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LABORATORY PRACTICE OF ORGANIC CHEMISTRY



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LABORATORY PRACTICE

OF

ORGANIC CHEMISTRY

BY

G. ROSS ROBERTSON

Associate Professor of Organic Chemistry in the University of California at Los Angeles

NEW YORK

THE MACMILLAN COMPANY

1937

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PREFACE

The main feature of this volume is an unusually extensive, but informal treatment of the principles underlying laboratory manipulations in organic chemistry. Part I consists largely of this theoretical material. Part II deals with synthetic experiments and a few examples of elementary qualitative and quantitative analysis. Essential explanations of principles are thus kept distinct from directions for experiments which a given instructor may not wish to use. Cross references are provided, however, in both parts. Sufficient experiments are included to cover the needs of a year course, with many options for superior students.

There is apparently a growing dissatisfaction with laboratory courses dealing only with organic preparations. One leading American university recently announced a substantial cut in this type of work. Another has completely eliminated synthesis from certain life-science curricula. The time thus saved is being devoted to qualitative and quantitative analysis, which in the opinion of the authorities concerned offer greater values in chemical training.

The author feels that this disparagement of organic synthesis really arises not from any inherent fault in the kind of work, but rather from inadequacy of class discussions of the principles governing such experimentation. Many of these principles may, to be sure, be found in somewhat abstract form in courses of physical chemistry—which many students unfortunately never reach. Although branded as elementary physical chemistry, this theoretical material is after all best illustrated in the organic laboratory. Phase changes and the acid-base relations are particularly good examples. In the author's laboratory, therefore, extra time is scheduled for lecture-discussions, and somewhat less for laboratory manipulation. Without apology the author frankly admits that portions of the text are beyond the mental reach of mediocre students; for example, the Duclaux analysis and the distinction between melting range and melting point.

But few experiments of the so-called "introductory" type, requiring no organic theory, are included. These few deal with

real, natural laboratory problems, such as calibration, melting point, empirical formula and the dehydration of alcohol. Special class exercises with artificial mixtures of substances are not favored. These arbitrary exercises do not command the respect of superior students, who repeatedly tell the author that they prefer to learn about a method in a place where that method is actually a part of a recognized synthetic procedure. Comparatively little space is devoted to test-tube experiments, which are perhaps best handled in lecture demonstrations or qualitative analysis. Experiments leading to definite exhibits, whether of preparations or analytical reports, are taken by students much more seriously than tests which end in the scrap jar or sink. Furthermore, they are much more easily administered by a busy instructor with laboratory assistants of varying competence.

Along with well-rehearsed old favorites a few novelties, such as the decarboxylation experiment, are offered; also several syntheses requiring especially good technic, such as propionaldehyde, methylmalonic acid, and particularly α-hydroxy-α-methylbutyric acid. The considerable use of toluene derivatives provides not only a combination of aliphatic and aromatic reactions, but also a more diversified experience with crystallization and reduced-pressure distillation than one gets with simple aliphatic compounds. Attention is called to notes on selection of experiments, and lists of supplies, in the Appendix, pp. 316, 317 ff.

Questions, problems and a number of equations have been included in both parts I and II. Occasionally representations of reactions are left incomplete, particularly where the balancing of an equation is of importance. In directions for preparations frequent use is made of molal and normal instead of simple metric units of quantity, again with the purpose of directing attention to the fundamental basis of calculation. Incidentally this policy aids in avoiding errors due to oversight of water of hydration, dilution of commercial reagents, etc., if bottles are properly labeled.

The author wishes to thank his colleagues in the chemistry department, and particularly Messrs. Wm. G. Young and C. Ernst Redemann for valuable suggestions and assistance in conducting trials of laboratory directions by students. Acknowledgment is also given of assistance by numerous students, both in

proposing and testing procedures. Recognition is also given of suggestions from well-known laboratory manuals, especially the valuable works of Adams and Johnson, Adkins and McElvain, L. F. Fieser, and Oliver Kamm.

G. Ross Robertson

Los Angeles, California
April, 1937

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PART I

CHAPTER I

INTRODUCTION

1. A student of general inorganic chemistry is likely to assume that a chemical reaction will go or stop of its own accord, without much relation to his own watchfulness. He has found, for example, that sodium hydroxide, a typical inorganic compound, reacts with sulfuric acid promptly and effectively whether his technic be good or bad. All that he needs is an adequate supply of the raw materials.

When this same student begins the study of carbon compounds he may never suspect that ethyl alcohol, an organic compound, will not always react with sulfuric acid exactly as the textbook portrays without special personal attention.

Perhaps it has never occurred to him that a mixture of reacting organic compounds might give him not half, possibly not one-tenth of the quantity of product called for by chemical arithmetic. He may not have foreseen the possibility of a rival side-reaction which would steal his raw materials and divert them to useless ends. Such conditions are of course matters of great concern to practical chemists. To the manufacturer they may spell the difference between dividends and bankruptcy.

Organic compounds have a peculiar set of habits. Usually they cannot stand high temperatures. Generally they melt and boil at relatively low temperatures. They usually do not ionize to a great extent in solution, and they often exhibit slow reaction rates. These closely related facts demand of the practical organic chemist a special skill in laboratory manipulation which depends on such factors as vapor pressure, melting and freezing phenomena, acidity, solubility, and general stability. With such requirements in view, this book is presented in two main parts: first a critical discussion of the principles of manipulation, and second a list of practical experiments in which many of these principles are illustrated.

It is not only the prospective chemist who is concerned with these practical matters. The physician is constantly handling

ethyl alcohol, ether, phenol and a host of more complex organic substances which are ever ready to play tricks on him if he does not understand their behavior. For example, a medical blunder once cost the life of a patient because the physician did not know how to neutralize the strongly acidic salt of an organic base before intravenous injection.

The modern refrigerating engineer spends much of his time studying the physical as well as the chemical behavior of the volatile organic liquids which circulate in his remarkable machines. The expert in insect control deals constantly with organic vapors, liquids, dusts, sprays and emulsions. The lacquer manufacturer demands an astonishing variety of organic solvents, plasticizers, resins and related carbon compounds. The dietitian probably never really understood the meaning of digestion until she successfully hydrolyzed an ester or an amide in laboratory vessels. The drug manufacturer, the cosmetician, the really expert photographer—all of these keep veritable storehouses of organic chemicals. Even the manufacturer of perfume needs to know the relation of Raoult's Law of vapor pressures to the behavior of his artistic product. Or if one prefer operations on a large scale, he need only turn to the petroleum industry for a comprehensive illustration of the combination of synthesis and analysis of organic compounds with the technic of distillation, filtration, clarification, drying, etc.

The Significance of Laboratory Workmanship

2. One does not learn the fundamental methods of the petroleum engineer, lacquer manufacturer or dye chemist merely by the simple mixing of reagents in test-tubes. A more practical program is desirable. In general, therefore, the student in this course is expected to present at the conclusion of each assignment a finished chemical product. A satisfactory yield of material of good quality thus affords one test, but by no means the only test, of laboratory workmanship.

A beginner, preoccupied in the task of following directions slavishly, may only too easily miss the point of these laboratory studies. Sometimes one may obtain acceptable results, particularly from the fully-described introductory experiments, without thorough knowledge of the underlying principles. In the long run, however, no real skill is acquired from such experimentation

unless the student *knows what he is doing and why.* The worker who cannot outline clearly the main reaction of the experiment going on before his eyes reveals himself to be a mere cookbook operator. When he is later confronted with inadequate directions, or entirely new problems, he is helpless. Furthermore, the very fact that he does not understand what he has been doing often makes it difficult or impossible for the instructor to diagnose his troubles.

The good workman makes mistakes also. Knowing what he is doing, however, he can either help himself, or give the instructor intelligible evidence upon which useful advice may be formulated.

The above doctrine of preparedness for laboratory work is taken so seriously in some institutions that a student is actually not allowed to withdraw necessary supplies from stock, or start work, until he has demonstrated in an oral or written quiz that he understands what he is about to do. Such a plan has much to commend it, if unreasonable delays and inconvenience can be avoided.

It is an open secret that the laboratory instructor in organic chemistry often identifies a good workman by discovering *clean apparatus, neatly assembled, on a clean laboratory desk.* To be sure, one could deliberately perform a satisfactory synthesis in disorderly surroundings. Experience shows, however, that in actual practice neither good quality nor quantity comes from slovenly experiments.

CHAPTER II

GENERAL LABORATORY REQUIREMENTS

NOTE. *The following details of general procedure apply to courses given in the author's laboratory. In view of differences elsewhere, follow only those sections of this chapter specified by your instructor.*

3. Notebooks. Each student keeps a bound notebook of adequate size (about 8″ x 10″). Loose-leaf books are not admissible. Such a requirement is merely in keeping with the standard practice of industrial and commercial laboratories as well as academic institutions. An original record of performance is desired, including reports of troubles as well as successful syntheses. "Write-ups" done at home after experiments are completed are discounted. In commercial practice, a chemist who would be naïve enough to offer such a write-up of his discoveries in a court of justice, for example in a patent case, would probably have his contribution thrown out of evidence. Mistakes should be frankly so marked in the notebook; they should be discussed if necessary, and the correction recorded properly. Do not tear out sheets carrying unsatisfactory data; this merely suggests that you have untidy habits of writing records.

The notebook should contain a systematic record, preferably done in ink, of all equations, quantities of materials used and produced, all numerical values which were used or determined, all essential calculations, and any critical comments which might be of value to one repeating the work. Optional additions to this record include answers to questions, and least important of all, pictures and abbreviated laboratory directions. The really competent laboratory worker examines the whole experimental procedure in advance, and plans his notebook entries so that there will be room for all data, particularly those in tabular form. Such a notebook is readily followed by a chemist, although there is no necessity of explaining details so fully as to satisfy a novice in organic chemistry.

4. Card Reports. When a synthesis or analysis is complete, and the notebook work is finished, the student is asked to write

a very brief summary of his results on a common office filing card (4 by 6 inches). This card report, together with the bottled organic preparation in case of synthesis, is exhibited to the instructor. If the work is accepted, the instructor merely retains the card as a record for his private files, without being troubled by the tedious clerical work of recording, one by one, the individual experiments as they are submitted. The bottled preparation is retained by the student unless instructions to the contrary are given.

When a synthesis is completed, and there is no further question of laboratory work with it, do not occupy the time and attention of the instructor or assistant with it unless the appropriate written work is done. No credit is given for chemical products without notes indicating thought upon the subject.

An example of a card report is the following:

Assignment No. 3 *John B. Smith*

ETHYL BROMIDE

$$C_2H_5OH + NaBr + H_2SO_4 \rightarrow C_2H_5Br + Na^+HSO_4^- + H_2O$$

Calculation based on 80 g. (80/103 mole) of NaBr:

$\frac{80}{103} \times 109 = 84.6$ g. Theoretical Yield

65 g. Actual Yield

$\frac{65}{84.6} = 76.8$ Percentage Yield

Boiling Range, 38–40°.

Please write number, name and title in the uniform positions indicated above, for convenience in examination of files.

5. The Finished Product. Not only should organic preparations be freed from recognized impurities, but they should be dry. Cloudiness in liquid preparations is usually evidence that the drying process was not properly conducted. Such cloudy liquids after a few hours often give up their emulsified water to the glass of the container. There will then be scattered water-globules upon the walls of the bottle, leading to the false impression that

the bottle had not been properly dried in the first place. Solids which have not been properly dried usually cling to the side walls of the bottle.

6. Use of Bottles. The standard of workmanship in preparing, bottling and labeling is exactly that of a good pharmacy. Liquids are invariably stored in narrow-mouthed bottles, solids in wide-mouthed. Preparations in the wrong type of bottle will not be accepted. Labels should be written or printed neatly in ink, and properly attached to the upper part of the bottle. A label should show the name of the student as well as the name of the preparation. There is no excuse for misplaced, pencil-scrawled labels at any time.

It is desirable to weigh the empty labeled bottle before adding the finished preparation. This so-called "tare weight" is entered on the label. One may then readily determine the net contents of the bottle at any future time regardless of partial use of the contents.

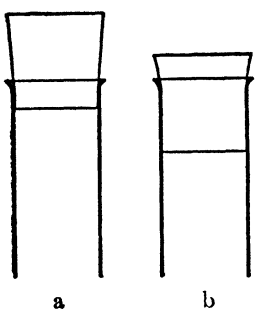


FIG. 1. FITTING OF CORKS

7. Cork Boring. Select a cork of ample size, as suggested in Fig. 1 a. Roll it in a cork press until it is decidedly softened, and so that it will fit deeply and securely as represented in b. Do not attempt to bore a hole until the rolling operation is finished. The standard tubular brass cork borer may now be employed.

The size of the circular cutting edge of the cork borer should, if possible, approximate the outside diameter of the tube which is to be inserted. In the less frequent cases where a rubber stopper is acceptable, a slightly larger borer may be required. It is advisable to sharpen the borer every second or third time it is used. Following the operation illustrated in Fig. 2, take care that there should not be too great a pressure applied at *A*, lest the cutting edge of the borer be nicked; nor at *B*, lest the cutting circle be burst.

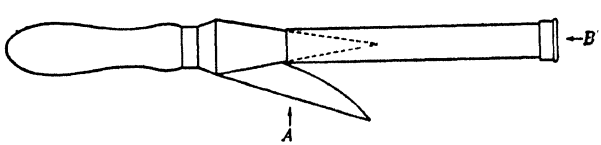


FIG. 2. SHARPENING A CORK BORER

Wet both borer and cork. With a continuous rotary motion, cut a hole beginning at the small end of the cork. As the borer advances through the cork, examine the tool three or four times to see that it is cutting a straight hole without slant. If much resistance is encountered, remove the borer and lubricate it with soap solution, or even with water. After the tool has been driven about half way through, finish the operation by either of the following methods, (*a*) or (*b*):

(*a*) Remove the borer from the hole, and bore from the other end of the cork. If the two holes are carefully aligned, a neat aperture is assured, with no torn or burst sections.
(*b*) Stand the cork upon an old cork, and continue the boring process until the opening is clear.

Do not press the borer into the desk or other hard object. Should the cutting edge be driven even once firmly against hard wood, it will require a special sharpening of the borer on a lathe to restore its normal efficiency.

An experienced worker, equipped with a well-sharpened borer, often completes the boring operation without reversal while the cork is held in the open between the thumb and two fingers. Only with care is it possible to make a complete clean cut without tearing the edges of the cork.

It would be surprising to many students to learn how readily vapors escape through crudely bored corks, and thus why yields of preparations often fall to low values.

Cleaning and Drying Glassware

8. Use of Solvents. A newly soiled beaker or flask is often easily freed from foreign matter by simple rinsing. Even in cases where both water and a freshly produced oily or tarry material are in contact with glass one may often eliminate the organic contamination promptly, since the glass is preferentially wetted by water rather than by tar. If through delay the water is allowed to evaporate, the tar reaches the actual glass surface and adheres tightly.

If practicable use the appropriate solvent on a soiled vessel before resorting to the official "cleaning solution." Inert tars of a hydrocarbon nature may often be loosened and removed with cleaning solvent, benzene or the like. Basic tars, as from preparations of the aniline type, may sometimes be removed with

hydrochloric acid. Acidic tars, such as phenolic residues, are handled with caustic soda solution. Many tarry impurities of the slightly oxidized type are often removed effectually with the aid of acetone. Frequently common soap solution is best of all.

9. Use of Abrasive Washing Powder. A high-grade household washing powder, commonly available in a sifter can, is very useful in cleaning laboratory vessels to which access with cloth or brush is possible. Punch only one hole in the top of the can, so that the powder may be directed into a narrow-mouthed vessel without spilling. Such a powder should have as its abrasive agent some material like volcanic ash which is not hard or coarse enough to scratch glass readily.

Ordinarily washing powder is mixed with a little water and rubbed on the soiled surface, as in household practice. In the organic laboratory, however, a different situation arises when a beaker or dish is very much soiled with a viscous, adherent tar. One may then substitute for the water a small amount of a volatile tar solvent of appropriate type, such as benzene or acetone. The paste of powder and solvent, including a large proportion of the former, picks up the offending impurity and buries it in the mealy, earthy mass. The solvent may then be allowed to evaporate without disadvantage. Water, preferably warm, will then join with the alkali or soap in the powder, disperse and remove the accumulation, leaving a clean vessel.

10. Chromic-Sulfuric Acid "Cleaning Solution." A mixture of chromic acid with concentrated sulfuric acid, whose preparation is described in § 176, is widely used for cleaning apparatus soiled with greasy or tarry matter, on account of its effectiveness both as "reaction solvent" and oxidizing agent. Its application is as follows: The soiled vessel is first washed with water should there be any possibility of soluble organic matter being present. If this precaution be neglected, and an appreciable amount of reducing substance such as alcohol be present, the entire supply of cleaning solution will be ruined the first time it is used. Such an outcome will be indicated by the change in color from reddish brown to dark green.

