a hydrazine, a hydroxylamine, or an aminophenol. All of these compounds are oxidized by Tollens' reagent, which, in turn, is reduced and gives a silver mirror.

Salts. The metal salt of a carboxylic acid can be decomposed by hydrochloric acid and the liberated carboxylic acid collected by filtration or separated by ether extraction. The salt of an amine and an acid can be decomposed by sodium hydroxide solution and the liberated amine collected by filtration or separated by ether extraction.

Glycols. Determine whether the compound is a 1,2-diol by application of the periodic acid test (Experiment 31).

Amines. Determine whether the amine is primary, secondary, or tertiary by application of the Hinsberg reaction (Experiment 50).

Phenols. Try the ferric chloride (Experiment 61) and bromine water (Experiment 61) tests.

Preparation of Solid Derivatives. After the functional group in the unknown has been identified, at least one solid derivative and preferably two or more should be prepared in order to complete the identification. Some of the more useful solid derivatives for the various classes of compounds are listed below:

Aldehydes and Ketones. Prepare the semicarbazone (Experiment 21), the oxime and/or the phenylhydrazone and 2,4-dinitrophenylhydrazone. Purify these and all other derivatives described subsequently by crystallization from a suitable solvent, and determine the melting points.

Alcohols and Glycols. To 1 g. of 3,5-dinitrobenzoyl chloride (Note 2) add about 1 g. of the unknown and heat the mixture on the steam bath for 20 minutes. Add 10 ml. of water and collect the solid ester by filtration. Wash the solid with dilute sodium carbonate solution and then with water. Crystallize the ester from petroleum ether and determine its melting point.

Carboxylic Acids. Prepare the anilide or *p*-toluidide (Experiment 36).

Esters. Saponify the ester, isolate the alcohol (or phenol) and acid, and prepare solid derivatives of each.

Amides and Nitriles. Hydrolyze the compound (Experiment 30), isolate the acid, and prepare a solid derivative.

Amines. Prepare the acetyl or benzoyl derivative (Experiment 50).

Phenols. Prepare the 2,4-dinitrophenyl ether (Experiment 62), benzoate (Experiment 62), or polybromo derivative (Experiment 62).

Aromatic Hydrocarbons or Halides. Prepare the mono- or dinitro-derivative (Experiment 48).

Salts. Decompose amine salts with sodium hydroxide solution, isolate the free amine, and prepare a solid derivative. Decompose metal salts of carboxylic acids with hydrochloric acid, isolate the free acid, and prepare a solid derivative.

Nitro Compounds. Reduce these to primary amines (Experiment 49) and prepare solid derivatives of the amines.

Literature Search. With knowledge of the melting point or boiling point of the unknown, the type of functional group present, and the melting point of at least one solid derivative, you should be able to identify the unknown by looking up tables of compounds and their derivatives in one or more of the following books:

Shriner, Fuson, and Curtin, *Identification of Organic Compounds,* Wiley.
Kamm, *Qualitative Organic Analysis,* Wiley.
McElvain, *The Characterization of Organic Compounds,* Macmillan.
Cheronis and Entriken, *Semimicro Qualitative Organic Analysis,* Crowell.
Huntress and Mulliken, *Identification of Pure Organic Compounds,* Wiley.

NOTES

1. To prepare the reagent, dissolve 2 g. of 2,4-dinitrophenylhydrazine in 15 ml. of concentrated sulfuric acid, then add this solution, with stirring, to 150 ml. of 95 per cent ethanol. Finally, dilute the solution to 500 ml. by addition of distilled water and filter. The filtrate is used as the test reagent.

2. If necessary, prepare 3,5-dinitrobenzoyl chloride as follows: Add 1 g. of 3,5-dinitrobenzoic acid and 1 drop of pyridine to 3 ml. of thionyl chloride and heat the mixture under reflux for 30 minutes. Remove excess thionyl chloride by distillation, and use the residue for making solid derivatives of alcohols.

QUESTIONS

1. The following observations are frequently made in the examination of unknowns. In each case, state what deduction may be made as to the nature of the compound being tested.

(a) A compound gives an orange precipitate when treated with 2,4-dinitrophenylhydrazine reagent, but it does not reduce Tollens' reagent.

(b) A compound gives a positive test with 2,4-dinitrophenylhydrazine reagent, and it reduces Tollens' reagent; however, it gives a negative test with Fehling's solution.

(c) An unknown is found to contain nitrogen. It is insoluble in water, 5 per cent hydrochloric acid, and 5 per cent sodium hydroxide solution. It does not undergo hydrolysis in hot sodium hydroxide solution. When an ethanol solution of the compound is treated with zinc dust and ammonium chloride and the resulting mixture filtered, the filtrate is found to reduce Tollens' reagent.

(d) An unknown contains nitrogen, and it is insoluble in water, 5 per cent sodium hydroxide solution, and 5 per cent hydrochloric acid. When boiled in 10 per cent sodium hydroxide solution, ammonia is evolved.

(e) A compound is insoluble in water and 5 per cent sodium bicarbonate solution, but it is soluble in 5 per cent sodium hydroxide solution. It gives a pronounced color with ferric chloride.

(f) A compound is insoluble in water, 5 per cent sodium hydroxide solution, and 5 per cent hydrochloric acid, but it is soluble in concentrated sulfuric acid. The compound undergoes hydrolysis when heated with sodium hydroxide solution.

(g) Elemental analysis of a compound shows that it contains bromine. The compound is insoluble in water, 5 per cent sodium hydroxide solution, 5 per cent hydrochloric acid and concentrated sulfuric acid.

(h) An unknown undergoes reaction with acetyl chloride to give a sweet smelling derivative, and it also gives a positive iodoform test. However, it gives a negative test with 2,4-dinitrophenylhydrazine reagent.

(i) Each of two different pleasant-smelling, water-insoluble organic compounds gradually dissolves when refluxed with sodium hydroxide solution with disappearance of the characteristic odor. In the case of the first compound, distillation of the resulting solution affords as the distillate, along with water, a compound which, when isolated free of water, reacts with acetyl chloride and gives a positive iodoform test, but does not give a positive Lucas test at room temperature.

In the case of the second compound, distillation of the basic solution affords pure water.

2. The compound $C_9H_{11}ON$ (A) is insoluble in dilute hydrochloric acid but soluble in a dilute sodium hydroxide solution. Phosphorus pentachloride converts A into an isomeric compound (B) which is no longer soluble in alkali. Hydrolysis of A with 10 per cent sulfuric acid gives $C_9H_{10}O$ (C) which is soluble only in concentrated sulfuric acid. C is converted into benzoic acid by vigorous oxidation, yields iodoform when treated with iodine in alkaline solution, and reacts with phenylhydrazine. B is converted by hydrolysis with 10 per cent sulfuric acid into acetic acid and C_7H_9N (D). D is soluble in water, gives a basic reaction, and is converted by nitrous acid into C_7H_8O (E) which yields benzoic acid when oxidized. What are the structures of A, B, C, D, and E? Show by means of equations the reactions involved. Identify any "name" reactions.

UNKNOWN REPORT

1. Physical Examination
   a. Physical State
   b. Color
   c. Odor
2. Physical Constants
   a. Melting point
   b. Boiling point
3. Elemental Analyses
   Elements present other than carbon and hydrogen
4. Solubility Behavior
   Compound is soluble in
5. Classification Tests

	Reagent	Observation	Inference
a.			
b.			
c.			
d.			
e.			
f.			

6. Possibilities. After you have determined the melting point or boiling point of the unknown and what functional group is present, list all of the compounds of that class which have a m.p. or b.p. within ±5° of that you have observed.

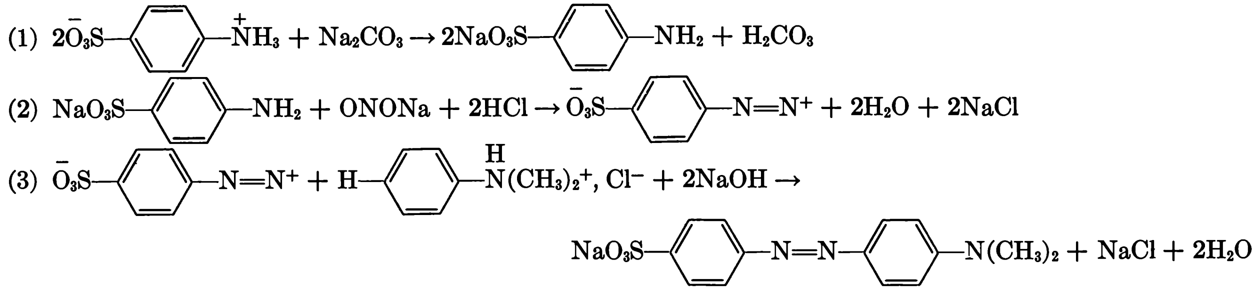
	Possibilities	B.P. or M.P.	Derivatives and Their Melting Points		
a.	Unknown				
b.					
c.					
d.					
e.					
f.					
g.					

7. Conclusion

EXPERIMENT 77

Dyes and Dyeing

I. PREPARATION OF METHYL ORANGE (AN AZO DYE)



Introduction. The preparation of an azo dye consists of the following operations:

1. The diazotization of an aromatic substance containing a primary amino group.
2. The preparation of a solution of some aromatic amino compound in dilute acid, or a solution of a phenolic substance in dilute alkali.
3. The mixing of the above solutions when the reaction (called **coupling**) takes place with the formation of the dye. Before coupling can occur, the solution must be alkaline or only slightly acidic.

In the preparation of methyl orange, sulfanilic acid is diazotized (step 1); dimethyl aniline is dissolved in dilute hydrochloric acid (step 2); and the two solutions are "coupled" (step 3).

0-50 *Procedure.* Dissolve 5 g. of sulfanilic acid and 2 g. of sodium carbonate in 100 ml. of water. Cool the solution to 0° by the addition of 150 g. of ice and add 2 g. of sodium nitrite dissolved in 15 ml. of water. A solution of 4 ml. of concentrated hydrochloric acid in 25 ml. of cold water is then slowly introduced. This process is known as **diazotization.**

Dissolve 3 ml. of dimethylaniline in 5 ml. of concentrated hydrochloric acid diluted with 15 ml. of water. Cool this solution with ice and pour it into the diazotized sulfanilic acid with continuous stirring. This process is known as "coupling" and is used for the preparation of all "azo" dyes.

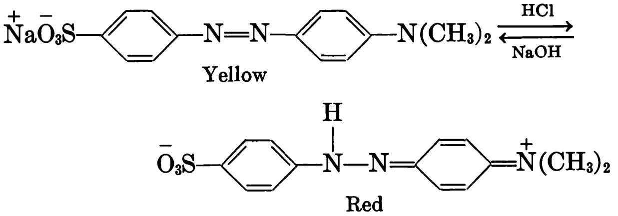
Some coupling occurs in the dilute acid solution and the dye thus formed imparts a red color to the solution. Complete the coupling process and, at the same time, convert the dye into its yellow sodium salt by the addition of approximately 40 ml. of a 10 per cent solution of sodium hydroxide.

At this point the solution is faintly basic to litmus paper. Add 30 g. of clean salt (NaCl), heat the contents of the beaker nearly to the boiling point, and set the solution aside (or in an ice bath) to cool. The dye separates in orange colored crystals which are collected on the Büchner funnel, pressed well, rinsed with a small quantity of ethanol and dried in the oven or spread out on paper to dry in the air. Do not attempt to take the melting point of the dye. Yield 8-9 g.

Tests with Methyl Orange

(*a*) *Helianthin.* To 0.2 g. of methyl orange add 10 ml. of water and 1 ml. of concentrated hydrochloric acid. Warm the solution and then cool it. The red crystals (inner salt) that separate are known as "helianthin." 50-55

The indicator action of methyl orange may be illustrated by the following formulas:



(*b*) *Cleavage of Methyl Orange by Reduction.* To 0.1 g. of methyl orange, contained in a small Erlenmeyer flask, add 30 ml. of water, 5 ml. of glacial acetic acid, and 3-4 g. of zinc dust. Keep the solution warm for a few minutes and observe the gradual loss of color. Equation. 55-65

All azo dyes undergo cleavage at the —N=N— bonding upon reduction to give two amino compounds whose identification provides valuable information toward the identification of an azo dye of unknown structure.