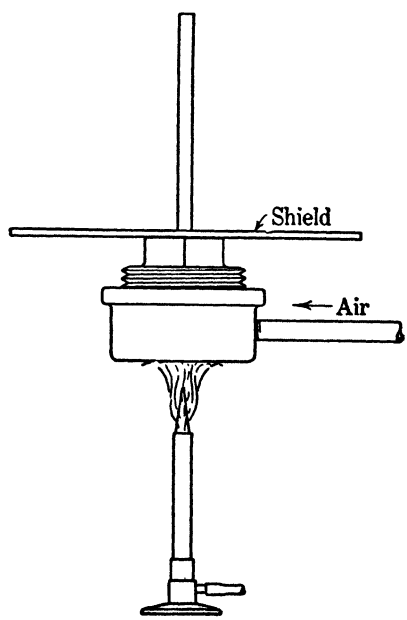
An ample supply of the cleaning solution is poured into the vessel to be cleaned. After care has been taken to wet all soiled surfaces with the acid, all but about 5 cc. is poured back into the stock bottle. The residual solution in the vessel is cautiously

diluted with about 5 cc. of water. The resulting heat of dilution, concentrated in a small volume of cleaning liquid, aids in a thorough cleansing of the glass surface. The vessel may now be washed and set away to dry.

11. Troublesome Cleansing Problems. Frequently the impurity has been scorched until it is largely tarry carbon, insoluble in all solvents. It is not removed by the simple treatment above described. If the vessel is a Pyrex flask it may safely be cleaned by the following more drastic method:

Place about 1 g. of sodium or potassium dichromate and about 5 cc. of cleaning solution in the flask. Heat over a bare flame, spreading the flame evenly, until the acid fumes strongly. Under such circumstances the hot chromic and sulfuric acids will oxidize even pure carbon itself.

12. Use of Chemical Knowledge in Cleaning Apparatus. For example, do not use chromic acid mixture to remove inorganic impurities, or contamination which cannot be oxidized. The stock example of foolishness is seen when one tries to remove the slaked lime from his absolute alcohol apparatus with chromic-sulfuric acid. The sulfuric acid, instead of helping to get rid of the lime, produces a mass of almost insoluble calcium sulfate which makes more trouble than ever. The chromic acid in this case is simply useless, since one cannot oxidize slaked lime.



HOT-AIR DRIER

13. The Drying of Glassware. In usual practice newly washed glassware is merely set aside in an inverted position and allowed to dry spontaneously. If immediate results are desired, the hot-air blast may be employed. A current of compressed air is led through a small cast-iron device heated with a Bunsen burner, as shown in the accompanying figure.

The air coming from such a heater is at a temperature varying from 150° to 200° C., and is effective in ridding flasks, condensers, etc. of water.

Pyrex ware may be dried upon the hot-air drier without special precautions. Ordinary glassware, on the other hand, occasionally cracks under such severe treatment. Test tubes, condenser tubes and adapters will usually survive the operation, but bottles should receive special attention. The outlet from which the hot air issues should never be allowed to approach closely to the side wall, or the bottom, of a bottle. Dropping funnels, separatory funnels, or similar ware carrying stopcocks *should never be heated* on the hot-air drier!

Use of Special Solvents. The above drying process may be hastened by rinsing of the vessel with alcohol before introduction of heated air. If cheap tax-free alcohol is not at hand, acetone is an excellent substitute. On account of its high volatility, acetone is actually superior, but suffers greater loss by evaporation and thus in general practice is expensive.

Organic laboratory workers frequently keep at hand a bottle of "wash alcohol" or "wash acetone," the contents of which are poured into successive vessels and then back into the bottle just before the vessels are dried. Care is taken not to use the wash solvent until the vessel is thoroughly cleansed from all impurities save those occurring naturally in the wash water. Residual water is now drained as completely as possible from the vessel, so that the wash solvent will not be diluted more than is absolutely necessary.

Warning. A fire or explosion hazard should be noted when a flask, rinsed with a volatile, inflammable solvent, is placed on the hot-air drier. As shown in the illustration, the heater is provided with a large asbestos board shield which prevents an explosive solvent-air mixture reaching the flame under the heater.

14. Drying by Evacuation. If no air heater is available, the vessel may be dried by cautious heating over a flame, followed by withdrawal of the hot moist air from the vessel with the aid of an aspirator. If a pump, or compressed air service is at hand, the moisture may instead be blown out.

15. Ovens. Where the expense and space can be allowed, steam-heated ovens are ideal for the drying of laboratory glass-

ware. The shelves in such ovens are made of coarse metal screen, in which the various vessels may be held in an inverted position until dry.

None of the above procedures yields really dry glassware, unless conducted under extreme desert conditions. When glass is cooled in ordinary air it accumulates hygroscopic moisture. In cases where extremely dry apparatus is essential, air should be passed through calcium chloride and then allowed to replace the ordinary air present in a newly heated and dried vessel.

CHAPTER III

TEMPERATURE CONTROL

Measurement of Temperature

16. Ordinary chemical thermometers are subject to errors of a degree or more, due to inaccuracy in calibration, irregularities in bore of tubing, or to changes in the glass subsequent to manufacture. Corrections may be made with sufficient accuracy for use in the elementary organic laboratory with the aid of water and naphthalene, two substances readily obtainable in a high degree of purity. In the experiment "Calibration of a Thermometer" (see § 178) these substances are used in boiling- or melting-point determinations intended to test the 0°, 100° and 218° marks on the thermometer.

17. Calibration by Transition Temperature. Anhydrous sodium sulfate (Na_2SO_4), Glauber's Salt ($Na_2SO_4.10H_2O$), and water cannot exist in one mixture under ordinary laboratory conditions except at the temperature of 32.4° C. Should heat be added to this system, the following reaction proceeds to the right.

$$Na_2SO_4.10H_2O + \text{heat} = Na_2SO_4 + 10H_2O$$

Should heat be withdrawn, the reverse reaction occurs. The temperature cannot rise or fall as long as all three components are present. If a thermometer be inserted in the mixture, it will soon register the constant temperature and thus any possible error at the 32.4° mark is revealed. For this purpose 25 to 50 grams of the slightly moistened decahydrate, gently heated until partially dehydrated, provides the equilibrium mixture cited in the equation above. The mixture, in the form of a thick slush, is well stirred with the thermometer under investigation.

Other standards are cited by Adams and Johnson (§ 170, Ref. 17).

18. Stem Correction. When a portion of the mercury column of a thermometer is not actually in the region heated to the temperature we are measuring, the reading will naturally fall below the true value, even though the calibration of the thermometer be absolutely correct for complete immersion. It becomes necessary to add a correction value to show how much higher the

protruding mercury column would rise if it were actually heated to the temperature of the medium under investigation.

The following formula yields the desired correction:

$$N(T - t)\ 0.000154$$

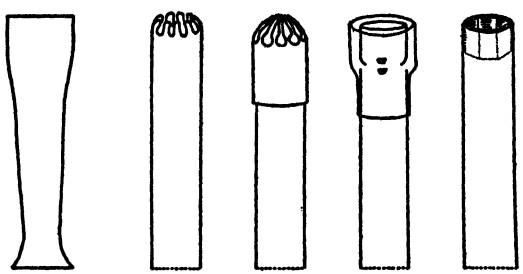
in which N is the length of that part of the column which actually protrudes from the region of heating (most conveniently measured in degrees); T is the (approximate) temperature of the thermometer bulb; t is the (approximate) average temperature of the protruding column; and 0.000154 is a constant, which is the coefficient of expansion of mercury in glass.

Neither N, T nor t can be precisely measured, but are estimated within 5 to 10 degrees. Such apparent inaccuracy is not serious, as shown in the following example.

A certain preparation of aniline boils at 182° (uncorr.). The temperature of the air is 30°, shown by a second thermometer hanging above. The bottom of the cork stands at the 90° mark.

$N = 182 - 90 = 92$	or approximately 90°
$T - t = 182 - 30 = 152$	or approximately 150°
$90 \times 150 \times 0.000154 = 2.08$	or approximately 2 degrees correction

The boiling point of this aniline preparation is thus estimated, with accuracy sufficient for ordinary laboratory work, as 182 + 2 or 184°.

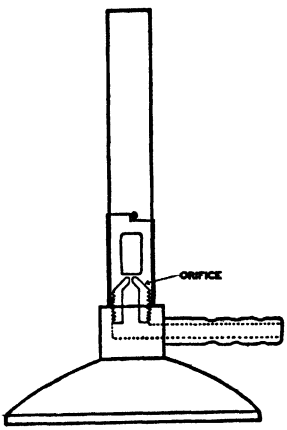


Courtesy *Journal of Chemical Education*

IMPROVED BURNER STACKS FOR USE WITH NATURAL GAS

19. Burners. Laboratory workers using artificial gas need have little concern about the type of burners used. The large fraction of free hydrogen in such domestic gas makes stable, hot flames easy to produce.

Western operators, using natural gas, encounter much trouble with the conventional Bunsen or Tirrill-type burner with 7/16-inch stack (vertical tube). Methane, of which natural gas largely consists, burns so slowly that the rapid current of gas in a narrow stack blows the flame out on the slightest provocation. In such cases a burner should be selected which has not only a stack of wider bore (1/2 to 5/8 inch), but also a device at the top to prevent blowout. The gas orifice in the base of the burner should be of specially small diameter. An over-size, dirty or improperly directed orifice is the usual cause of the "soft," inefficient blue, or even yellowish, flame often obtained from a defective burner in spite of good ventilation at the air-ports. Further details are given by the author in the *Journal of Chemical Education*, 9, 1963 (1932).

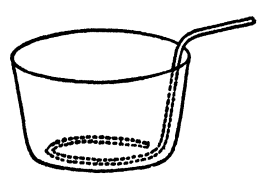


Courtesy *Journal of Chemical Education*

BUNSEN BURNER

HEATING BATHS

20. Water or Steam Baths. It is frequently desirable to heat a laboratory vessel to temperatures up to 100° C., without risk of running to higher temperatures. If steam-cones, copper water baths or like special devices are not at hand, ordinary sauce pans or open kettles will serve. Where no fire hazard is involved, a pan may be heated over the gas flame. If inflammable liquids are to be heated in a vessel placed in the water bath, the introduction of steam from piped laboratory service is to be recommended. The steam is led through a piece of commercial 5/16-inch copper tubing about 20 inches, or 50 cm., long. The tube is bent into the form of a loop as shown in the accompanying illustration. The entering steam, encountering the cold copper tube, condenses quietly without the disturbing noise produced when the steam enters through a tube of poorly conducting material such as glass or rubber.



STEAM-HEATED WATER BATH

Baths for Higher Temperatures

21. Sand Bath. For controlled temperatures above 100° material less volatile than water must be chosen. In many laboratory directions written in Great Britain and on the Continent, the sand bath is often prescribed. Such a bath serves well as a support for the relatively fragile Bohemian and German flasks which were formerly the best available. Students using the more substantial borosilicate or Pyrex ware should always consider the substitution of more convenient methods.

The principal shortcoming of the sand bath is seen in its lack of flexibility of control. When the sand bath becomes too hot, it may of course be removed; but it is not easily restored to position when needed again.

22. Fusible-Metal Baths. Much better than the sand bath is the fusible-metal bath. In this arrangement a low-melting alloy is placed in a hemispherical iron bowl, and the flask is partially immersed in the fused metal. Unfortunately this neat method is too costly. In a low-melting alloy it is necessary to use a large fraction of bismuth, which is both expensive and of high density.

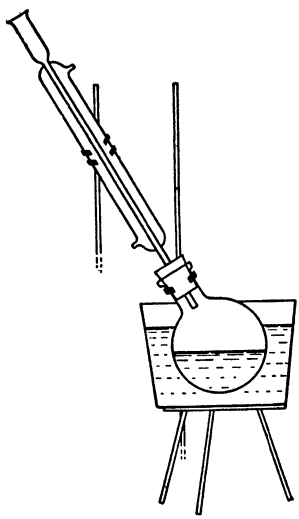
23. Oil Bath. Oil serves as an inexpensive substitute for fusible metal. For this purpose solid, hard-hydrogenated cottonseed oil, and technical stearic acid are serviceable, the former being slightly preferable. Common (liquid) vegetable oils, such as cotton, corn, rape seed and olive, are almost as satisfactory in performance, but are not so easily preserved when out of service. Petroleum products such as paraffin wax or lubricating oil are undesirable or even dangerous. Either they have high vapor-pressures, as with paraffin, or if not so volatile, they are tarry and messy. The vegetable oils will not take fire under 300° C., whereas paraffin will ignite and give a dangerous conflagration far below that temperature.

Hard cottonseed oil, heated to high temperatures, soon turns to a chocolate hue, and becomes opaque. Such discoloration does not ruin the material. Students are cautioned not to throw away any oil-bath material without consulting the storekeeper.

For baths used in melting-point apparatus, see § 136.

24. Reflux Condenser. The act of boiling a liquid reaction mixture accomplishes two desirable aims, namely, increase of

reaction rate through elevation of temperature, and agitation, which is required if the mixture be not completely homogeneous. A reflux or return condenser is attached to prevent loss of volatile material while the reaction proceeds.



REFLUX CONDENSER

As almost evident from the accompanying illustration, particular care should be taken to roll and bore the cork properly, lest there be serious loss of vapors in a prolonged experiment. The lower end of the condenser tube should project 2 cm. or more below the stopper, but not down into the body of the flask.

A vertical mounting of the condenser is of course more convenient than the oblique position as pictured. Unfortunately the recondensed liquid often does not drain back promptly in such a position. A considerable column of liquid accumulates, and may be blown entirely out of the top of the apparatus. An inflammable liquid thus blown out falls directly upon the flame, and a fire is certain. Even relatively safe solvents like toluene (C_7H_8, boiling-point 111°) become dangerous under such misuse.

In cases where the refluxed liquid boils above 150°, an air-cooled condenser may be employed. A Liebig condenser not served by a stream of water is not a substitute for the simple air-cooled device. Its empty outer jacket would serve as a heat insulator rather than as means for cooling.

QUESTIONS

1. Calculate the thermometric stem correction for a case where a liquid is being distilled under the following conditions: bottom of the cork at the minus-10° mark; reading of the thermometer 105°; temperature of the air outside 35°.

2. Suppose that the outfit mentioned in question No. 1 were operated at reduced pressure, resulting in a thermometer reading of 5° instead of 105°. Calculate the stem correction.

3. Give two reasons why stem correction is more important in the distillation of high-boiling liquids than with low-boiling liquids.

4. In which case do you think the water-cooling of a condenser is more efficiently carried out, when the condenser is attached in the normal position for distillation, as in Fig. 1, § 25, or in the reflux position? Why?

5. Why should a burner with a small orifice give a hotter flame than one with a larger opening for gas?

6. Which do you think would be the more efficient type of heating bath for temperatures under 100°, the water bath or oil bath? Why?

CHAPTER IV

ISOLATION AND PURIFICATION OF A LIQUID SUBSTANCE—PRACTICAL METHODS

Technic of Simple Distillation

25. Simple distillation from a flask through a condenser is illustrated in Figs. 1, 2, 3. Several details of technic should be noted:

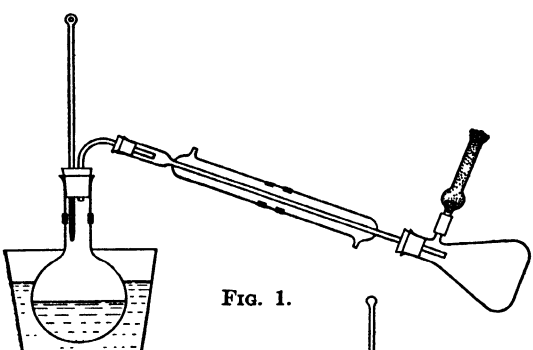


Fig. 1.

Apparatus for Distillation

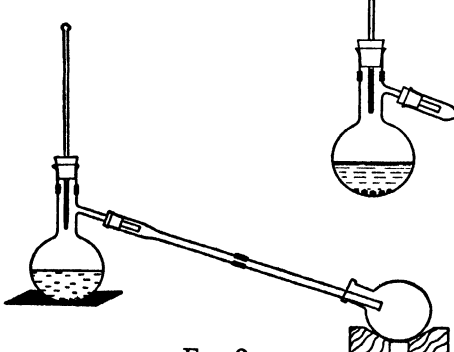


Fig. 2.

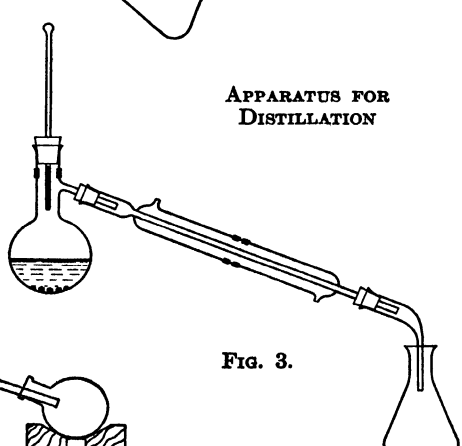


Fig. 3.

All clamps or rings which are directly attached to the glassware should stand at right angles to the desk front. The thumbscrew holding each ring should be directly behind the vertical rod

support. No oblique angles should be required until the final adjustment of the flask and condenser is made to the point of delivery.

The common practice by the novice of clamping a distilling-flask tightly and then trying to fit its side-stem to an unsupported condenser frequently ends in grief. The side-stem snaps off. Flask and condenser should be independently clamped in as nearly as possible the correct position—then slipped together to a proper fit.