II. DYEING CLOTH

A. Direct Dyeing of Wool and Silk 65-85

In 400-ml. beakers prepare (1) a solution of 0.2 g. of Malachite Green in 200 ml. of water, and (2) a solution of 0.2 g. of Crystal Violet (or Methyl Violet) in 200 ml. of water.

Heat the two solutions to boiling and immerse in each a piece of cotton cloth, one of wool, and one of silk, each of which is 2-3 inches square. After 2 minutes remove the cloth with a glass rod; avoid getting the dye solution on your hands or dripping it upon the laboratory table, and wash out the excess dye in a gentle stream of water at the sink. Is the color "fast" in each sample? Dry the samples on a string tied between two iron stands and fasten them in your notebook with pieces of Scotch tape. Save the dye solutions for Part B.

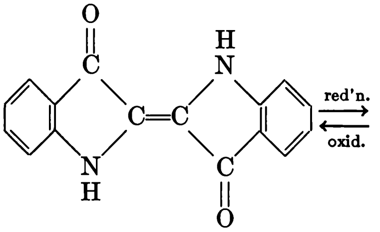
85-105 B. Dyeing Cotton with the Aid of a Mordant

Prepare a solution of 1.0 g. of tannic acid in 200 ml. of water and immerse in it two small pieces of cotton cloth. Let the cloth remain in the solution at room temperature while you prepare a solution of 0.2 g. of tartar emetic in 200 ml. of water. By means of a glass rod remove the pieces of cloth from the solution of tannic acid to an empty beaker and, with the aid of a spatula, press out as much of the tannic acid solution as possible.

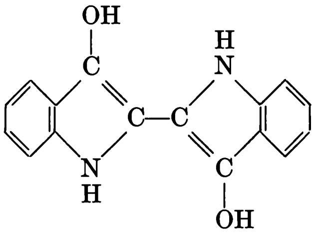
Fasten the tannic acid in the pieces of cloth by dipping them in the solution of tartar emetic and again pressing out the excess solution as before. Now immerse one piece of the mordanted cloth in the Malachite Green dye bath, the other in the Crystal Violet bath. Dye the cloth at or near the boiling point of the solutions for 2 minutes and wash and dry the samples of dyed cloth as in Part A. Does the mordant aid in fixing the dye in the fiber? Fasten the specimens in your notebook.

105-130 C. Dyeing with Indigo-A Vat Dye

The "vat" dyes, of which indigo is the classic example, are insoluble in water but become soluble upon reduction to the "leuco" dye. The "leuco" forms of such dyes may or may not be colorless; for example, the solution of leuco-indigo (often called indigo-white) is green. Cloth impregnated with the solution of the "leuco" dye develops a "fast" color when oxidized in the air.



Indigo
(Insoluble in water)



Leuco-indigo
(Soluble in water)

Procedure. In a small Erlenmeyer flask place 0.1 g. of blue indigo powder (or 0.5 g. of the 20 per cent indigo paste), 0.1 g. of sodium hydrosulfite ($Na_2S_2O_4$), 2 pellets of sodium hydroxide (about 0.15 g.), and 10 ml. of water. Stopper the flask to exclude air and shake it gently 2-3 minutes. Note that the solution acquires a dark-green color as the indigo dissolves. Dilute the solution with 50 ml. of water.

From a piece of cotton cloth, cut a strip 2 inches wide by 10 inches long. Hold the strip at one end and dip the lower half or two thirds of the cloth into the leuco-indigo for 10-15 seconds and then hang the cloth on a support to oxidize in the air. After a few minutes wash the cloth under the tap. Is the blue color fast? Fasten a sample of the dyed cloth in your notebook.

Reduction and Reoxidation of a Dye

In a 1-liter flask dissolve 10 g. of glucose and 10 g. of sodium hydroxide in 500 ml. of water. To the well-shaken solution add 1 or 2 ml. of a solution of methylene blue in order to impart a distinct blue color to the solution.

When this solution is allowed to stand quietly for about 1 minute, the blue color disappears because the dye is reduced to its leuco form by the alkaline solution of glucose. When the flask is shaken vigorously so that the dye may be oxidized by good contact with the air, the blue color reappears, only to fade again when the flask is allowed to remain at rest. This "now you see it, now you don't" demonstration may be repeated many times.

Cleaning the Glassware

Dye stains may be removed from the glassware by brushing with a thin paste made of bleaching powder and water. Remove any dye spots from your hands likewise by application of a little of this paste; finally remove the odor of chlorine from your hands by washing them with a little alcohol.

QUESTIONS

1. What structural formula would you assign to a dye made by diazotizing the amine listed in column A and coupling it with the compound opposite it in column B.

	A	B
(a)	*p*-aminodimethylaniline	*β*-naphthol
(b)	*α*-naphthylamine	*α*-naphthol
(c)	sulfanilic acid	*p*-cresol
(d)	sulfanilic acid	resorcinol
(e)	benzidine	4-amino-1-naphthalenesulfonic acid

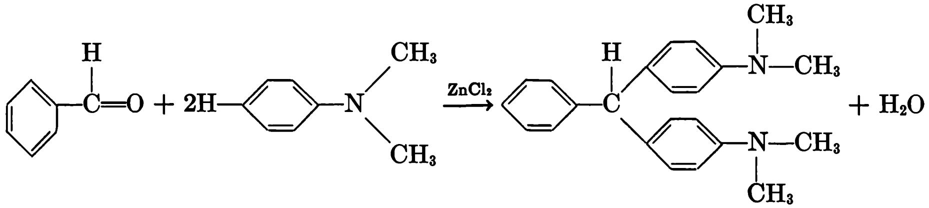
2. What structural formula would you assign to an azo dye which upon reduction gave:

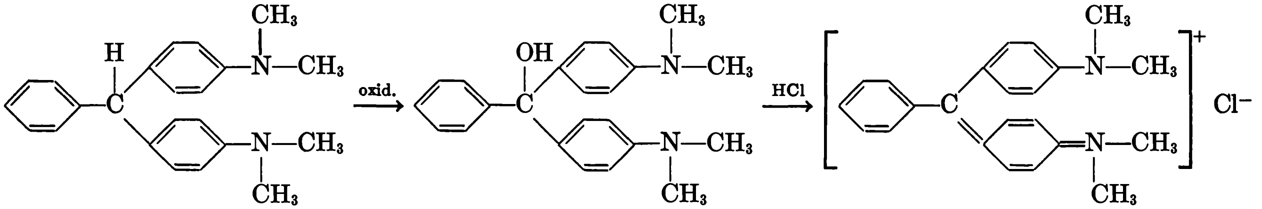
(a) aniline (1 mole) and *p*-aminophenol (1 mole)
(b) sulfanilic acid (1 mole) and 1-amino-2-naphthol (1 mole)
(c) benzidine (1 mole) and 3,4-diamino-1-naphthalenesulfonic acid (2 moles)

EXPERIMENT 78

Malachite Green, Phenolphthalein, and Fluorescein

I. Preparation of Malachite Green


Leuco Base of Malachite Green


Leuco Base of Malachite Green

Carbinol Base of Malachite Green

Malachite Green (A salt)

Introduction. It has been said that in giving an examination in Organic Chemistry one should not ask a student to write the answers to a series of questions, but rather should send him to the laboratory to prepare a specimen of Malachite Green. If the student can make this dye without getting it all over the laboratory as well as himself, he is an excellent chemist. Many students have failed so woefully on such a test that in many universities the experiment, though highly instructive, is often omitted from the list of assignments.

The procedure that follows is short and only a modicum of care is needed to ensure that not so much as one drop of the dye solution will be spilled on one's clothing or upon the laboratory table.

0-60 *Procedure.* Place 4 ml. each of benzaldehyde and dimethylaniline along with 2 or 3 g. of coarsely powdered fused zinc chloride into a 250- or 500-ml. distilling flask. (The sticks of fused zinc chloride should be broken quickly in a dry mortar because the material rapidly absorbs water from the air. Keep the bottle of zinc chloride closed.)

Lower a thermometer into the flask so that the bulb rests on the bottom. Warm the flask with a small semi-luminous flame of the Bunsen burner until the thermometer registers a temperature of 130°-140°. Maintain this temperature by intermittent application or removal of heat for 10 minutes by the clock. The flask now contains the leuco base of Malachite Green along with the zinc chloride and some unchanged benzaldehyde and dimethylaniline.

Allow the flask to cool somewhat and add 150 ml. of water measured from a graduated cylinder. Connect the flask with a condenser and remove water by distillation until 125 ml. of water has been collected. This distillation "boils out," or steam distills, the excess benzaldehyde and dimethylaniline. The leuco base of Malachite Green remains in the flask as a gummy blue-green mass. The prefix *leuco-* means "white" but the leuco form of a dye may or may not be colorless; its color, however, if far less intense than that of the corresponding dye.

Oxidation of the Leuco Base to the Dye. Add 3 ml. of concentrated hydrochloric acid to the contents of the distilling flask and shake the mixture for 30 seconds to dissolve as much of the leuco base as possible. Add 150 ml. of tap water, shake well, and then add 3 g. of lead dioxide (PbO_2). Note the immediate deepening of the color. Shake the flask for 2 minutes to mix the materials well and then add about 3 g. of sodium sulfate to precipitate the lead as lead sulfate.

Heat the solution nearly to boiling and filter part of the solution (about 15 ml.) into a large test tube. Add a piece of woolen cloth to this solution and heat it until it boils for 1 minute. Remove the cloth with a glass rod and wash it at the water tap. Dry the cloth and fasten it in your notebook with Scotch tape. Pour all solutions of the dye directly into the drain pipe in the sink and wash the dye down the drain.

Cleaning the Glassware. To clean the glassware proceed in the following manner:

(1) Wash the flask several times with water at the sink, pouring the dye solution directly into the drain pipe.

(2) Pour 20 ml. of concentrated hydrochloric acid into the flask, rotate the flask to wet the sides well, and add 150 ml. of water. Heat this solution nearly to boil-

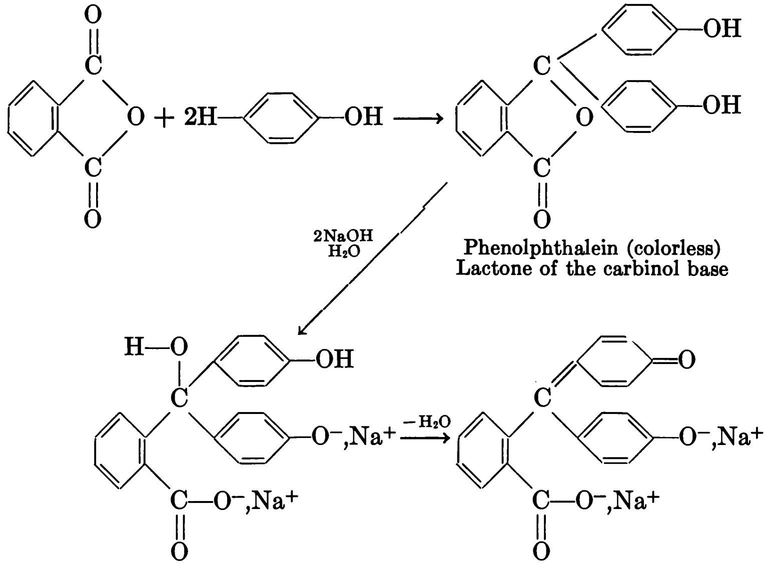
ing and shake the flask to dissolve as much as possible of the dye remaining on the upper part of the flask. Wash the flask well at the sink.

(3) Remove the remaining dye by total immersion of the flask in the crock of bleaching solution, which will be placed near the sink. (The bleaching solution contains $CaOCl_2 + Na_2CO_3$.) After several minutes remove the flask with the old pair of tongs provided for the purpose and wash the flask well with water.

(4) The test tube and funnel may be washed with water at the sink and then immersed in the bleaching solution.

(5) Remove any spots of dye on your hands by application of a little of the bleaching solution and allowing it to remain for one or two minutes. Wash well and remove the odor of chlorine from your hands by an alcohol rub.

II. PHENOLPHTHALEIN



Phenolphthalein (colorless)
Lactone of the carbinol base

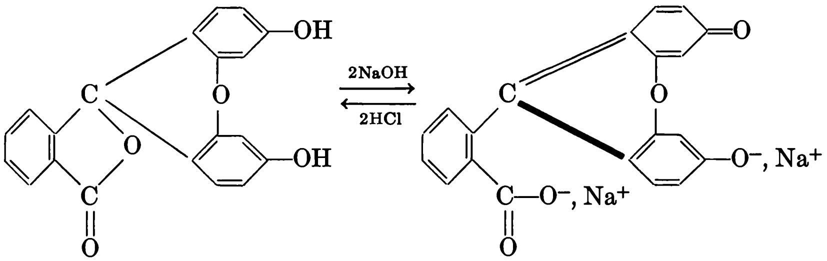
Carbinol base
(Disodium salt)

Phenolphthalein (red)

Introduction. Malachite Green, prepared in Part I, is a typical example of the triphenylmethane dyes. The phthalein dyes are so closely related structurally to those of the triphenylmethane classification that the two types may well be studied collectively. Note that the colorless form of phenolphthalein may be considered the lactone of the carbinol base of the dye.

60-80 *Procedure.* In a test tube mix 0.3-0.4 g. of phenol with about 0.2 g. of phthalic anhydride. Add 3-4 drops of concentrated sulfuric acid, stir the mixture with a stirring rod, and heat the mass to a temperature of approximately 160° for 2-3 minutes. The substances will react with gentle ebullition. Pour the hot melt into 50-60 ml. of water. Make a portion of the solution alkaline and then reacidify it. Does the solution give the change of color that is characteristic of phenolphthalein?

III. FLUORESCEIN



Fluorescein (acidic)

Fluorescein (sodium salt)

Introduction. If resorcinol (*m*-dihydroxybenzene) replaces phenol in the preceding experiment, the dye formed, known as fluorescein, contains in its molecular structure an oxygen linkage between the two phenolic nuclei. Solutions of fluorescein have a greenish-yellow fluorescence.

80-100 *Procedure.* Repeat the above experiment replacing the phenol with resorcinol. After the reaction mixture has been poured into water, make the solution alkaline and examine the solution by direct and by reflected light.

QUESTIONS

1. Show how Michler's ketone and phenylmagnesium bromide may be used for the preparation of Malachite Green.

2. Show how Michler's ketone may be condensed with dimethylaniline in the production of Crystal Violet.

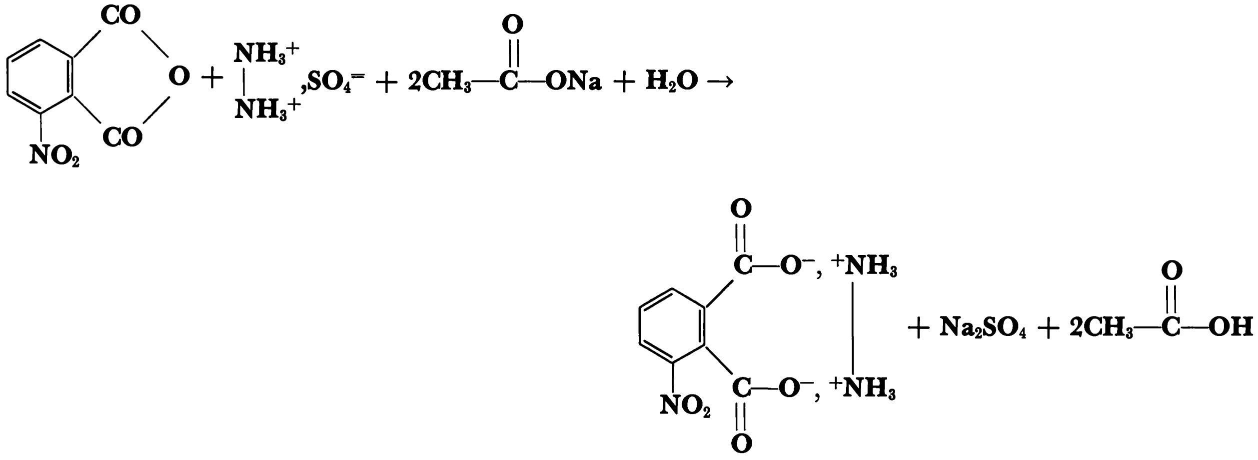
3. (a) What may be formed by the reduction of Malachite Green; (b) by the reaction of Malachite Green with sodium hydroxide solution?

4. (a) Compare the formula of Crystal Violet with that of Pararosaniline. (b) Show how Pararosaniline may be converted into the parent hydrocarbon, triphenylmethane.

5. Write structural formulas for:
(a) 4-hydroxytriphenylmethane
(b) 4,4′-dihydroxytriphenylmethane
(c) 4,4′,4″-trihydroxytriphenylmethane
(d) eosin
(e) mercurochrome

EXPERIMENT 79

I. 3-Aminophthalhydrazide ("Luminol")



II. Chemiluminescence

Introduction. All chemical reactions proceed with the evolution or absorption of energy. In most instances the energy evolved or absorbed is in the form of heat, although many experimenters from time to time have noticed that visible radiation was produced when various chemical reactions were conducted in a darkened room. In most instances of this kind the intensity of the light emitted is low. The oxidation of 3-aminophthalhydrazide in alkaline solution, however, gives one of the most brilliant displays of chemiluminescence on record and has the added advantages that, in contrast to certain other compounds which exhibit this phenomenon, the materials are easily obtained, are safe to handle, and are used in very dilute solutions.

Today's experiment is a small-scale adaptation of the procedure given by Huntress, Stanley, and Parker.[1]

These authors not only describe the preparation of 3-aminophthalhydrazide but also present a discussion of chemiluminescence that will be of interest.