Pieces of rubber tubing should be fitted upon the jaws of clamps which are to hold glassware. Inasmuch as rubber is easily damaged by heat, such glassware, particularly the boiling flask, should be clamped at the coolest place that is practicable.

Fire Hazards in Distillation

26. Inflammable Solvents. Liquids which introduce fire hazards during distillation may be divided roughly into three classes.

(*a*) *Diethyl Ether, Petroleum Ether, and Carbon Disulfide.* These solvents, with boiling points below 50°, are dangerously inflammable. No flame whatsoever is permissible under or near the distilling apparatus. Even a flame as much as ten feet distant may ignite ether if a continuous table-top lies between the flame and the exposed ether, and a gentle draft is blowing in the appropriate direction.

Use either piped steam service, or bring a supply of boiling water from a distance. In research operations, or wherever the expense is warranted, special electric hot plates, in which the heating elements are thoroughly covered, may be used to distil ether. With carbon disulfide even a hot plate is not permissible. Only steam may be used; see § 81.

Ether which has stood for some time may contain an explosive impurity; see § 69.

(*b*) *Benzene, Ethyl and Methyl Alcohols, Di-isopropyl Ether.* These solvents, intermediate in volatility between ordinary ether and water, may of course be distilled most safely by the method described in (*a*) above. The piped steam service, however, may be replaced by a gas-heated water bath. An outfit similar to that shown in Fig. 1, § 25, is used, but the calcium chloride tube is replaced by a length of gas hose. The open outer end of this hose

is allowed to hang over the edge of the desk. If through oversight, or failure of condenser water service, the inflammable vapors are not properly condensed before entering the receiver, they escape from the hose at a point where ignition is unlikely. Methyl alcohol (b. pt. 65°) and di-isopropyl ether (68°) deserve special care of this kind.

Unfortunately the steam bath, while satisfactory for distillation of the above solvents when they are in a comparatively pure state, is often not adequate for complete expulsion of these liquids from their mixtures with less volatile liquids. For example, in later situations the need will arise for elimination of di-isopropyl ether from extracts. For example, see aniline, § 264. In such a case the boiling point of an ethereal extract of such a liquid will gradually rise from its initial value near 68°. Before the ether has all passed over, however, the temperature approaches 100° so closely that distillation practically ceases. It is now necessary to change from steam heat to the gas flame. Before this change is made, however, the main yield of recovered ether, already in the receiver, is removed to a safe distance and placed in a stoppered bottle.

The steam bath is now replaced with wire gauze, and a gas flame applied to the distilling-flask. Any possible fire from this point on cannot be very serious, since the residual ether is of small consequence.

(*c*) *Toluene* (*b. pt. 111°*). Inflammable solvents with boiling points above 100° of course cannot be distilled from the steam bath. In a case like that of toluene, a Pyrex distilling-flask, immersed in an approved oil bath, may be employed, preferably in fire-proof quarters. The flask is connected to the water-cooled condenser, stoppered filter-bottle and rubber tube hanging from the desk, as described in (*b*) above. The oil bath is of course gas-heated.

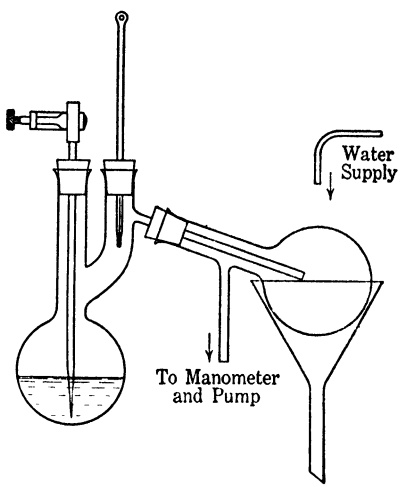
With such an outfit the danger of cracking and downfall of the distilling bulb and its inflammable contents is practically nil. Ordinarily an oil bath will not cause the "scorching" and sticking of organic matter and consequent cracking of glass (see § 64). Admittedly there is still chance for a big fire in case of gross carelessness, but not such a personal hazard as would exist in a case where flaming toluene fell upon the table and splashed. If he must distil quantities of such a solvent, the student is warned

that he should make sure of the location of fire extinguishers before starting operations.

Distillation under Reduced Pressure

27. In view of the hazard of collapse of an evacuated flask, goggles or stout wide-rimmed spectacles should be worn during a reduced-pressure distillation. Particular care is also taken that there be not the slightest crack or other defect in the distilling flask. Flat-bottomed flasks are of course not admissible in such procedures. Pyrex ware is particularly desirable.

The two-necked "Claisen" flask is commonly used for reduced-pressure distillations, in order that both a capillary air-tube and a thermometer may be used. An ordinary distilling-flask may also be employed; but in such case a two-holed rubber stopper or some other makeshift is required.



Apparatus for Reduced-Pressure Distillation

A capillary glass tube is introduced into the neck of the Claisen flask. This tube is prepared with the aid of a large blast-lamp flame in such a manner that it has an extremely small bore, but a substantial external diameter. A piece of common 6- or 7-mm. glass tubing is heated, with continuous rotation, until a section of several centimeters' length has become soft. Under these conditions the tube shrinks to a small thick-walled capillary. At this point the tube is drawn out until its external diameter is about 0.5 mm., and the internal diameter as small as possible.

When properly installed with its tip almost at the bottom of the flask, the capillary tube introduces the constant supply of air bubbles needed for prevention of bumping. At the same time, the air current is so small that it does not seriously interfere with maintenance of low pressure in the flask. If the air current is too

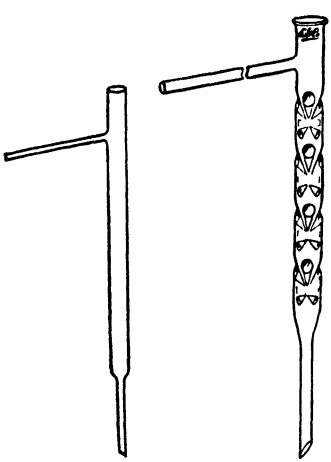
large, it may be controlled by the attachment on the outside of a piece of fresh soft rubber tubing fitted to a Hofmann screw clamp.

The side-stem of the flask should pass well into the bulb of the receiver to prevent diversion of uncooled vapors directly into the manometer and pump. The outside of the receiver should be gently scrubbed with household abrasive washing powder just before the distillation is started, so that the stream of cooling water will cling to the glass and spread properly over its entire surface.

If rubber stoppers of good quality are available, one may replace the flask type of condenser as shown in the illustration with the conventional Liebig condenser. In such case of course a filter-bottle or distilling-flask is attached to the end of the condenser. The resulting outfit will somewhat resemble that shown in § 228 for acetyl chloride.

The Claisen flask should always be heated by an appropriate bath rather than over the wire gauze. Either the water bath, for use at lower temperatures, or the oil bath for higher temperatures, should be employed. Bumping is minimized in the more uniform heating possible by such procedure.

Fractional distillation at reduced pressure requires peculiar apparatus, described in more advanced works of practical organic chemistry. See Gattermann-Wieland, Lassar-Cohn, or Houben, for details.



FRACTIONATING COLUMNS

For a discussion of the theory of reduced-pressure distillation see § 38.

28. Distillation with Fractionating Column. The column, which usually has the general form represented in the illustration, is fitted to the flask with a cork stopper. In cases where cork or rubber would be attacked seriously by the boiling liquid, tinfoil or leadfoil may be used to cover the cork. Where this provision is unsatisfactory, as with strongly acid mixtures, a substitute stopper may be constructed from asbestos and sodium silicate. Best of all—though expensive—is the ground-in glass stoppered

connection, available now in standard interchangeable form from the manufacturers of both Pyrex and European laboratory ware.

The mercury bulb of the thermometer should of course be just below the delivery stem of the column. Care should be taken, however, that the thermometer be not thrust down far enough to collide with the packing material of the column. In the case of the Vigreux column one may only too easily knock off one of the delicate inner tubes, or indentations, and perhaps entirely ruin the column.

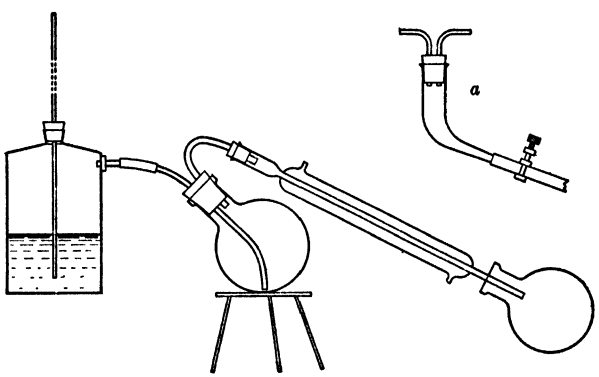
An irregular piece of glass is ordinarily put in the bottom of the Hempel column to prevent the beads from dropping through. Some Hempel columns, on the other hand, have indentations at the base which render the separate glass piece unnecessary.

Ordinarily the operator watches a distillation rather closely and continuously in order that the rate may be kept low without entire suspension of production of distillate. In this way the sharpest separation is afforded. In extreme cases the burner is continuously manipulated so that the rising vapors in the column barely reach the side-stem, and a very slow dropping of distillate is obtained. This method is employed in our experiment with acetamide in which that substance is freed from water with minimum loss of acetic acid, a liquid slightly less volatile than water (see § 247).

For the theory of the use of a fractionating column, see § 56.

Steam Distillation

29. If a supply of steam is not available in the laboratory, a can or even a flask may be used as a boiler. In such case a small glass



Apparatus for Steam Distillation

tube 50 to 75 cm. in length should be included as a safety valve. When placed in the position shown in the figure, it will show by the escape of steam when the water level in the can falls below a safety line, set about 2 cm. above the bottom. Furthermore the tube serves as protection in case the ordinary outlet from the apparatus should become obstructed for any reason.

The substance to be steam-distilled is placed in the middle flask. By setting this flask at an angle one can prevent to a large extent the splashing of impure boiler liquid into the tube leading to the condenser.

The connecting tubes may well be of large (8 to 10 mm.) glass tubing. This size permits a more rapid passage of steam, and thus a more rapid distillation. Since the liquid is more actively stirred, a better yield ratio is attained. Moreover, the use of large connecting tubes makes it more difficult for liquid, splashed from the impure mixture, to be forced over into the receiver.

If piped steam service is furnished in the laboratory, use the assembly of adapter, tubes and Hofmann screw clamp, as shown in *a* of the figure. This accessory serves as a water trap between the steam valve and the main distilling flask.

For the theory of steam distillation see § 63.

CHAPTER V

ISOLATION OF LIQUID. THEORY

Distillation of a Single Substance

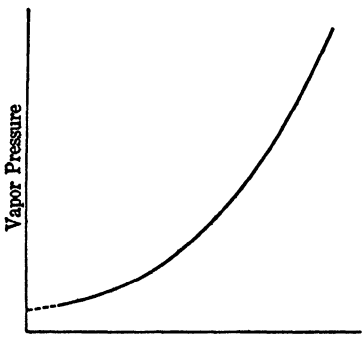
30. When a pure substance is heated it normally shows an increasing tendency to pass into the gaseous state. It is said to exert **vapor pressure.** If the substance is not confined, it should eventually disappear, its molecules escaping from the mass, one by one. If the substance—in the present case a liquid—is in a partly-filled distilling-flask, most of the departing molecules remain in the vicinity, collide with one another, and frequently bounce back into the liquid.

At any given temperature the escaping tendency, and thus the rate of escape of molecules per unit surface of the exposed liquid, are constant. The rate of return, however, grows with increasing concentration of the newly produced vapor. Soon the rate of return just equals the rate of escape, and equilibrium is attained. The vapor pressure becomes constant, and is subject to measurement with a suitable gauge.

If the temperature is now elevated, the rate of escape rises, thus compelling a new and increased vapor concentration. Soon the rate of return again matches the rate of escape, and a new equilibrium is attained. The vapor pressure is greater than before. From experiments of this type thousands of numerical values of vapor pressure for various substances at various temperatures have been determined, and recorded. Examples of these are seen in § 410. While recorded in the literature simply as "vapor pressure," each of these numerical values refers to a vapor pressure at equilibrium.

The air, which originally constituted most of the gaseous material above the liquid in the flask, has gradually been displaced by the new vapor. For example, when liquid and vapor came to equilibrium at the pressure of 100 mm. of mercury, 100/760 of the total vapor was of the new substance, and the residue of 660/760 was air. In this simple calculation the standard external atmospheric pressure of 760 mm. is assumed. In general, the

variable fraction of the total gaseous pressure which is due to one particular species of molecule is called the **partial vapor pressure** of that component under the conditions at hand, without necessity of equilibrium.



VAPOR PRESSURES OF A LIQUID

Further increase in temperature eventually causes the vapor pressure to reach 760 mm. The partial vapor pressure becomes the whole pressure. The air is practically all displaced. Further heating will of course tend to elevate the pressure above 760 mm. Before the pressure exceeds 760 mm. by a measurable amount, however, the vapor will overcome the resistance of the external atmosphere and pour out of the flask.

Since the heating of such a vessel is usually done from below, the bottom of the flask will be the first to reach the maximum temperature, i.e., the point at which the vapor pressure is just about to exceed 760 mm. If now a bubble can be started, a sudden expansion of vapor will occur under the liquid surface. In other words, the liquid boils.

31. Boiling Point. Since a liquid is now being transformed into a gas in relatively large quantity, much heat is absorbed. The temperature no longer rises. On the other hand, it cannot fall even the smallest amount lest boiling stop at once. There is thus fixed a single definite temperature, to be known as the (normal) "boiling-point" of the substance. If the substance is a really pure and stable compound, and is handled in highly refined research apparatus, there is no fundamental reason why the boiling point could not be determined with great accuracy—perhaps to the hundredth or thousandth of a degree. The boiling point is thus a valuable mark of distinction of the given substance. It is unlikely that another substance would have exactly the same boiling-point.

Unless otherwise specified, the boiling-points of substances, as reported in the literature, are supposed to refer to standard atmospheric pressure, 760 mm. Where another pressure was used,

its value in mm. of mercury is usually printed in parentheses, or small type, after the reported figure for boiling point.

32. Bumping. It is often difficult to conduct the boiling process smoothly. The liquid "bumps," alternately ejecting excessive amounts of vapor—perhaps blowing spray into a condenser—and then lying for a time without ebullition. The presence of crystalline salts, and sometimes the existence of a peculiar colloidal condition, seem to be connected with the habit of bumping.

Whatever be the original cause of trouble, the immediate occasion is likely to be the lack of a supply of air or other gaseous material at the point from which the bubbles should be starting. In the everyday kitchen the cook is seldom troubled by bumping, since most of the vegetable and animal products which he uses are full of cavities from which a host of minute bubbles may slowly emerge, each serving as the starting-point of a major steam bubble. Furthermore, the kitchen vessel is likely to be roughened by use. It probably has much air adsorbed upon its rough surface. Mere pouring of liquids into such a vessel does not displace the adsorbed air; but when heating is conducted, much of the adsorbed air comes off and promotes a smooth boiling process. The fact that metal is a better conductor of heat than glass may also influence the situation.

33. Remedies for Bumping: Boiling Stones. The organic laboratory worker, using smooth glass vessels, often finds no such supply of adsorbed air available, and naturally introduces a special supply. The result may be accomplished by introduction of some objects which will slowly give off many small quantities of air as boiling proceeds. Bits of unglazed clay plate, fine capillary glass tubes, scraps of platinum, and even anthracite coal have been used for this purpose. The platinum is useful by virtue of its well-known habit of adsorbing large quantities of gases. The clay plate may also adsorb air, and also has numerous cavities in which air is merely occluded.

Each particle or potential bubble of air, emerging from the clay plate, exists at a pressure somewhere near 760 mm. Immediately the liquid, at 760 mm. vapor pressure itself, delivers vapor in relatively large quantity to the air bubble. The total pressure—air plus vapor—inside the bubble promptly rises above 760 mm. At once a rapid expansion occurs with the assistance of the ample

heat supply close at hand. A vapor bubble is promptly expelled, and boiling proceeds quietly.

It is thus advisable to place boiling stones at the outset in vessels in which distillation is to be conducted. (See § 175 for details of preparation of the stones.) In case a distillation is interrupted, it is advisable to add one or two new stones before the heating is resumed. Otherwise trouble may arise from the fact that the first supply of stones, partially freed from air by heating, will absorb liquid so thoroughly upon cooling that they no longer readily release the air still contained in their innermost parts.

Beginners are warned at this point not to drop stones into a liquid which has already been heated to boiling without earlier provision of boiling stones. In such a case the liquid may already be at a temperature above its normal boiling point. A sudden outburst of vapor and spray may throw acid, or flaming liquid upon the worker. When the operator realizes that he needs boiling stones, he should wait at least two minutes after the burner is removed before applying the remedy.

34. Air-Supply at Reduced Pressure. As described in § 27, a capillary tube is introduced when distillation is to be conducted at reduced pressure. Unfortunately the process of evacuation of a distilling-flask tends to remove both adsorbed and absorbed gases from boiling-stones, rendering the stones of little or no value.

35. Heating Methods. Bumping may often be prevented, or at least reduced in violence, by the use of a heating bath instead of the simple system of burner and wire gauze. An oil bath or water bath permits many of the bubbles of vapor to rise from points around the edge of the liquid, and not all from the bottom of the flask. In reduced-pressure distillation this plan is particularly advised, and often absolutely necessary, even with the assistance of a capillary tube.

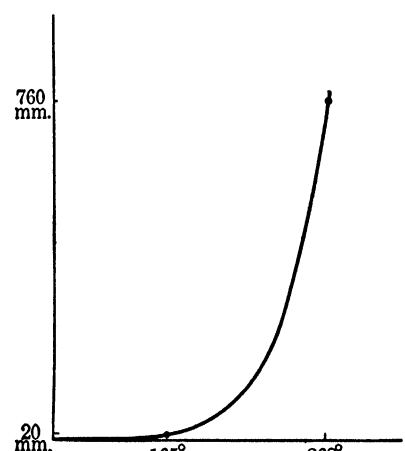
36. Prevention of Bumping by Evolution of Hydrogen. If an aqueous reaction mixture is either faintly alkaline or faintly acidic, the addition of one or two pieces of zinc often gives protection from bumping. The liquid reacts very slowly with the zinc, yielding minute hydrogen bubbles and thus permitting smooth ebullition. Naturally such a method is employed only in cases where the addition of a small amount of zinc salts is not harmful.

37. Use of a Condenser. When a liquid of boiling point below 150° C. is distilled, the vapors are led into a condenser (Liebig or similar type) through which water may circulate. In cases where the liquid boils between 120° and 150° some workers advise filling the condenser with water, and shutting off the stream before actual distillation. If the liquid boils below 120°, the water is allowed to circulate.

On the other hand, if the liquid boils above 150°, the water-jacket is not only unnecessary, but introduces the hazard of cracking of glass. A simple air-cooled tube replaces the Liebig condenser. In cases where the temperature of a single distillation varies over a wide range from values far below 150° to those above 150°, the water-cooled condenser would ordinarily be exchanged for one of air-cooled type as the higher figures were approached. Where such an exchange is inconvenient, a water-cooled condenser with inner tube of Pyrex glass is used for the whole operation, with reduced hazard of breakage.

Distillation under Reduced Pressure

38. Examination of the accompanying vapor pressure-temperature diagram for capric acid ($C_9H_{19}COOH$) shows that the boiling point of the substance may be substantially lowered by operation at pressures under 40 mm., a process readily carried out with simple apparatus. It happens that capric acid decomposes somewhat at 268°, its normal boiling point. A reduction of pressure to 20 mm., accomplished with the aid of a common water pump, permits distillation at 165°, a temperature so low that the substance is recovered with little or no decomposition.



Vapor Pressures of Capric Acid

While distillation at 20 mm. is usually not difficult, it is not always as smooth as at 100 mm. and higher. Bumping is more likely to cause trouble. A consideration of the change in volume of a liquid evaporated at 20 mm.,

in contrast to the change at 100 or 760 mm. throws light on this situation. For example:

Suppose the capric acid above cited is distilled at 760 mm. Aside from the danger of decomposition, a simple calculation shows that each cubic millimeter of the liquid, arbitrarily taken as a portion being distilled at a given moment, expands about 250-fold when it goes into the vapor state. 0.25 cc. of vapor is produced. This 0.25 cc., appearing at the bottom of the distilling flask, naturally forms a bubble of moderate size which rises and escapes without great disturbance.

Let this experiment be now repeated at 20 mm. The one cubic millimeter portion of liquid now evaporates at a much lower temperature. This factor alone would, to be sure, tend to reduce the size of the bubble about to be produced. At 20 mm., however, a great expansion is necessitated by simple "Boyle's Law" effect. The small portion becomes about 8 cc.,—roughly an eight thousand fold increase in volume. So great an expansion tends to cause violent ebullition, excessive splashing, and bumping.

To minimize these difficulties the two-necked Claisen flask offers some assistance. In such a flask (see § 27) it is relatively difficult for splashings of liquid to be carried mechanically to the side-stem.

Of equal importance to the bumping problem is the choice of heating methods. Direct heating of a reduced-pressure flask, applied under wire gauze from a common Bunsen flame, is to be avoided. Such heating encourages the oversize bubbles to be formed at a low level, where they tend to lift the whole mass of liquid out of the boiler. As these bubbles rise, they are relieved of hydrostatic pressure, and thus tend to burst out with accelerated violence. Such relief of pressure would not be of any relative importance in a distillation at 760 mm.; but at low pressures the difference in pressure between top and bottom of a liquid is of significance. In distillations at extremely low pressures, such as 0.01 or 0.001 mm., the very weight of liquid in a flask would be more than enough to counteract the upward pressure of a potential bubble. In such cases, accordingly, no bubbling is expected, and the distillation really becomes a low-pressure evaporation.

The Claisen flask is therefore immersed in a heating bath—using water for temperatures under 100°, oil for higher temperatures.

Much of the evaporation in such a case occurs around the edge of the liquid. Furthermore, the use of the oil-bath with distillations at high temperatures eliminates the risk of overheating a flask at one point, and reduces the danger of violent collapse of the flask with possible injury to the operator. A distilling flask should be examined carefully for cracks before mounting in an oil bath. Occasionally a Pyrex flask, carelessly handled, strikes some hard pointed object, which makes a tiny fractured spot with radiating cracks. Such a flask, being of specially good glass, may not fail under ordinary treatment, and the flaw may not be noticed. Under reduced pressure, however, an accident is possible.

It is the custom in chemical literature to report as accurately as possible the pressure at which a given substance was distilled. In ordinary distillation an error of two or three millimeters in the measurement of pressure is of no great significance. For example, at 757 mm. the boiling point of an organic compound may be only two or three tenths of a degree below the standard figure for 760 mm. At reduced pressure, however, the vapor-pressure curve is much flatter, and a change of two millimeters may make a great difference in boiling point. Of course such differences are obvious and easily determinable if one has a good pressure gauge in connection with the apparatus; but there is still opportunity for deceptive error if the capillary tube in the Claisen flask is not well controlled.

Suppose a distillation is being conducted in apparatus where the pressure gauge, or manometer, reads 20 mm. It happens that the capillary bore is too large, admitting far too much air. The vapor passing from the flask to the condenser is not pure, but contains perhaps 10% of air. The partial pressure of the air inside the flask is 2 mm. The partial pressure of the organic vapor is accordingly 20 less 2, or 18 mm. The liquid under these conditions will "boil" not at the temperature appropriate to 20 mm., but at the very different temperature for 18 mm. Not only are the resulting numerical data erroneous, but the excess of air may sweep unduly large quantities of product entirely through the apparatus. The air may also tend to oxidize the hot organic vapors to an excessive degree, though not necessarily with visible result.

39. Pumps for Reduced-Pressure Distillation. The common aspirator, or filter-pump, is generally employed for evacuation of reduced-pressure apparatus. In ordinary weather such a pump

will permit distillation at a minimum of about 20 mm. Theoretically the aspirator is capable of reducing the pressure to a value equal to the vapor pressure of the water in the pump at the temperature of the supply. (See § 410.)

In cold weather, when the domestic water supply comes out directly from under ice, it may be possible to reduce the pressure in a filter pump to a value as low as 8 mm. (theoretically to 4.57 mm., the vapor pressure of melting ice). In summer it is often difficult to lower the pressure below 30 mm.

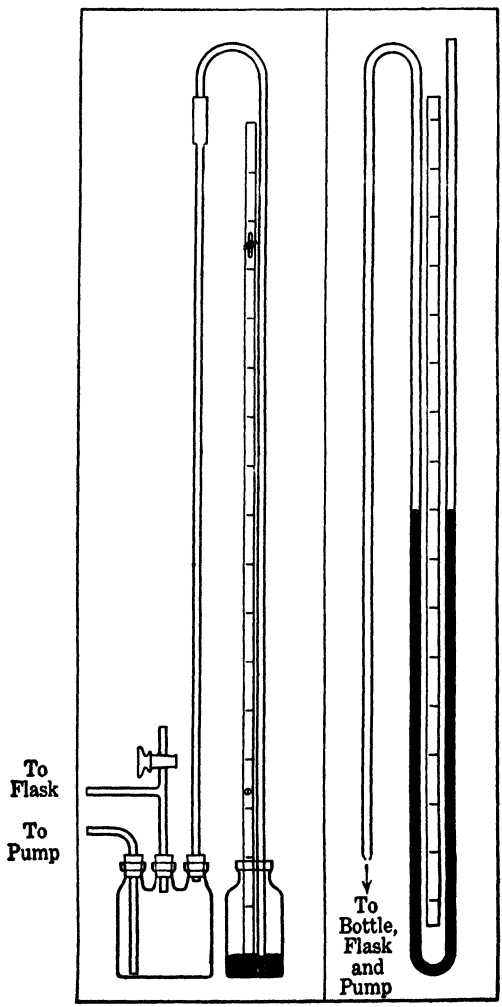


FIG. 1 FIG. 2

MANOMETERS

For lower pressures piston pumps were developed in Europe, and more recently, in America, rotary devices operating in oil reservoirs. These appliances not only permit distillation at pressures far below one millimeter, but are proving valuable to physicists who have use for pumps which will evacuate to 0.001 mm. and even lower for vacuum-tube research.

When a mechanical pump is used in the organic laboratory care must be taken to insert a safety trap or other vessel between the pump and the distilling appa-

ratus. In such manner vapors are caught and not allowed to get into the pump, where they might contaminate the oil and corrode the metal parts of the pump. Such a trap may consist of an intermediate vessel chilled with ice and salt, or better yet with solid carbon dioxide.

40. Manometers (Pressure Gauges). Perhaps the best everyday practical device for measuring reduced pressures is one which, peculiarly, seems not to be offered commercially. It is essentially a vertical tube, slightly over 760 mm. long, dipping into a mercury well, as shown in Fig. 1. The distilling outfit is attached to the other end of the tube with an intervening safety bottle. When the system is evacuated, mercury rises out of the well to the height representing the degree of evacuation. The difference between the height of the mercury in the manometer, and that of the standard mercurial barometer, equals the pressure of the distillation. This manometer is easily cleansed. The device shown in Fig. 2, while not so readily cleansed, is a somewhat neater assembly, and is superior to the closed-tube manometer, shown in Fig. 3.

The short, closed-tube manometer, universally sold in the apparatus market, is almost useless in the ordinary student laboratory. When clean, it is of course satisfactory and even more convenient than the taller model; but after a short period of actual chemical laboratory practice, air, water, or other volatile material is certain to creep around the bend at the bottom. As soon as vapor reaches the closed space (to the right in Fig. 3) all pressure readings are thrown into serious error.

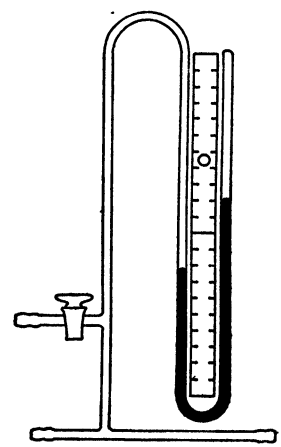


FIG. 3. CLOSED-TUBE MANOMETER

For specific directions and details of practical procedure, see § 27.

DISTILLATION OF MIXTURES

Single-Phase Systems

41. Non-Volatile Impurities. The attempt may now be made to distil a liquid such as water in which is dissolved some non-

volatile material like sugar. It will be more difficult for water-vapor to escape from the surface of the sugar solution than from pure water. Sugar molecules seem to be more or less in the way, causing reduction of vapor pressure. At 100° the pressure will fall short of 760 mm. In order that the solution may boil, the temperature must be raised.

Boiling-point elevation, like several other fundamental phenomena to be described in succeeding pages, is governed by **Raoult's Law,** a principle of major importance:

The partial vapor pressure of a component in a solution varies directly with its mole fraction.

For example:

1000 moles of water at its normal boiling point (100°, 760 mm. pressure) is taken as the basis for experimentation. One mole of this quantity is now replaced with 342 grams, or one mole, of sugar, with consequent reduction in the amount of solvent by exactly 0.1 mole per cent. Experiment now shows that the vapor pressure of the new solution is just 0.1% lower than before, the difference of course being 0.76 mm. More directly expressed in conformity with Raoult's Law, the vapor pressure of the water component has been reduced from its full normal value to 99.9% of that value, or 759.24 mm.

Increase of the fraction of sugar to 0.2 mole per cent (2 moles of sugar to 998 moles of water) lowers the aqueous vapor pressure to 99.8% of 760, or 758.48 mm., and so on.

Such regularity of behavior occurs in almost any solution containing very low concentrations of the non-volatile impurity. With more concentrated solutions substantial deviations from the rule appear, depending on the kind of impurity present.

A regular fall in vapor-pressure, as above described, naturally suggests an equally regular rise in boiling point as the mole-fraction of water is decreased. Thus in very dilute solutions the boiling point of water rises at the rate of about 0.3° per mole per cent. of solute, or 0.53° for one mole in 1000 grams of water. This observation suggests the well-known method of determining molecular weight by elevation of boiling point.

The careful worker in organic chemistry will therefore be on his guard against recording a boiling point in a case where the boiling liquid may contain dissolved impurities. It is possible, however, to determine the boiling point of a substance in such a case by

the method of **recondensation.** The liquid, in which any impurities are of non-volatile type only, is boiled in a flask with a long neck. A thermometer is mounted with the mercury bulb up in the neck at some distance from the boiling material. As the solution boils, vapor may be emitted at an elevated temperature, in agreement with Raoult's Law; but in passing up through the neck of the flask it is cooled to its true boiling point if the distillation be conducted at a moderate rate. Part of the vapor now recondenses and flows down over the lower part of the thermometer. Under such conditions, the thermometer, if accurately calibrated and completely immersed in condensing vapor, will show the true boiling point. (See § 181.)

42. Mixture of Two Liquid Substances. Miscible Liquids. A mixture of two similar liquid substances which do not react with each other is often called an "ideal solution," and obeys Raoult's Law rather closely. A mixture of *n*-pentane and *n*-heptane, two inert hydrocarbons of like character, is an example. Knowledge of the vapor pressures of these substances at different temperatures will make it possible to predict the behavior of various mixtures during distillation.

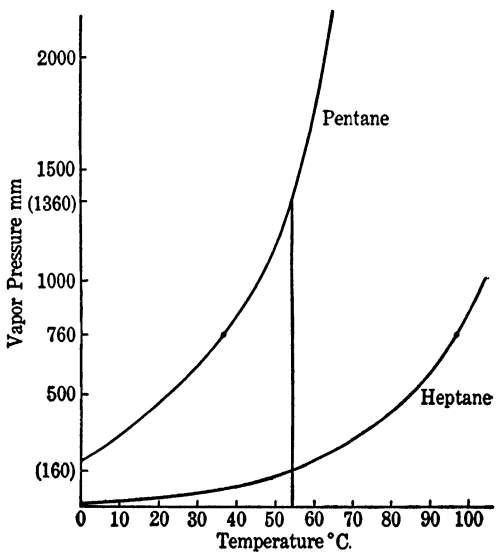


FIG. 1. VAPOR PRESSURES

For simplicity, an equimolal mixture of *n*-pentane and *n*-heptane is first chosen. From the data given in § 410, graphically plotted in Fig. 1, the boiling-point may now be estimated.

According to Raoult's Law the partial vapor pressure of the pentane will be just one half of the value shown in the table or graph for any given temperature, since just one half of the molecules are of that species. Similarly the partial vapor pressure of

heptane will be one half of the tabular value for heptane. Adopting a simple "cut-and-try" method one soon discovers that at 54° the sum of the two partial pressures happens to be just 760 mm. That is

$$(\tfrac{1}{2} \times 1360 \text{ mm.}) + (\tfrac{1}{2} \times 160 \text{ mm.}) = 760 \text{ mm.}$$

Therefore 54° is the boiling point of the equimolal mixture.

A somewhat broader treatment of this type of calculation is illustrated in a second example: What mixture of pentane and heptane will boil at 60°?

Let x mole per cent. of pentane, and y mole per cent. of heptane constitute the mixture. Using proper data from § 410:

According to Raoult's Law, at 60° the partial vapor pressure of pentane will be $x\%$ of 1605 mm., the vapor pressure of pure pentane. Similarly, the partial pressure of heptane will be $y\%$ of 208 mm. The sum of these partial pressures, of course, must be 760 mm. if the mixture is to boil—

$$\left(\frac{x}{100} \times 1605\right) + \left(\frac{y}{100} \times 208\right) = 760. \qquad (1)$$

But $x + y$ by assumption equals 100%; or in more formal algebraic statement

$$\frac{x}{100} + \frac{y}{100} = 1. \qquad (2)$$

Solving (1) and (2) as simultaneous equations,

$$x = 39.5 \text{ (mole per cent. pentane)}$$

and

$$y = 60.5 \text{ (mole per cent. heptane)};$$

or, in terms of ordinary metric weight, a mixture of 284 grams of pentane and 605 grams of heptane will boil at 60°.