I. 3-AMINOPHTHALHYDRAZIDE ("LUMINOL")

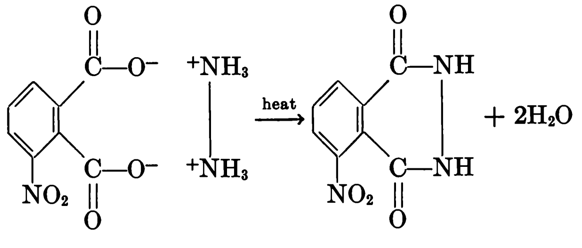
Procedure. Into a 25 x 200 ml. test tube introduce 1 g. of 3-nitrophthalic anhydride, 0.7 g. of hydrazine sulfate, 1 g. of hydrated sodium acetate, and 4 ml. of water. Support the tube at an angle of about 45° on an iron stand by means of a clamp and heat the mixture to boiling. Note that the escaping steam carries with it the vapors of acetic acid.

The hot suspension now contains hydrazine 3-nitrophthalate. The composition of the salt formed by hydrazine and 3-nitrophthalic acid apparently is not known with certainty. The structure shown in the equation is one possibility.

In order to convert the salt (hydrazine 3-nitrophthalate) to 3-nitrophthalhydrazide (belonging to the amide family of compounds), a temperature considerably above the boiling point of water is required. To attain this temperature introduce 5 ml. of glycerol and a boiling chip, insert a thermometer whose bulb rests on the bottom of the tube, and heat the tube to remove water. No stopper is used; the mouth of the tube is left open to facilitate the escape of steam.

Boil the contents of the tube rather vigorously but do not apply heat so rapidly that excessive bumping occurs. Stir the contents of the tube with a stirring rod and note the rise in temperature. After a temperature of 120° is attained the thermometer reading rises quickly to 200°. At this point heat the tube gently and intermittently so that a temperature of 200°-220° is maintained for 3 or 4 minutes. During this period the contents of the tube acquire an orange-yellow color.

Allow the tube to cool to about 100° and add 40 ml. of water. Warm the tube over the Bunsen burner to accelerate the coagulation of the light yellow 3-nitrophthalhydrazide and set the tube in an ice bath for a few minutes.



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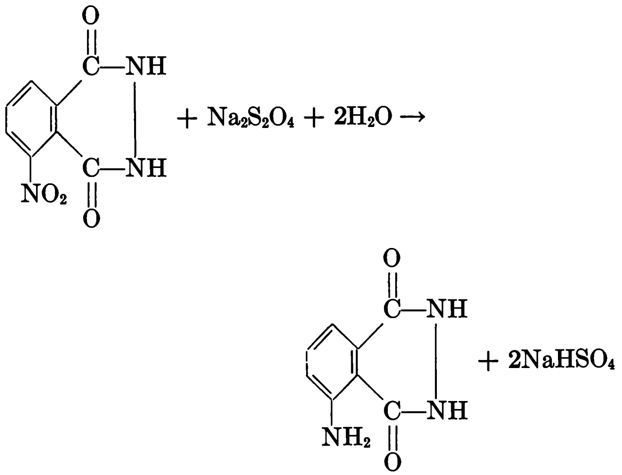
[1] E. H. Huntress, L. N. Stanley and A. S. Parker, *J. Chem. Educ.*, **11,** 142-145 (1934).

As soon as the 3-nitrophthalhydrazide has settled well, pour off the supernatant solution and shake the residual yellow powder with another 40-ml. portion of water. Warm the mixture, if necessary, to increase the rate of sedimentation, and, after chilling in ice, decant the clear upper solution from the 3-nitrophthalhydrazide which remains in the bottom of the tube.

Reduction of 3-Nitrophthalhydrazide to 3-Aminophthalhydrazide. The nitro compound is now contained in the test tube along with a little water. Add to the contents of the tube 5 ml. of a 10 per cent solution of sodium hydroxide. To the red solution thus obtained add 3 g. of sodium hydrosulfite as a reducing agent and heat the contents of the tube to boiling.

Maintain a temperature at or near the boiling point for 3-4 minutes. The red color of the solution quickly gives way to the yellow color of the 3-aminophthalhydrazide, some of which usually precipitates almost immediately. The quantity of this precipitated amino compound increases when the contents of the tube are cooled and acidified with glacial acetic acid (about 2 ml. of the acid will be required).



"Luminol"

Collect the 3-aminophthalhydrazide ("Luminol") on a small Büchner funnel and wash it twice with 25-ml. portions of water. Remove the filter paper with the "Luminol," and place both the paper and moist product on a watch glass. Use part of the moist "Luminol" for Part II and place the watch glass (or Petri dish) containing the remainder in an oven to dry. The recorded melting point of 3-aminophthalhydrazide is about 310°.

II. Chemiluminescence

Prepare the following solutions:

A. Dissolve a quantity of the moist "Luminol" estimated to contain 0.1 g. of the dry material in 10 ml. of 10 per cent sodium hydroxide solution and dilute the solution to 1 liter.

B. Dissolve 0.5 g. of potassium ferricyanide $[K_3Fe(CN)_6]$ in 75-100 ml. of water, add 15 ml. of ordinary 3 per cent hydrogen peroxide solution, and dilute the solution to 1 liter.

Take these solutions to a room that can be darkened where you have at hand a reagent bottle of hydrochloric acid and one of sodium hydroxide solution. Place a 6-inch funnel in the mouth of a large flask (3-5 liters), turn off the lights, and mix solutions A and B by pouring them through the funnel into the large flask. The chemiluminescence appears as soon as the solutions are mixed. The light emitted will illuminate the room so that you can now easily locate your bottles of reagents.

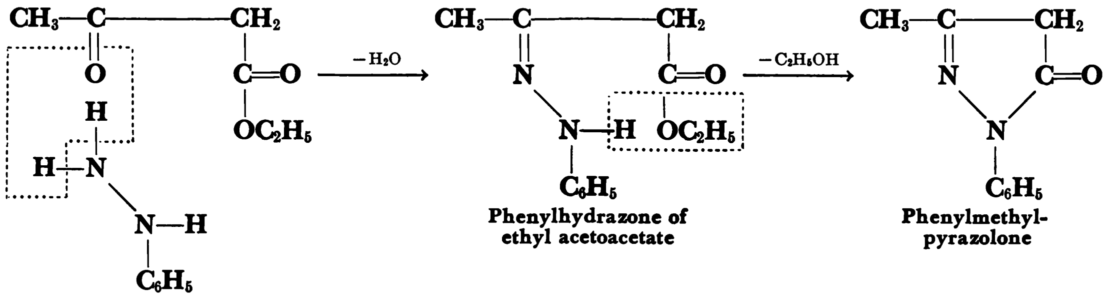
Add to the mixed solutions in the large flask a little sodium hydroxide and note that the chemiluminescence is intensified. Then acidify a portion of the luminescent solution with hydrochloric acid and note that the emission of light ceases and that it reappears if the solution is again quickly made alkaline.