It is evident from Fig. 1 that the boiling point of a 50 mole-per cent. mixture lies closer to the boiling point of pentane than its mere mole-fraction might suggest. In cases where the two components are widely variant in boiling point, the tendency of the boiling point of the mixture to be low is more noticeable. For example, a mixture of ether (b.pt. 36°) and aniline (b.pt. 184°) has a very low boiling point. This behavior in part explains the fact that ether is easily separated from aniline by distillation.

Figure 2 shows the boiling points of all mixtures of pentane and heptane. It is known commonly as a "boiling point—composition" diagram. The continuous line of the graph gives the boiling point for every possible composition. The dotted line gives the composition of the vapor which comes by distillation from each possible mixture. For example, the mixture of 39.5 moles of pentane and 60.5 moles of heptane boils at temperature A (60°); and the vapor which comes from such a distillation is marked by a point on the dotted curve at the same horizontal level, viz., A'.

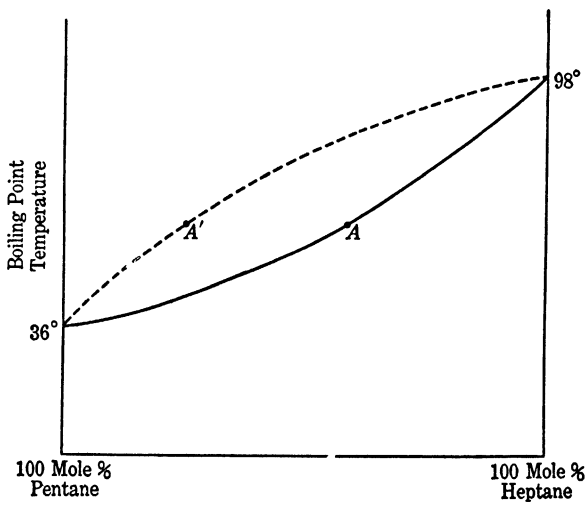


FIG. 2. BOILING POINT—COMPOSITION DIAGRAM

The numerical value of A' may of course be determined experimentally. It is readily obtained also from vapor pressure data. Raoult's Law shows that 39.5% of 1605 mm. or 634 mm. is the partial vapor pressure of pentane, and 60.5% of 208 mm. or 126 mm. is the partial vapor pressure of heptane. Now in conformity with Avogadro's Law, at constant temperature the *number of molecules* in a gas is measured by the pressure of that gas. Therefore 634 molecules of pentane will come over by distillation in company with every 126 molecules of heptane. The vapor, and thus the first distillate will be much richer in pentane than the original 39.5% mixture. It will contain at the start 83.4 mole per cent. of pentane.

43. Behavior of the Mixture during Distillation. It is clear that 83.4% pentane cannot be removed from 39.5% pentane without immediately disturbing the conditions present in the boiler. With loss of pentane the boiling-point rises, and the distillate becomes increasingly richer in heptane; but the distillate being produced at any given moment is always richer in pentane than the boiler liquid existing just at that moment. The temperature, at first just 60°, rises steadily and approaches 98° as the boiler goes dry.

Two practical conclusions may be drawn at once. First: a rising temperature of boiling means that *at least two* substances are present. That is, the liquid is certainly not a pure substance—or if originally pure, it has decomposed at least partially. Second: a "straight" distillation does not give a satisfactory separation of two components. Two improvements of method are possible; (*a*) to distil repeatedly into a succession of receivers, as described in § 55, or (*b*) to employ a fractionating column (§ 56).

44. Note. Students frequently report that the boiling temperature of a liquid fell at some time during distillation. No such phenomenon as a drop in boiling point is recognized in properly conducted distillation. The worker must have permitted the flame to be blown aside by a draft, or in some other way he allowed the flask to become cool, with resulting back-flow of cool air from the condenser. The fall in temperature thus has no significance whatever in the distillation.

45. Deviations from Raoult's Law. Many liquid mixtures do not obey Raoult's Law. In some cases the vapor-pressures are greater than those calculated from tables and mole-fractions. A **positive deviation** from the law is then recognized. In other cases the vapor pressures are abnormally low, indicating a **negative deviation.** An example of each of these will be discussed.

46. Positive Deviation. Whenever two liquids, though miscible and mutually non-reactive, are quite different in fundamental makeup, a positive deviation often occurs. Apparently the two liquids have an abnormally great tendency to escape from one another. Were that tendency greater, they might part in two liquid phases like ether and water. Under certain conditions, however, they actually stay together as a single liquid phase, but manifest their mutual "dislike" of each other by exerting abnormally high combined vapor pressures in mixtures.

Since these mixtures tend to have such high vapor pressures, they have correspondingly low boiling points. So great is the depression of boiling point that in certain ranges of composition the mixture may boil at temperatures even below the boiling point of the more volatile of the two components.

47. The system ethyl alcohol-water is the best known case of positive deviation. At one composition (95.57%) aqueous ethyl alcohol boils at a temperature below the boiling point of pure ethyl alcohol. For convenience in oral explanation, this value is rounded off to "96%" in the following paragraphs.

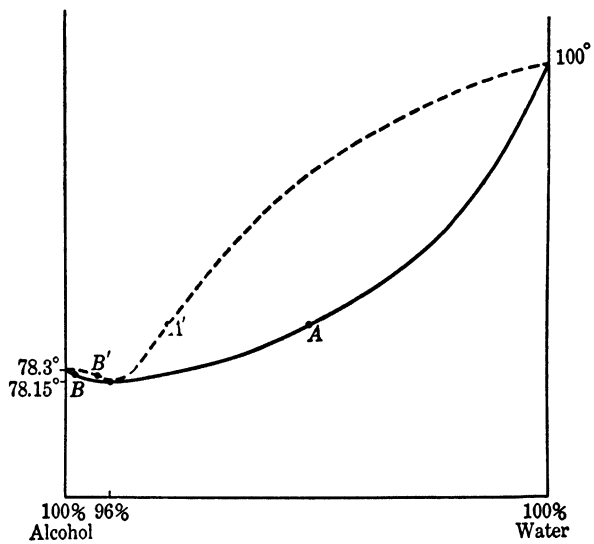


FIG. 1. BOILING POINT—COMPOSITION DIAGRAM FOR ETHYL ALCOHOL AND WATER

Figure 1 shows the boiling point of 96% alcohol to be only 0.15° below the boiling point of pure alcohol; nevertheless this small difference is enough to make considerable trouble in both the industrial and laboratory processes of preparing pure ethyl alcohol. The phenomenon makes it impossible to produce pure ("absolute") alcohol by any kind of fractional distillation of mixtures of alcohol and water alone. It may be noted that commercial ethyl alcohol is seldom of so high a percentage as 96%, but commonly contains a slightly greater content of water.

In Fig. 1 it is seen that aqueous alcohol of 50% composition (A) will yield a distillate (A') richer in alcohol—just as one would expect in a case where Raoult's Law was obeyed. On the other hand, 98% alcohol (B) yields a distillate (B') richer in water—richer in the *less volatile* component. If 96% alcohol is distilled, vapor of exactly the same (96%) composition comes over. The boiler contents do not change. Evidently therefore the entire quantity of liquid could be distilled without change in temperature or composition. Such a mixture is commonly called a "constant boiling mixture," "azeotropic mixture," or when composed of just two substances, a "binary mixture."

An azeotropic mixture may easily deceive an original investigator into thinking he is dealing with a pure substance. Unfortunately there are many such mixtures known. Most of these are of the minimum boiling type above described, and a few of maximum boiling point as described in § 49 below. Distillation engineers must be constantly on their guard in the operation of processes involving mixtures of solvents.

48. Repeated Distillation of Aqueous Alcohol. The repeated partial distillation of any mixture of alcohol and water will eventually yield a distillate of the azeotropic composition. It is assumed that a certain residue is set aside, or discarded, each time, from the distilling flask. For example, a fermented fruit juice, containing 5% of alcohol, upon simple distillation might yield a 20 or 25% solution of alcohol, there being a substantial rejection of aqueous boiler residue, or "slop," as the distiller calls it. Repeated redistillations, with successive rejections, will gradually raise the percentage to 96%, but not higher. If a fractionating column is included in the apparatus this advance from 5% to 96% may be made in fewer steps—in two distillations, or perhaps even in one operation. Again there is no possibility of getting above the 96% mark.

Where really pure alcohol is desired, one may employ chemical means, usually with the aid of quicklime, as explained in § 197. Industrially the result is accomplished much more expeditely by the introduction of a third solvent, benzene, into the aqueous alcohol. When the three-component mixture is distilled through proper fractionating apparatus, a "ternary" azeotropic mixture of the three substances passes over until the water is exhausted.

A second azeotropic mixture, this time of benzene and some alcohol, then goes over until the benzene is practically exhausted. Further distillation yields absolute alcohol.

49. Negative Deviation. Sometimes the sum of the partial vapor pressures of two components is abnormally low, illustrating negative deviation from Raoult's Law. The boiling point curve will run high instead of low. In the case pictured in Fig. 2 there is a constant-boiling mixture of 20% acetone and 80% chloroform.

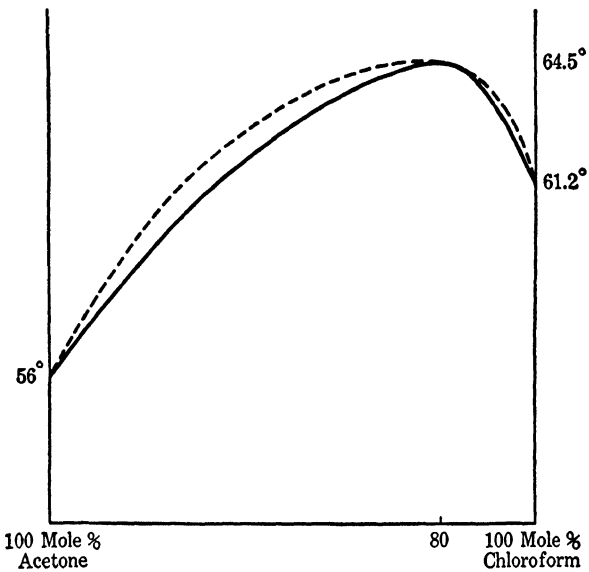


FIG. 2. BOILING POINT—COMPOSITION

Distillation of an acetone-chloroform mixture will proceed in a manner contrary to that with alcohol and water. Any mixture of the two components, when boiled, will itself gradually become more and more like the azeotropic mixture. Either acetone or chloroform, as the case may demand, escapes in relatively large proportion, leaving a boiler residue which finally attains the composition of 20–80.

Relatively few of the high-boiling types of azeotropic mixtures are known in the field of organic chemistry. This fact is probably related to the ordinary cause for negative deviation. Usually the two components in such a case combine chemically to a

certain extent, forming a relatively non-volatile compound. Naturally the residual free component materials, present actually in reduced mole-fraction, exert low vapor pressures. Whence the boiling points are high.

50. Several common inorganic acids, when mixed with water, yield high-boiling azeotropic solutions. The 20.2% solution of hydrochloric acid is a noteworthy example. So faithfully does this reagent change to the 20.2% value that a standard solution of the acid may be prepared with a high degree of precision merely

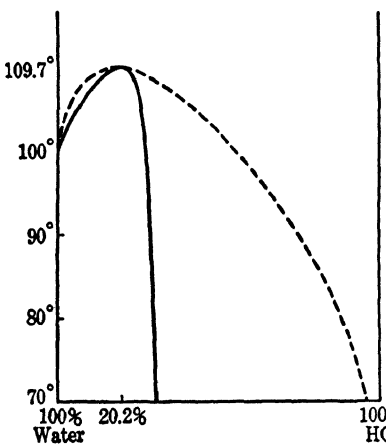


FIG. 3

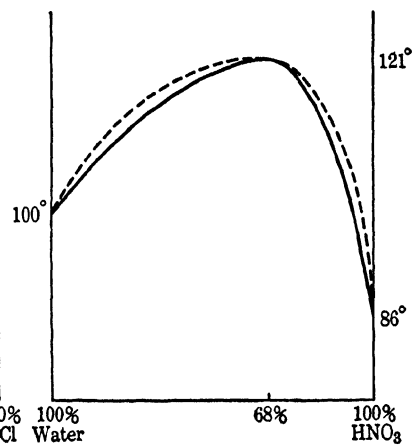


FIG. 4

BOILING POINT—COMPOSITION DIAGRAMS

by distilling any aqueous solution of the acid until the boiler residue, and thus the current distillate, are of constant, and thus azeotropic composition. Arrival at the 20.2% point is of course expedited by starting with a solution of nearly that concentration. Slight corrections for barometric variations must also be considered. Conditions for such a system are seen in Fig. 3. Similarly, ordinary commercial nitric acid is a 68% azeotropic solution of HNO_3 in water, as in Fig. 4. Hydrobromic and hydriodic acids have like behavior.

51. The following are a few examples of the many constant-boiling mixtures which are known. Information on others may be obtained from Robinson, *Fractional Distillation*, and *International Critical Tables*, Vol. 3, p. 318 (McGraw-Hill Company).

Components	B.Pt.	Comp.	Constant B.Pt.
Benzene Ethyl alcohol	80.6° 78.3°	68% 32	68.25°
Benzene Cyclohexane	80.6° 80.8°	55% 45	77.5°
Carbon tetrachloride Methyl alcohol	77° 65°	79% 21	55.7°
Ethyl acetate Ethyl alcohol	77° 78.3°	69% 31	71°
n-Propyl alcohol Toluene	98° 111°	53% 47	91°
Formic acid Water	101° 100°	77% 23	107.1°
Phenol Aniline	181.5° 184.4°	42% 58	186.22°

Deviations from Raoult's Law in Very Dilute Solutions

52. Duclaux Constants. In the experiment on "Identification of an Acid" (see § 242) an aliphatic acid is identified virtually by measurement of the rate at which it escapes from a very dilute (2%) solution when the latter is distilled. 100 cc. of the dilute solution is used; and the percentages of the total quantity of acid which pass over in the first, second, and third 10 cc. of distillate, respectively, are estimated. These percentages are known as Duclaux constants. Some acids escape relatively rapidly, and thus have large constants; others seem to be less active, and have low constants.

Duclaux Constants

Acid and Boiling Pt.	First 10 cc.	Second 10 cc.	Third 10 cc.
Formic (101°)	3.95	4.40	4.55
Acetic (118°)	6.8	7.1	7.4
Propionic (141°)	11.9	11.7	11.3
n-Butyric (164°)	17.9	16.9	14.6
n-Valeric (187°)	24.5	20.6	17.0
iso-Butyric (155°)	26.0	20.9	16.0
iso-Valeric (177°)	28.7	23.1	16.8
n-Caproic (202°)	33.0	24.0	19.0

The table reveals the peculiar fact that the acids of lowest boiling point have the smallest Duclaux constants. Still more striking are the large values for high-boiling, relatively non-volatile acids of the valeric-caproic class.

Strict adherence to Raoult's Law would of course require that water, which is more volatile than any of the acids in question, should pass over in a distillation of dilute acid proportionately faster than the acid. The first 10 cc. of distillate would therefore contain more than 10% of the water originally present in the system, and thus less than 10% of the acid. The case of acetic acid at least approximately complies with this presumption, since only 6.8% of the acid component is distilled in the first 10 cc.

The behavior of *n*-butyric acid is strikingly different. Since the Duclaux constant is above 10, it follows that a dilute solution of butyric acid, upon distillation, would yield a distillate *enriched in the less volatile* component. When such information, gotten from distillations at different concentrations, is plotted on a conventional boiling point-composition diagram, it necessarily follows that butyric acid and water exhibit at some point the phenomenon of azeotropic *minimum* boiling point, of the type illustrated in Fig. 1, § 47. The high Duclaux constant (17.9) is thus seen to be the direct result of a marked positive deviation from Raoult's Law.

Formic acid, on the contrary, has an exceptionally low constant, despite the fact that it is the most volatile acid. In this case, however, it is likely that an unusually large proportion of the acid is held back as a less volatile hydrate. A negative deviation results, with low vapor pressures, and a maximum azeotropic boiling point of the type described in § 49.

53. Irregularities. Caproic acid, with a large Duclaux constant, would undoubtedly form a minimum-boiling azeotropic mixture if its solubility in water were sufficiently great. Actually the acid is not miscible with water in all proportions, so that the zone of azeotropic mixtures happens to be excluded. In such a case the process of Duclaux distillation approaches in physicochemical character a normal steam distillation, in which two dissimilar components escape rather independently.

The above discussion of course is primarily intended to throw light on the particular analytical method under discussion; but it also has outside applications. Laboratory workers frequently

have occasion to prepare a volatile organic compound in a dilute reaction mixture, and naturally attempt to isolate the desired substance from the water by fractional distillation. A consideration of these principles may show whether the principal yield of the substance is to be expected in the early fractions, or the late ones—quite aside from the boiling point of the pure substance itself.

54. References on Distillation. A discussion of the principles of distillation is usually to be found in a standard text of physical chemistry. In addition, several special treatises and articles may well be consulted:

Findlay, Alexander, The Phase Rule (Longmans).
Robinson, Clark S., Fractional Distillation (McGraw-Hill).
Young, Sidney, Distillation Principles and Processes (Macmillan).
Evans, P. N., Ind. Eng. Chemistry, **8**, 260 (1916). A discussion of alcohol-water mixtures.

Fractional Distillation

55. Distribution into Multiple Receivers. Simple distillation of a mixture of two liquids normally yields at first a fraction rich in the volatile component; at the end a fraction rich in the less-volatile component. Repetition of such a distillation, into multiple receivers, effects a sharper separation. In such a process various distillates are poured back at intervals into the boiler and redistilled. The actual scheme of performance is too complicated to permit of an intelligible explanation in general terms. It is perhaps better to outline the procedure concretely in an imaginary case, supplying plausible data to show the progress of the separation:

Suppose a mixture of 500 cc. of *A*, boiling point 80°, with 500 cc. of *B*, boiling point 100°, is distilled into four receivers, each receiver taking in its turn 250 cc. of distillate. It is assumed for simplicity that there is no loss of material during the entire process, and no azeotropic mixture possible.

FIRST DISTILLATION

	FRACTION 1	FRACTION 2	FRACTION 3	FRACTION 4
Boiling Range	84–87°	87–90°	90–93°	93–96°
Yield	250 cc.	250 cc.	250 cc.	250 cc.

Since the boiling ranges of these fractions depend upon the amount of condensate which flows back from the upper walls of the boiler, the above figures might vary in actual practice. The schedule is merely a reasonable illustrative assumption.

Fraction No. 1 is now returned to the boiler and redistilled. About 200 cc. of this passes over at a *lower* and *narrower* range of temperature, arbitrarily taken at 82–84°. When the 84° mark is reached, the distillation is interrupted. Fraction No. 2 is now placed in the boiler along with the residue of No. 1. Distillation is resumed, and about 75 cc. of distillate collected over the same range, 82–84°. Fraction No. 3 is now added and from this only 25 cc. is obtained, 82–84°. Finally fraction No. 4 enters, and this yields only 10 cc., 82–84°. The residual boiler contents are now distilled into three fractions to be labeled Nos. 2, 3, 4 below. It is noted that the first and last fractions are large, and each has a relatively *narrow* range of boiling temperature.

SECOND DISTILLATION

	FRACTION 1	FRACTION 2	FRACTION 3	FRACTION 4
Boiling Range	82–84°	84–91°	91–96°	96–98°
Yield	310 cc.	180 cc.	190 cc.	320 cc.

The process is repeated three times with results as follows:

THIRD DISTILLATION

	FRACTION 1	FRACTION 2	FRACTION 3	FRACTION 4
Boiling Range	81–83°	83–90°	90–97°	97–99°
Yield	370 cc.	125 cc.	130 cc.	375 cc.

FOURTH DISTILLATION

	FRACTION 1	FRACTION 2	FRACTION 3	FRACTION 4
Boiling Range	80–82°	82–90°	90–98°	98–99°
Yield	425 cc.	70 cc.	75 cc.	430 cc.

FIFTH DISTILLATION

	FRACTION 1	FRACTION 2	FRACTION 3	FRACTION 4
Boiling Range	80–81°	81–90°	90–99°	99–100°
Yield	480 cc.	20 cc.	20 cc.	480 cc.

Fractions Nos. 1 and 4 in the fifth run are nearly pure *A* and *B*, respectively. Fractions Nos. 2 and 3, being of mixed composition, may be discarded, unless there is a new batch in prospect, in which case they would merely be added to the new raw material.

It is seldom that a scheme such as that outlined above is used without the aid of a fractionating column. The addition of the column would simply mean that the results above shown would be gotten in fewer runs. The principle of repeated distillation is valuable, however, even though it may be applied only to a partial extent in actual laboratory practice. There are also other schemes of dividing, pouring back, etc.; cf. Robinson's *Fractional Distillation*.

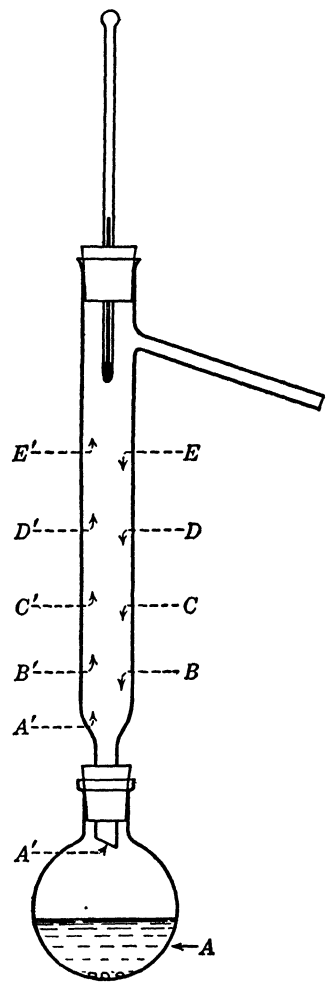


FIG. 1. FRACTIONATION

56. Distillation through a Fractionating Column. The explanation of the operation of a fractionating column, at best somewhat complicated, may be simplified at first by the experiment of omitting the glass beads or similar obstructions normally provided in such a column. This is the equivalent of distillation from a flask with a long neck. The mixture distilled in this case is to be one of benzene (b.pt. 80.6°) and toluene (b.pt. 111°), two similar hydrocarbons. A fairly close agreement with Raoult's Law may be assumed. Figure 2 shows the appropriate boiling point-composition data.

Let *A* (of Fig. 2) represent the composition of the original mixture in the flask. *A'* as usual represents the composition of the vapor coming at equilibrium from the liquid *A*.

The vapor *A'* naturally rises, strikes the walls of the relatively cool column, and is partially recondensed. Since *A* originally

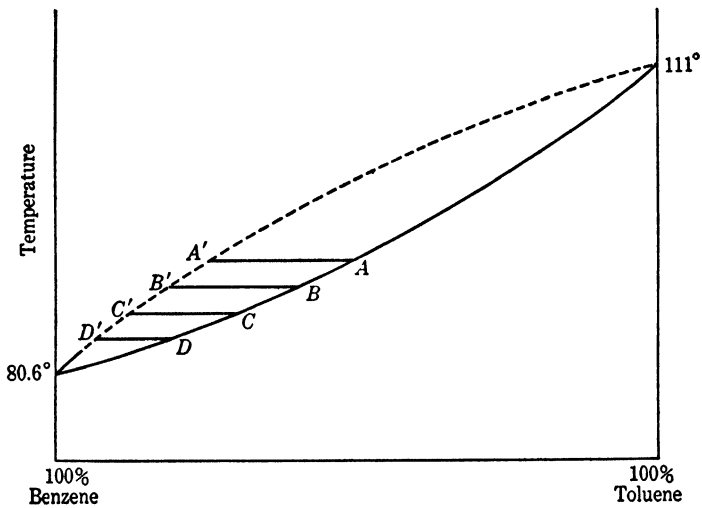


FIG. 2. BOILING POINT—COMPOSITION DIAGRAM

produced the equilibrium vapor A', by reversal of process at the initial moment when condensation begins A' will produce a very small amount of condensate of composition A. The newly-formed A runs back into the boiler. In order to extract a supply of A from a vapor of A' composition, however, it is plainly necessary to strip the vapor A' of a relatively large part of its toluene content. The residual vapor will be correspondingly richer in benzene, although reduced in total quantity. Let its composition be shown as B', which necessarily is nearer to the benzene axis of Fig. 2, and lower on the temperature scale.

Vapor B' rises to a higher level in the column, and again partial recondensation occurs. Another quantity of condensate, relatively rich in toluene, runs back into the boiler. The residual vapor is altered in composition to the state C'; then to D', E', etc. Finally at the top of the column almost pure benzene emerges into the sidestem and passes to the condenser. At the same time the temperature has been falling continuously until it has almost reached 80.6°.

Unfortunately so little vapor actually reaches the top that the process is very inefficient. Nearly all goes back as condensate to the boiler. A more rapid and more distinct separation is desired. The column is now packed with beads, and the distillation repeated with a new supply of the original benzene-toluene mixture.

57. Effect of Adding Beads. The ascending vapor of composition A' as usual suffers partial recondensation at the bottom of the column. It thus produces some liquid A and itself becomes B'. Again the surviving vapor B' rises, this time for a short distance through the glass beads, and produces as usual some liquid B. So far the process resembles that in the simple column.

Liquid B, however, does not drop into the boiler immediately. It is detained by the beads for a short time, but soon reaches the lowest level of the column, where the atmosphere about the beads consists of vapor A'. Figure 2, however, shows that liquid B is not at equilibrium with A'; nor is it at the same temperature as A'.

Whenever a liquid and a vapor, each made up of the same components, but not at equilibrium with each other, are nevertheless allowed to meet each other, there will be a transfer of material from one phase to the other in the attempt to reach equilibrium. In the case at hand B contains too much benzene for the equilibrium state. It will give up part of its benzene to the rising vapor A'. Similarly A', rich in toluene, will give up some of that component to liquid phase B.

Figure 3 shows the changes which A' and B have just undergone. A', stripped of part of its toluene, and slightly cooled at

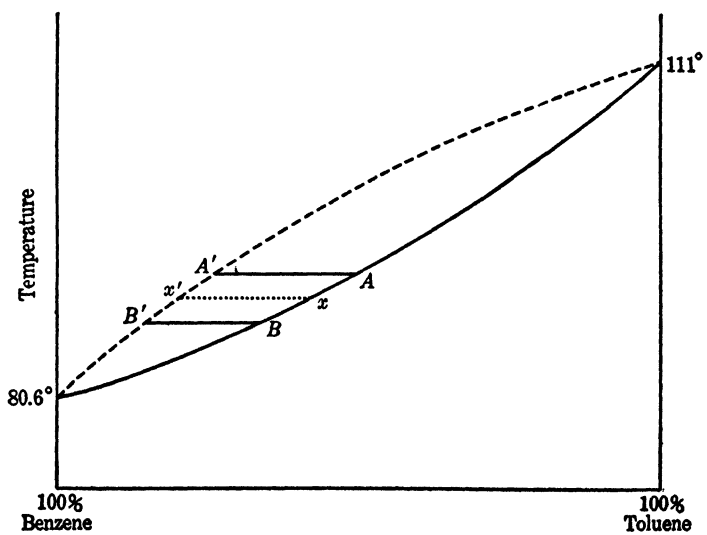


FIG. 3. DISTILLATION WITH A COLUMN CONTAINING BEADS

the same time, changes to an intervening mixture x', while B, newly enriched in toluene, and somewhat warmer, becomes x. But x' and x happen to be on the same horizontal line, and thus by graphical definition are at equilibrium. The process of interchange is at an end. Liquid x falls into the boiler.

The important fact in the above scheme of operations is that A' has been improved in benzene content (shift from A' to x') with *little or no loss in volume*, and of course without the use of any additional length of column. The credit goes to the beads for their service in detaining the falling liquid B, and in breaking up its mass into units of greatly increased surface. Interchange of components becomes easier.

The above account of the behavior of A, A' and B through to x' and x may now be repeated up in the next level of the column, with application to that part of the vapor reaching such a level. Vapor x' rises to a point where it encounters a still cooler liquid such as C, which in turn has already previously been condensed from vapors still higher in the column. x' in due time would be transformed into a vapor continuously richer in benzene as upward progress through the column is made. It must be realized after all that each shift from A' to x', etc., is an infinitesimal step, in terms of mathematics. Obviously a rigorous treatment of the problem leads into the calculus, with complicated possibilities, especially when a variety of engineering problems enters the field.

58. Temperature Change. Changes in **temperature** have much to do with the behavior of the system, as well as changes in composition. Accordingly, the operation of the column may be redescribed from the viewpoint of temperature:

As before, vapor A' rises into the column, is cooled, and yields a partial condensate of A. The residual vapor B' again rises, yielding another partial condensate B. The relatively cool B slowly falls into the hotter zone of A' vapor. The temperature in this zone is above the boiling point of the falling liquid B. Naturally therefore B will boil, just as it would boil if placed in the midst of heated air from a burner. As it boils, B of course gives up vapor rich in benzene, and itself becomes rich in toluene.

The "boiling" of B caused by the heat transferred from A' is only half the story, thermally speaking. Since B is cooler than A' it serves as a sort of condenser upon which hot A' may deposit some of its less volatile substance. If now the evaporation of B

just matches in quantity the condensation of other material upon B, no significant change in volume of either B or A' will occur—but a great change in composition.

Unfortunately the presence of beads in the Hempel column, while in one sense a valuable factor, at the same time introduces difficulties. Much liquid is held up in the column—so much that the boiler may go dry before much distillate is collected. That part of the liquid held in the beads simply cannot be distilled without change of apparatus.

Industrially the hold-up of liquid in a column is a matter of little concern. Plenty of material lies in reserve. There is accordingly no serious objection to the use of very long columns, perhaps 75 or 100 feet high, running the entire height of a tall factory building. With such equipment so much interchange of volatile and involatile components is possible that in the end a sharp fractional "cut" may be obtained. It may thus be readily practicable to separate two liquids whose boiling points lie only ten degrees apart. In the laboratory, on the other hand, it might be difficult to separate liquids if their boiling points were within thirty degrees of each other.

Such products as gasoline and kerosene are prepared with the aid of fractionating columns. Ingenious designs are worked out, in which ascending vapors pass through "bubble-caps," "plates," and other types of obstacles which cause them to meet a long succession of splashing liquid masses. By careful regulation a continuous process may be evolved whereby a constant inflow of crude liquid stock, and a constant output of uniform distilled product may be maintained.

59. In the laboratory the problem in some ways is more troublesome. To avoid the hold-up of liquid in beads, numerous fancy glass modifications of the ordinary column have been devised. Among these the Vigreux has attained popularity, not only because it does not hold up much liquid, but also because it is of fairly rugged type of construction. It is not extremely efficient, however. The device consists of a simple tubular column (Hempel model) in which inward indentations have been made with a slender carbon pencil.

The Friedrich column is reported to be more efficient. In it the vapors ascend through a long spiral passageway. This passageway is arranged by winding a silver, copper or even a glass

rod about a closed hollow glass cylinder, and then slipping this complete assembly into an empty Hempel-type column.

The comparative efficiency of distillation with and without a column is illustrated by curves showing the boiling points at different times during a distillation. In the adjoining figure, boiling temperature is plotted vertically, and the yield (at each temperature measurement) horizontally. The liquid distilled was a mixture of 36% methyl alcohol and 64% water. Curve *A* is that obtained when the mixture is distilled from a simple flask. Curve *B* is that obtained by slow distillation with a special fractionating column. (See Cooper and Fasce, *Ind. Eng. Chemistry*, **20**, 420 (1928).)

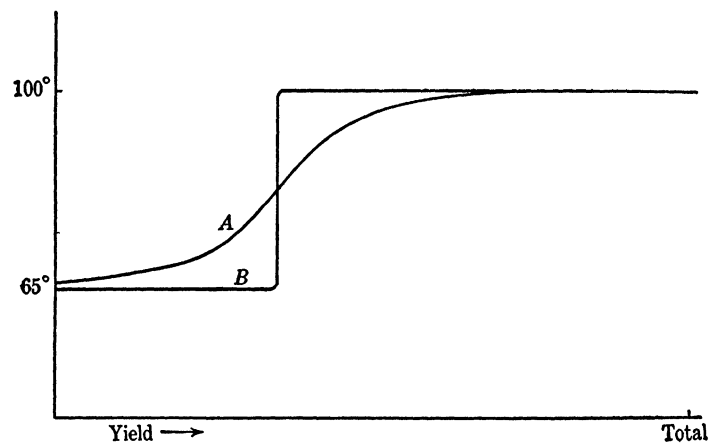


FIG. 4. DISTILLATION OF A MIXTURE OF METHYL ALCOHOL AND WATER

Curve *B* indicates that the temperature of distillation, as measured at the top of the column, remains almost constant at 65°, the boiling point of methyl alcohol, until nearly 35% of the original solution has been distilled. While the next few drops of distillate are being collected, the temperature rises rapidly to 100°, indicating that little remains in the boiler except water. Finally the second horizontal portion of the curve shows that practically pure water is being collected.

In practice the sudden change from such a temperature as 65° to a much higher value like 100° may not proceed smoothly unless heat is at once applied more intensely. A low adjustment of the burner, adequate for the low-temperature part of the

process, may not suffice to distil water. Thus the sudden exhaustion of the volatile substance may cause a suspension of distillation. Cool air surges back from the condenser, causing the thermometer to behave erratically and indicate temperature values which have no significance in the experiment. These phenomena are illustrated in the acetone experiment (§ 224).

60. When two liquids show a slight positive deviation from Raoult's Law, not quite sufficient to cause an azeotropic minimum boiling point, separation may become relatively easy despite a small interval between the normal boiling points. Contrariwise, irregular cases where the vapor and liquid curves lie close together present difficult problems in fractional distillation.

One of the most serious problems in the operation of laboratory columns is that of excessive cooling. In cases where a common Hempel column, 30 or 40 cm. long, does not give the desired fractionation, one naturally proposes a long column—perhaps one or two meters in length—or as long as the ceiling height in the laboratory permits. Unfortunately it is difficult to get an ordinary vapor through so long a column. The whole mass is recondensed. To remedy this situation one may insulate the outer surface of the column with magnesia-asbestos "lagging" in the manner commonly practiced with steam pipes.

A good discussion of laboratory equipment for fractional distillation is given by Simons and Wagner, *J. Chem. Education*, **9**, 122 (1932).