EXPERIMENT 80

Heterocyclic Compounds

Phenylmethylpyrazolone, Furfural, and Pyridine

(1)



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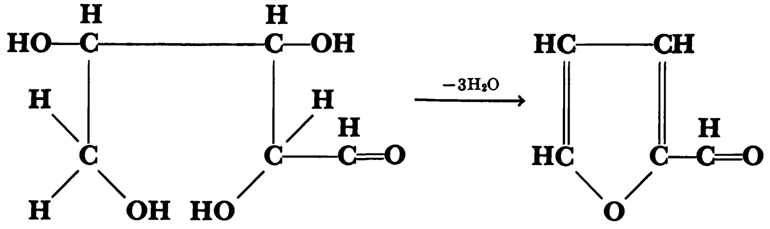


I. Preparation of Phenylmethylpyrazolone

0-20 In a large test tube (25 x 200 mm.) mix 6.5 g. (6.5 ml., 0.05 mole) of ethyl acetoacetate with 5.4 g. (5 ml., 0.05 mole) of phenylhydrazine. Note that a little heat is evolved and that the original clear solution soon becomes turbid owing to the separation of droplets of water in the formation of the phenylhydrazone of ethyl acetoacetate. Fit the tube with a cork stopper through which is inserted a piece of glass tubing about 18 inches long.

20-80 Heat the tube in a bath of molten paraffin wax (see Figure 31, page 139) for 1 hour at a temperature of 135°-145°.

[During this period in the preparation of phenylmethylpyrazolone, go on to Parts II and III.]

80-120 When the heating period has been completed, pour the contents of the tube into a small beaker, cool the beaker in cold water and stir the material with 30-40 ml. of ether. As soon as crystals form, chill the beaker in ice and collect the product on the Büchner funnel. Recrystallize the phenylmethylpyrazolone from alcohol or hot water. Yield 6-8 g. M.p. 127°.

Test the solubility of phenylmethylpyrazolone in 5 per cent sodium hydroxide solution by warming 0.2 g. of the compound with a few ml. of the alkaline solution. Cool the solution and acidify it with acetic acid. Result.

Test the solubility of phenylmethylpyrazolone in a warm 10 per cent solution of hydrochloric acid. Cool the solution and make it basic by addition of ammonium hydroxide solution. Result? How do you account for the amphoteric nature of phenylmethylpyrazolone?

II. Properties of Furfural 20-60

Introduction. The commercially important aldehyde, furfural, is obtained by heating oat hulls, crushed corn cobs, and other materials containing pentosans with sodium chloride and 10 per cent sulfuric acid solution in water. Note the similarity of the molecular structures of furfural and benzaldehyde, particularly the lack of an *alpha* hydrogen atom in each of the molecular formulas. The following short experiments serve to show the similar properties of these two aldehydes.

Procedure. Redistill 10 ml. of commercial furfural for use in the following tests.

(*a*) *Action of Tollens' Solution.* Warm a few drops of furfural with 5 ml. of Tollens' solution. Does any reduction take place? Equation.

(*b*) *Reaction with Ammonia.* Place approximately 1 ml. of furfural in a test tube and add 5 ml. of concentrated ammonium hydroxide solution. Close the mouth of the test tube with a stopper, shake the tube thoroughly and let it stand for a few minutes. The reaction is similar to that which takes place between benzaldehyde and ammonia. Equation.

(*c*) *Auto-oxidation and Reduction.* Shake 1 ml. of furfural in a test tube with 5 ml. of a 20 per cent solution of sodium hydroxide. What are the crystals which separate? What other product is produced? Equation. Does benzaldehyde give a similar reaction?

60-80 III. PROPERTIES OF PYRIDINE

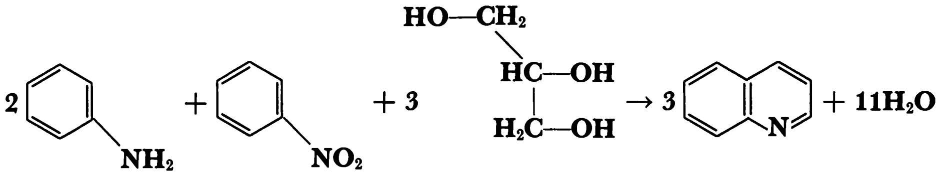
(*a*) *Action on Litmus Paper*. Shake a few drops of pyridine with 5-10 ml. of water and test the solution with litmus paper. Write an equation for the reaction of pyridine and water.

(*b*) *Reaction with Ferric Chloride Solution.* To the solution of pyridine prepared above add a few ml. of ferric chloride solution. What is the brown gelatinous precipitate? Equation.

(*c*) *Addition of Methyl Iodide*. Add 1 ml. of pyridine to 1 ml. of methyl iodide. Result. Write the equation to show the formation of the methylpyridinium iodide (a quaternary ammonium salt).

EXPERIMENT 81

Preparation of Quinoline by the Skraup Synthesis



Introduction. In the conversion of a molecule of aniline into a molecule of quinoline three additional carbon atoms must be supplied by a reactant, other than the aniline, and an oxidizing agent must ordinarily be used to effect ring closure. In the Skraup synthesis, glycerol, which presumably is converted into acrolein by the sulfuric acid used, supplies the needed three carbon atoms and nitrobenzene serves as the oxidizing agent. The aniline produced by reduction of the nitrobenzene is likewise converted to quinoline.

0-60 *Procedure.* In a 500-ml. flask mix 6 g. of powdered ferrous sulfate, 10 ml. of nitrobenzene, and 18.6 g. (18 ml., 0.2 mole) of aniline. Then add in small portions, and with constant shaking of the flask, 25 ml. of concentrated sulfuric acid. The reaction between the aniline and sulfuric acid is so highly exothermic that it may be necessary to cool the flask somewhat, although, for convenience in mixing, the temperature of the mixture should remain high enough to maintain the contents of the flask in a fluid condition. Finally, again with constant shaking of the flask, add 50 g. (40 ml.) of glycerol.