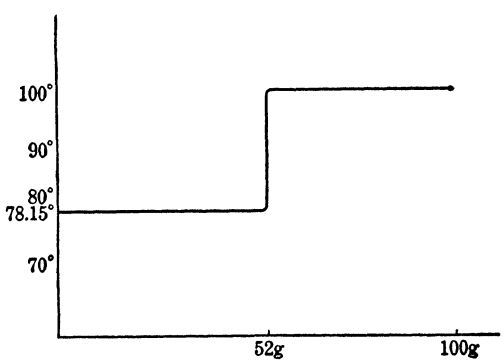


FIG. 5. DISTILLATION OF 100 G. OF A 50% SOLUTION OF ETHYL ALCOHOL THROUGH AN EFFICIENT COLUMN

61. Azeotropic Mixtures with Fractionating Column. If the constant-boiling mixture of two components is distilled through a column, no change in composition occurs. The fact that a column has been interposed in the line has no bearing upon the situation and the results obtained are the same as those from a simple distilling flask.

On the other hand, if the mixture of these particular components does not have the azeotropic composition, fractionation will occur. For example, if aqueous ethyl alcohol (50%) should be distilled through an ideal, highly efficient column, 96% alcohol would be steadily received in the condenser until the boiler was completely stripped of alcohol. The boiling temperature would then rise to 100°, and water would then pass over until all the remaining liquid had been distilled, as shown in Fig. 5.

If the mixture is one of substances which show negative deviation from Raoult's Law, but is not of azeotropic composition, there will also be fractionation. This time the *first* distillate will be of one pure component. For example (Fig. 6):

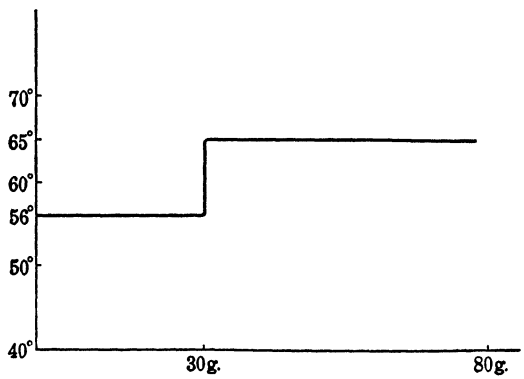


FIG. 6. DISTILLATION OF ACETONE-CHLOROFORM MIXTURE THROUGH A COLUMN

As already noted chloroform (b.pt. 61.2°) and acetone (b.pt. 56.6°) form a constant-boiling mixture (b.pt. 64.7°) when mixed in the ratio of 80% and 20% respectively. Suppose a mixture of 40 g. of chloroform and 40 g. of acetone is distilled through an ideal column. At first the receiver collects pure acetone, until 30 grams has passed over. The balance is of the azeotropic composition; so the temperature will now suddenly rise from the boiling point of acetone, 56.6°, to 64.7°. At this new point the entire remainder of the liquid will go over uniformly.

62. Fractionation under High Pressure. Recently it has become of industrial interest to distil fractionally mixtures of substances having very low boiling points. For example, the separation of propane, boiling point −45°, from its natural mix-

ture with isobutane, boiling point −11°, and *n*-butane, +1°, is desirable in the manufacture of liquefied fuel gas for domestic use in the country. Such an operation might be conducted at high expense with the aid of liquid air or solid carbon dioxide. If on the other hand, the mixture of hydrocarbons is confined in high-pressure steel apparatus, the range of boiling temperature may be elevated to common temperatures. Obviously the boiling kettle, fractionating column, condenser and receiver must all be under pressure. The product is pumped into steel tanks for retail sale.

Steam Distillation

63. The distillation of two non-miscible liquids in one vessel affords an excellent method of vaporizing a relatively involatile substance at a low temperature. Usually one of the liquids is water; therefore the practical problem is to cause a relatively high-boiling organic liquid to pass over with steam at a temperature near 100°. The organic substance in question may be unstable at its own normal, but high boiling point. The possibility of its distillation with steam in the vicinity of 100° is thus attractive.

Before considering the customary process of using an external steam service, it is perhaps better to describe the behavior of two non-miscible liquids when boiled together in one flask. Although one of the liquids is usually water, such a limitation is not at all necessary in the following discussion.

The very fact that neither of the two liquids dissolves appreciably in the other is evidence at once that they do not obey

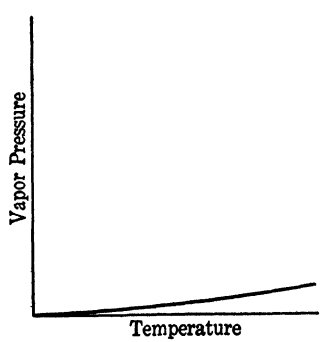


Fig. 1

Vapor Pressures of Iodobenzene

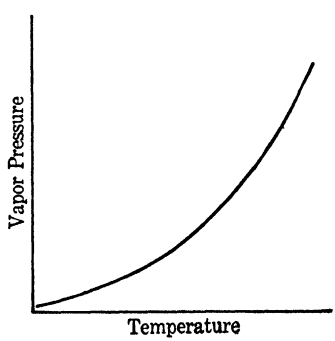


Fig. 2

Vapor Pressures of Water

Raoult's Law. The situation may almost be regarded as an extreme case of "positive deviation" in which the combined vapor pressures are abnormally high. An example is seen in the distillation of a mixture of iodobenzene and water, two mutually insoluble liquids, whose vapor pressures are represented in Figs. 1 and 2.

Iodobenzene and water behave independently of each other, although in the same vessel. Each exerts its own full vapor pressure in addition to that of the other component. Necessarily the combined vapor pressures of the two will reach 760 mm. before the temperature reaches 100°. To find the boiling point of the mixture, invert Fig. 1 and place it directly below Fig. 2, using the same horizontal or temperature axis, as in Fig. 3.

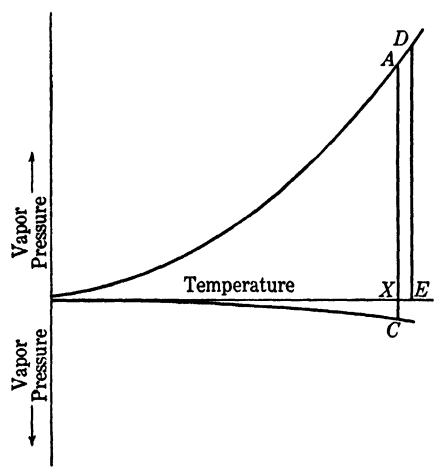


FIG. 3. VAPOR PRESSURES OF IODOBENZENE AND WATER

The line DE is graphically equal to 760 mm. pressure. For the sake of simplicity move DE along to the left and downward until it just fits between the curves for iodobenzene and water, as at AC. The intersection X marks the point where the sum of the vapor pressure of water (AX, 714 mm.) and that of iodobenzene (XC, 46 mm.) is 760 mm. This condition happens to occur at a temperature of 98.25°. The boiling-point of this two-phase system is thus 98.25°. It does not matter how much of each liquid is present in the mixture. The above figures apply as long as both kinds of material are present.

If the iodobenzene is now replaced with a relatively non-volatile substance like bromonaphthalene, the boiling point of the mixture will be nearer to 100° than in the case of iodobenzene. The higher the normal boiling point of the organic component, the more closely the temperature of steam distillation approaches 100°. A low-boiling liquid, on the contrary, will boil together with water at a lower temperature. For example, a mixture of toluene

(b.pt. 111°) and water boils at 85°. In general the boiling point of a mixture of non-miscible liquids is below the normal boiling point of the more volatile component.

The variation of boiling point noted in cases of this type causes difficulty in the identification of certain organic substances when they are first distilled from crude reaction mixtures. For example, when *n*-butyl bromide is distilled from a mixture of sulfuric acid, butyl alcohol, water and organic salts, as described in § 208, the boiling point of the mixture proves to be low. It gives no definite clue to the composition of the distillate prior to the purification of the desired product.

64. Efficiency of Two-Phase ("Steam") Distillation. The lines AX and XC in Fig. 3 measure the relative yields of water and iodobenzene, respectively, as collected in the receiver. In this case there will be 46 moles of iodobenzene obtained for every 714 moles of water. The truth of this simple deduction hinges upon Avogadro's Law. Barring slight deviations from the simple gas laws, each molecule, regardless of size or kind, exerts the same individual vapor pressure—or partial vapor pressure—after escaping from the boiler. The partial vapor pressures of 46 and 714 mm. thus simply measure respectively the relative numbers of each species of molecule passing to the condenser.

In the case above cited the ratio of 46 to 714 at first seems unfavorable in the attempt to obtain a large yield of iodobenzene in a short time. When one notes, however, that 46 moles of iodobenzene weigh 9.38 kg., whereas 714 moles of water weigh only 12.85 kg., the contrast is seen to be not great. The distillation is efficient, as over 42% of the distillate will be of the desired iodobenzene.

In practice it is not customary to boil a mixture of water and the desired substance. As indicated in the practical directions for conducting the process (§ 29) steam is usually generated in a separate vessel. No change in principle is involved, however. The passage of a current of steam into an organic liquid at once introduces liquid water. The turbulent mixture of water, organic compound and mixed vapors may be regarded as the practical equivalent of the contents of a simple flask where two liquids are being boiled together.

Actually the practice of using an outside source of steam is preferable. Direct heating of a glass vessel containing the two

liquids might cause decomposition of the organic component. It might cause bumping. In cases where the process is being used to purify a tarry preparation, direct heating might cause fracture of the flask at a point where the tar would stick and become scorched.

65. Distillation with Superheated Steam. Occasionally a liquid has so slight a vapor pressure at 100° that no adequate quantity can be obtained without the distillation of an unreasonably large volume of water as by-product. In such a case distillation with superheated steam may be employed.

Steam is passed through hot tubes and raised in temperature to 125°, 150° or such higher temperature as may be necessary. It is then passed through a refractory liquid and carries large quantities of the desired vapors into the condenser. In the ideal case represented in Fig. 4 a distillation with superheated steam

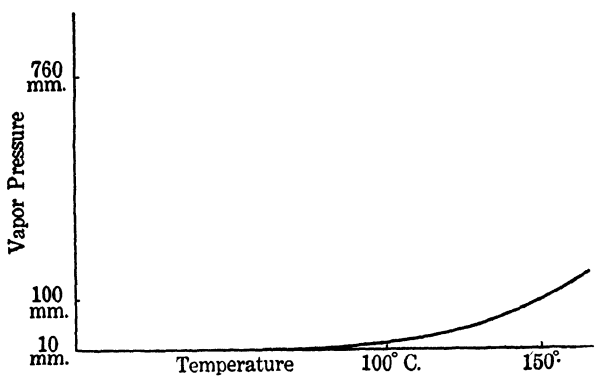


FIG. 4. USE OF SUPERHEATED STEAM

at 150° would give about ten times the yield obtained by operation with ordinary steam at 100°. An actual case is seen in α-bromonaphthalene, a liquid not readily amenable to ordinary steam distillation. This liquid may be distilled in small amounts in the laboratory by the expedient of gently heating the substance itself by means of an oil bath surrounding the containing vessel. The temperature of the oil bath is of course much above 100°. Ordinary steam is passed through the flask, and thus sweeps the desired vapors on through the apparatus.

In distillation with superheated steam the yield does not depend upon the ratio of the vapor pressures of the two liquids involved.

Instead there is a constant total pressure which is not necessarily above 760 mm. Of this total pressure a variable part is that of the steam-distilled liquid. For example in the last illustration, Fig. 4, if ordinary steam were passed through the liquid, the condenser would deliver 10/760 mole of the organic substance with each 750/760 mole of water. If on the other hand the steam were superheated to 150°, the condenser would deliver 100/760 mole of the organic compound and only 660/760 mole of water. This shows approximately eleven times the efficiency of the first process.

PROBLEMS ON DISTILLATION

(See §410, on vapor pressures, and §51, on azeotropic mixtures, for necessary data.)

1. What is the vapor pressure of a mixture of one mole of *n*-pentane, one mole of *n*-heptane, and one mole of *n*-octane at 20°?

2. If a mixture of two moles of bromobenzene and one mole of *p*-dibromobenzene were distilled under reduced pressure at 100°,

   (a) What would be the pressure in the distilling flask?
   (b) What would be the mole-fraction of bromobenzene in the first drop of distillate which came over?
   (c) What would be the percentage composition (by weight) of the first drop so collected?

3. Estimate the boiling point of a 60 mole per cent solution of *n*-pentane in *n*-octane at a place where the barometric reading is 735 mm.

4. Calculate (*a*) the mole fraction of heptane in that mixture of *n*-heptane and *n*-octane which boils at 100°, and (*b*) the weight percentage of *n*-octane in the first vapor coming from this boiling mixture.

Deviations from Raoult's Law

5. Suppose a mixture of equal weights of carbon tetrachloride and methyl alcohol were completely distilled from a simple boiler without a fractionating column or equivalent in any form:

   (a) In what way would the composition of the first few cc. of distillate differ from that of the original mixture?
   (b) How would the last few cc. differ from the original mixture?

6. Suppose a solution of 10 grams of formic acid in 90 grams of water were distilled. How would the composition of the distillate change during the distillation?

7. Referring to question No. 6, how would the composition change if the original mixture had been a 90% solution of formic acid in water?

Fractional Distillation

8. Suppose an equimolal mixture of *p*-dibromobenzene and α-bromonaphthalene were to be separated by fractional distillation. Which temperature would permit the sharpest separation, 110° or 210°?

9. One sample of a pentane-hexane-heptane mixture (light petroleum distillate) was exposed to the air until half of the material had evaporated. Another sample of the same mixture was distilled in the ordinary manner, without fractional reflux, until half of the material had passed into the condenser. Do you think that the contents of the distilling flask at this point would have the same composition as the residue from simple evaporation? Why?

10. In cases where a fractionating column is being used, why is the separation of two liquid components more readily effected by *slow* distillation than by a more rapid operation?

11. What does the position of the sidestem on a distilling flask have to do with the efficiency of fractional distillation from such a vessel?

12. In the case of a liquid mixture obeying Raoult's Law, how does the liquid in the topmost beads in a Hempel column during distillation differ from that at the bottom of the column?

13. Suppose you distilled a mixture of 50 g. of phenol and 50 g. of aniline through an ideal column at a constant rate. Sketch approximately the curve which you would expect to obtain, plotting time elapsed against boiling points.

14. Answer a question like No. 13 in which ethyl alcohol and ethyl acetate are substituted for the phenol and aniline respectively.

Steam Distillation

15. Make a reasonable approximate estimate of the boiling point of each of the following equimolal mixtures:

(a) *n*-propyl bromide and water
(b) ethyl bromide and *n*-propyl bromide
(c) *n*-heptane and water
(d) α-bromonaphthalene and water.

16. Suppose a mixture of ten moles of bromobenzene and ten moles of water were distilled until one mole of the former had passed into the receiver. How much water would simultaneously be distilled?

17. If *p*-dibromobenzene were steam-distilled under pressure at 110° C., what weight of the substance would be carried over with each 100 g. of water distilled?

18. Suppose bromobenzene were steam-distilled at a certain high altitude where water boils at 94°. Would the yield of bromobenzene, per liter of water distilled with it, be greater or less than it would be in a distillation at sea level?

CHAPTER VI

WASHING AND EXTRACTION OF ORGANIC PREPARATIONS

66. Fundamentally the operations of extraction and washing are alike. In each case a mass of material, solid or liquid, is mixed with a solvent which thereupon withdraws from that mass one or more constituents whose removal is desired. If the substance so withdrawn is valuable, and is thus being preserved, the process is commonly termed extraction. If the material so withdrawn is an undesired impurity, the process is called washing.

Washing

67. A solid organic preparation is washed usually just as it lies upon a filter, the wash liquid being allowed to fall upon the finely divided mass and pass through. A liquid preparation is usually shaken with the wash liquid in a separatory funnel. The wash liquid is necessarily one not miscible with the preparation. Usually it is of polar type, while the preparation is of the non-polar oily type. In this normal case the procedure is as follows:

A separatory funnel of ample capacity is mounted in a ring supported on a common stand. The barrel and plug of the stopcock are dried with cloth and lightly treated with stopcock lubricant. The non-polar organic liquid and the wash solvent are then mixed thoroughly in the funnel, after which the two layers or liquid phases are allowed to separate. If the wash solvent is denser than the organic liquid it may conveniently be run out through the stopcock, and the process repeated as often as desired.

If the organic liquid is more dense, as in the case of ethyl iodide which has just been washed with dilute aqueous sodium hydroxide, the denser liquid is run out into a flask for temporary storage, and the wash liquid *decanted from the top of the funnel.* In no case does proper technic permit both liquids to pass through the stopcock and funnel stem. If the washing is to be repeated the once-washed liquid is of course returned to the funnel.

Extraction

68. In extraction the desired organic compound is usually but not necessarily in an aqueous solution, while the second or extracting liquid is commonly of the non-polar type. As usual the two liquids are placed together in a separatory funnel.