Clamp the flask securely to a ring stand and support it by means of a wire gauze resting on a ring. Fit a reflux condenser to the flask and heat the flask gently by waving a small, semiluminous flame of the Bunsen burner beneath it. Agitate the flask as much as possible and continue heating the flask cautiously until an exothermic reaction begins. The burner is then removed and the reaction allowed to proceed spontaneously. Be prepared to cool the flask in a bath of ice and water if the rate of boiling should become excessively rapid. When the automatic reaction has subsided, heat the contents of the flask to boiling for 40 minutes.

60-75 *Removal of Excess Nitrobenzene.* Cool the flask somewhat, add 200 ml. of water, and pour the liquid into a larger flask for steam distillation. The collection of about 100 ml. of distillate, requiring about 10 minutes, will serve to remove any nitrobenzene that was not utilized in the reaction. This distillate is discarded.

75-105 *Conversion of Excess Aniline to Phenol.* Cool the contents of the steam-distillation flask to 25°-30° and add a solution of sodium nitrite until a drop of the solution on starch-potassium iodide paper shows that an excess of sodium nitrite is present. (Note: Nitrous acid liberates iodine from potassium iodide; iodine and starch give a blue coloration.) Ordinarily about 5 g. of sodium nitrite is sufficient.

Warm the flask to 50° for the evolution of nitrogen from the diazonium salt and then, with constant shaking and cooling of the flask, make the contents alkaline by the slow addition of a cold solution of 40 g. of sodium hydroxide in 100 ml. of water. If a test drop of the well-shaken liquid is not alkaline to litmus, more sodium hydroxide must be added.

105-170 *Isolation of the Quinoline.* Subject the contents of the flask to steam distillation and collect 400-450 ml. of distillate. This will require about 40 minutes. Pour the distillate into a 500-ml. separatory funnel and remove the lower layer (10-12 ml.) of quinoline. Then extract the water suspension twice with 15-ml. portions of carbon tetrachloride, combine the extract with the first portion of quinoline, and dry the combined material over a little solid sodium hydroxide. Decant the liquid from the drying agent and distill it. The carbon tetrachloride boils at 77° and the quinoline at 237°. Quinoline is a pale yellow liquid with a disagreeable odor. Yield 10-12 g.

QUESTIONS

1. What compound will be produced by the Skraup process if the aniline used is replaced (a) by *p*-anisidine, (b) by *o*-bromoaniline?
2. How may nicotinic acid be obtained from quinoline?

Special Reagents

Tollens' Reagent. Thirty grams of silver nitrate are dissolved in 500 ml. of water and a solution of ammonium hydroxide is added until the precipitate of silver oxide which first forms is barely redissolved. Dilute the solution to a liter. The solution may be used in this form. If greater sensitivity is desired a portion of the solution should be mixed immediately before use with an equal volume of a 5 per cent solution of sodium hydroxide. Upon standing or heating, this mixture deposits a black precipitate which is explosive.

Fehling's Solution. Dissolve 34.64 g. of pure copper sulfate ($CuSO_4 \cdot 5H_2O$) in 350-400 ml. of distilled water and dilute the solution to 500 ml. Label this solution Fehling's Solution I.

Prepare another solution containing 173 g. of Rochelle salt and 65 g. of sodium hydroxide in about 350 ml. of water and dilute the solution to a volume of 500 ml. Put this in a bottle labeled Fehling's Solution II.

Use equal volumes of I and II in making a test. One ml. of the mixed solutions will oxidize 0.005 g. of glucose.

Benedict's Qualitative Reagent. Prepare solution A by dissolving 173 g. of sodium citrate and 100 g. of anhydrous sodium carbonate in about 600 ml. of water and dilute the solution to 850 ml. Prepare solution B by dissolving 17.3 g. of crystalline copper sulfate ($CuSO_4 \cdot 5H_2O$) in 100 ml. of water and diluting the solution to 150 ml. Add solution B to solution A and mix well for the preparation of Benedict's solution.

Schiff's Reagent. Dissolve 1 g. of fuchsine (rosaniline) in 350-400 ml. of warm water. Cool the solution and pass sulfur dioxide through it until the solution is colorless or only a pale yellow. Dilute to 1000 ml. Keep the solution in amber-colored bottles.

Molisch's Solution. Ten grams of α-naphthol are dissolved in 100 ml. of ethyl alcohol or chloroform.

Iodine in Potassium Iodide. Dissolve 5 g. of iodine in 200 ml. of water containing 10 g. of potassium iodide. This solution may be used in this concentration for making iodoform tests. When used for the detection of starch, a portion of the solution should be diluted to 10-25 times its original volume.

Potassium Mercuric Iodide. Dissolve 14 g. of mercuric chloride and 50 g. of potassium iodide in 1 liter of water.

Millon's Reagent. Ten grams of mercury are dissolved in 20 ml. of hot concentrated nitric acid and the resulting solution is diluted with 30 ml. of water.

Ammoniacal Cuprous Chloride. Ten grams of cuprous chloride are dissolved in 100 ml. of concentrated ammonium hydroxide and the solution diluted to 500 ml. If solid cuprous chloride is not at hand it may be prepared as described in Experiment 59. The precipitate of cuprous chloride there formed is removed by filtration and dissolved in ammonium hydroxide.

Lucas' Reagent. Dissolve 136 g. of anhydrous zinc chloride in 105 g. of concentrated hydrochloric acid, with cooling.

2,4-Dinitrophenylhydrazine Reagent. Three grams of 2,4-dinitrophenylhydrazine are dissolved in 15 ml. of concentrated sulfuric acid, and this solution is then added, with stirring, to a solution of 20 ml. of water in 70 ml. of 95 per cent ethanol. The mixture is stirred thoroughly and filtered. The filtrate is used as the test reagent.

Periodic Acid Reagent. Dissolve 0.5 g. of paraperiodic acid (H_5IO_6) in 100 ml. of distilled water.

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