Great care should now be exercised when the funnel is stoppered and shaken for the extraction, particularly if the liquid is warm. The sudden evolution of new solvent vapor—such as of diethyl ether—is very likely to lift the stopper and blow a spray of the liquid mixture into the face of the operator. To avoid this, it is well to shake the funnel gently, relieve pressure cautiously at the stopper, and repeat the operation until no further vapors tend to escape forcibly. Finally the well-stoppered funnel is vigorously shaken to permit the maximum possible transfer of the desired substance to the ether or other solvent.

When the two layers have separated distinctly, the next operation depends on relative densities, just as noted in the case of washing:

(*a*) *Extracting Solvent of Lower Density.* Run the denser aqueous liquid into temporary storage, and *decant* the extracting solvent from the top of the funnel.

(*b*) *Extracting Solvent of Higher Density.* Run off the solvent as soon as the extraction has been performed, leaving the aqueous solution in the funnel.

Diethyl ether has been the principal solvent employed for extraction in organic laboratories for many years. As suggested in § 126, it has special value because it is able to dissolve a small amount of water. The main virtue of ether, however, lies in its low boiling point (35°). It is very easily expelled from the ethereal extract.

In elementary practice the extreme volatility and inflammability of diethyl ether lead both to wasteful evaporation and fire hazard. Recently di-isopropyl ether has been offered commercially. Its higher boiling point (67.5°) solves some of the problems of use of ether, and the solvent is recommended in this course.

69. Explosion Hazard from Ether Peroxide. When an ether is allowed to stand for some time in contact with air, a small fraction of the solvent combines with oxygen to form a danger-

ously explosive ether peroxide. The hazard from peroxide is greatest just at the end of a distillation of impure ether, when the peroxide compound becomes concentrated in the distilling flask. The presence of peroxide in ether is detected by shaking a sample of the solvent with an equal volume of 2% potassium iodide and a few drops of dilute hydrochloric acid. Iodine is liberated. The undesirable compound is eliminated by distilling the ether in steam from a flask containing sodium hydroxide solution. Beware of ether which has been standing for several months in a partly-filled bottle, exposed to light and air. Not only the ethyl, but also isopropyl and other ethers form such peroxides. See discussion by E. F. Degering, *J. Chem. Education*, **13**, 494 (1936).

70. Theory of Extraction. Economy of time and material raises this question:

Given a certain quantity of solvent, should this be used in one operation, or should it be divided into portions for repeated extraction? The extraction of phenol from aqueous solution will serve as an illustration.

Phenol, being soluble in both ether and water, is distributed between the two solvents as soon as the extracting solvent and the aqueous solution are shaken together. The ratio of the concentration of phenol in ether to that in water is known as the **distribution coefficient,** or distribution ratio. Such a coefficient not only varies widely with different solutes and solvents, but varies more or less with temperature and total relative amount of solute present. For simplicity in an illustrative calculation, it is assumed herewith that the distribution coefficient of phenol in ether and water is 3. That is, the concentration of phenol in an ether layer is about three times that in the adjacent water layer. In dilute solutions this is approximately the same as saying that phenol is three times as soluble in ether as in water, comparing ratios of solute to solvent. This assumption facilitates calculation without serious error in general reasoning.

Given 40 g. of phenol dissolved in 1000 cc. of water. As a first experiment this is extracted with 1000 cc. of ether used in one portion. The two liquids are shaken together as usual.

Let x be the weight of phenol remaining behind in each cubic centimeter of the water. Then $3x$ will be the weight of phenol

in each cc. of the ether. The total quantity of phenol is then readily set down:

$1000 \times x = 1000x$ grams of phenol in water
$1000 \times 3x = 3000x$ grams of phenol in ether
Total $4000x$ grams, which of course must equal 40, the weight originally given.

Therefore

$$x = 40/4000 = 0.01 \text{ g.}$$

and

$$3000x = \textbf{30 g. of phenol extracted.}$$

This is a 75% recovery in one operation.

Suppose the extraction experiment be repeated with a new supply of 40 g. of phenol in 1000 cc. of water. This time the 1 liter supply of ether is divided into two equal portions, with extraction in two operations:

First Extraction:

$1000 \times x = 1000x$ g. of phenol in the water layer
$500 \times 3x = 1500x$ g. of phenol in the ether layer
Total $2500x$ grams, which equals 40 g.
$x = 0.016$, and
$1500x = \textbf{24 g. of phenol extracted.}$

This is a 60% recovery, 16 g. being left in the aqueous solution.

Second Extraction:

A similar equation will hold, but this time applying to the solution containing only the residual 16 grams of phenol:

$2500x = 16$ g.
$x = 0.0064$ g.
$1500x = 9.6$ g. of phenol extracted.

Addition of the two extract yields, 24 + 9.6, gives **33.6 g., a distinctly better total yield.**

In like manner one may easily prove that still better yields may be obtained by dividing the extracting solvent into three or more portions.

A more formal treatment of the principle may be applied as follows:

Let

K = distribution coefficient
S_1 = solubility of a substance in the extr. solvent
S_2 = solubility of a substance in water
a = original wt. of substance sought
x = wt. of substance obtained on one extraction
v_1 = volume of extracting solvent
v_2 = volume of water,

Then

$$S_1 = \frac{x}{v_1} \quad \text{and} \quad S_2 = \frac{a - x}{v_2} \quad \text{and} \quad K = \frac{S_1}{S_2}$$

and

$$K = \frac{x}{v_1} \quad \text{divided by} \quad \frac{a - x}{v_2} = \frac{xv_2}{v_1(a - x)}$$

$$Kv_1(a - x) = sv_2$$

from which

$$x = \frac{Kv_1a}{v_2 + Kv_1}.$$

In our first example,

$$x = \frac{3 \cdot 1000 \cdot 40}{1000 + (3 \cdot 1000)} = 30 \text{ grams.}$$

In general, a very few extractions will suffice if the distribution coefficient is large. On the other hand, if the coefficient is much less than unity, many extractions will be required.

71. Drying by Extraction. A peculiar application of the principle of extraction is found in the method of drying slightly polar liquids, such as diethyl ether to be used in Grignard syntheses. First the ether is washed to remove alcohol and other impurities, thus incidentally becoming saturated with water. It would now require an excessive quantity of solid calcium chloride to serve as drying agent at this stage in the process, and ether would be lost in the mass of drying agent. On the other hand, an excess of saturated aqueous calcium chloride, shaken with the wet ether, will extract a definite fraction—much over 50%, but of course not all—of the water from the ether. In this manner most of the water is removed without mechanical trouble, and the drying may be finished with a small quantity of solid calcium chloride.

It should of course be noted that by such procedure ether cannot possibly be completely freed of water, even by numerous

repeated extractions, since the extraction solvent (saturated calcium chloride solution) contains as a normal component the very substance one seeks to extract; that is, water. Thus the conventional algebraic calculations will not hold in the simple form already given.

72. Devices are obtainable in the market which permit the simultaneous extraction of material and return of the recovered solvent to the extracting vessel. The liquid which has just been mixed with the material to be extracted is automatically carried to a vessel where the solvent is evaporated. The vapors of the solvent are condensed in the ordinary manner, and the distillate allowed to return to the scene of the original extraction. The Soxhlet extractor is a good example of such a device. It is possible to extract a mass of material with the equivalent of many liters of solvent, although the actual quantity of solvent in the apparatus may be limited to some small value like 100 cc.



SOXHLET APPARATUS FOR EXTRACTION

QUESTIONS

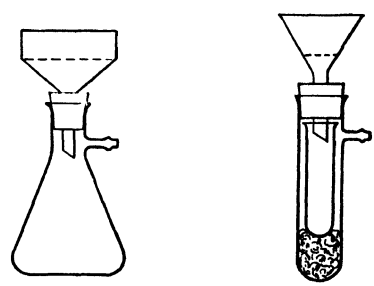
1. The distribution coefficient of a certain organic acid in ether and water is 2. What weight of the acid could be extracted from a solution of 1 gram of the acid in 100 cc. of water, if—
   (a) 50 cc. of ether were used in one portion?
   (b) the same amount of ether were used in two 25 cc. portions?
2. Which would require the more numerous extractions from aqueous solution, hydroquinone or toluidine? Why?
3. Which substance would have the higher distribution coefficient in chloroform and water, butyl amine or aniline? (Note difference in basic strength.)
4. Which would have the higher distribution coefficient in chloroform and water, ethyl acetate or butyl butyrate?
5. Why does the danger of blowing out of the stopper of a separatory funnel disappear after the first few shaking operations, even though fresh ether be added?
6. Why is it often desirable to add salt to a solution which is to be extracted?

CHAPTER VII

ISOLATION AND PURIFICATION OF A SOLID PRODUCT

73. Filtration. When a desired solid substance has separated from a reaction mixture, filtration usually follows. Much time is saved by the application of reduced pressure, or suction filtration. Ordinarily the Buechner funnel, as shown at a in the illustration, is employed. If the quantity of material is small, the Hirsch funnel is used, as in b. In the latter case a special inner receiver is shown, thus illustrating a situation where both the solid product and filtrate are not only small in quantity, but are of value and are to be preserved with minimum loss in transfer.

74. Use of Buechner Filter. The circular piece of filter paper used in the Buechner funnel should be just large enough to cover the entire perforated plate, without crumpling of the edges of the paper. Where crystals of appreciable size are to be collected, any common grade of porous filter paper is acceptable. Later when suspensions of decolorizing carbon are to be filtered, paper of finer texture should be employed. Sometimes two sheets may be used together.



a b

BUECHNER AND HIRSCH FILTRATION APPARATUS

Suction is now applied with the aid of a connection of rubber tubing. This tubing must have a thickness of wall sufficient to withstand complete evacuation without collapse. Without interruption of suction, a small amount of solvent is poured upon the paper. The appropriate solvent of course is like that from which the crystals are to be separated. Care is now taken that the paper clings tightly and uniformly to the plate, without chance for solids to slip under the paper and pass into the filtrate below.

The solvent, which promptly runs through the paper, is now

removed from the flask in case its presence with the filtrate would be undesirable. Suction is resumed, and the reaction mixture promptly poured upon the paper. Ordinarily the mother liquor passes down rapidly, and if it is valuable it is set aside in a separate vessel before the crystals are washed.

Frequently one is unable to transfer the entire contents of the crystallizing vessel to the funnel in one operation. Crystals adhere to the sides of the vessel. It is now convenient to take out part of the filtrate, and use it to flush the residual crystals into the funnel. This operation may naturally be repeated as often as necessary without loss.

After the filtrate has been set aside the funnel is replaced in operating position. The washing process now depends to some extent upon the solubility of the crystals in the wash solvent. If the crystals are insoluble, and water is used for washing, it is satisfactory simply to pass large volumes of water through the crystal bed under continuous suction. If on the other hand the solvent is of appreciable cost, or of a character likely to dissolve the crystals, it is better first to moisten the crystal bed with a limited portion of the solvent *without suction*. After a moment or two in which the solvent permeates the whole mass, paper and crystals alike, suction is actively applied, and the washings passed into the flask below.

In such cases it is desirable to press down the crystal mass. This limits the amount of wash liquid required for the operation. A glass stopper of "mushroom" type, held in inverted position, is convenient for this purpose. There is usually a supply of such stoppers in the storeroom, salvaged from broken bottles.

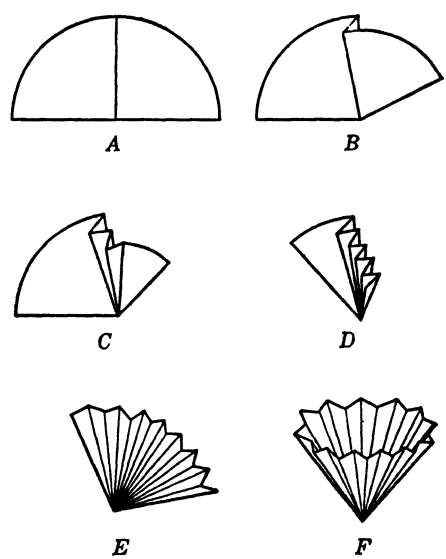
If the final crystalline mass is not easily shaken out of the funnel, it may be blown out if the advance precaution be taken to wash the funnel tip and thus rid it of any offensive substance which should not reach the mouth. In such a procedure the funnel is inverted closely over the dish which is to receive the product.

75. Precautions. If a filter flask without safety bottle is connected directly with a filter pump, one must be careful not to turn off the water before disconnecting the suction hose. Failure to observe this warning usually results in a backwash of water from the pump into the filtrate itself.

If the flask is connected to a piped vacuum system, great care must be taken to avoid over-filling the flask with mother liquor. Carelessness of this sort results in the passage of filtrate into the vacuum line with possible injury to vacuum equipment.

76. Use of a Fluted Filter. Occasionally a solid product is so finely divided that it tends to work its way through the pores of the filter when suction is applied. In other cases colloidal, viscous material is present, and the attempt to filter forcibly drives the viscous material down upon the filter in an impervious, varnish-like layer, blocking further passage of filtrate. One may then resort to the fluted filter. This device is prepared from loosely-fabricated filter paper in the manner shown by the accompanying diagram.

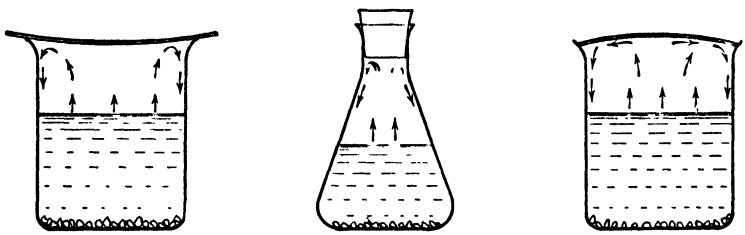
77. Preparation of a Fluted Filter. Select a circular piece of filter paper of two to two and one-half times the diameter of the conical funnel to be used. In folding this paper in fluted form, be very careful that the hands are dry, lest a weak point develop at the bottom of the finished cone. It is well not to fold the paper too sharply near this point—but very sharply in the wider folds above.



FOLDING OF A FILTER

When the folding operation is finished and the filter opened out, its pointed bottom should be very carefully moistened just before the filter is placed in the funnel. The whole paper cone may then be pushed down gently into the funnel so that there will be a slight constriction of folded paper at the place where the hazard of breakage is greatest. In cases where the liquid undergoing filtration is strongly acidic or alkaline this precaution is particularly valuable.

78. Recrystallization—Choice of Vessel. Following the isolation of a crude solid product by filtration, the process of recrystallization from solution is ordinarily employed. That is, the material is first dissolved in a heated solvent; then the resulting solution is cooled, whereupon the desired compound reappears in



RECRYSTALLIZATION IN COVERED VESSELS

crystalline form. For this process a beaker or flask is chosen rather than the evaporating dish or "crystallizing dish" frequently used in inorganic chemistry. When a hot, saturated solution is allowed to cool in an open dish, more or less of the solvent evaporates, and there is a tendency for impure crusts to grow at the margin of the solution. Cooling is therefore conducted in a closed space.

Under such circumstances crystals will likely form first on the bottom where the initial cooling is most rapid. Furthermore, vapors of solvent will be automatically distilled for some time from the hot surface of the liquid to the upper walls of the vessel which are cooled by the atmosphere and thus act as a condenser. The freshly-condensed solvent continually washes down the walls, and may even cause a layer of very dilute solution to form at the top. Under such conditions crystals will be less likely to grow at the top where they are least desired.

When a beaker is used, it is of course convenient to place the watch-glass cover convex side down. Occasionally it is important that the solution be not agitated by the drops of recondensed solvent falling into the center of the liquid and starting crystallization at the top. If a watch-glass of suitable size is available, the optional setting, convex side up, is of course appropriate; or the flask method may suffice.

79. Choice of Solvent. One naturally chooses a solvent which dissolves the solid compound freely when heated, but only spar-

ingly in the cold. If the appropriate solvent for a given case is not known, the theroretical discussion given below (§ 84) should be noted. See also §§ 118 and 186.

80. Procedure in Recrystallization. A small amount of the solvent is heated to the boiling point in a beaker or flask. If the solvent is inflammable, a flask under reflux condenser is employed, and a water-bath used for heating the material (see discussion of fire hazards in § 26). Next as much as possible of the crude solid is dissolved in the small portion of heated solvent. This preliminary operation gives a rough idea of the amount of solvent required for the whole operation. Following such preliminaries, successive portions of solvent and solute are added until the whole quantity of solid has been dissolved in the minimum volume of solvent. If the substance has the habit of crystallizing rapidly, it is advisable to add solvent slightly in excess of the above requirement. This will allow time to filter before crystals could appear in an inconvenient place.

The boiling, saturated solution may contain insoluble impurities. If these impurities are not colloidal, but consist merely of relatively coarse material such as filter paper fibers, cork fragments, etc., the solution should be filtered rapidly through the Buechner funnel. If the impurity is colloidal, a fluted filter is occasionally used. Usually it is better to treat such a turbid mixture with decolorizing carbon, and then to filter it through the Buechner filter. See § 88 for details of the process of decolorization.

If the beaker or flask containing the filtrate from the above-described procedures is now covered as shown in the illustration, and allowed to stand, the desired crystalline preparation should accumulate. In case large crystals are desired, the crystals and liquid should be heated to the boiling temperature, and until all crystals are redissolved. The heating is then discontinued, and the vessel—still covered by the watch glass, or loosely stoppered, as the case may be—is wrapped with a towel to prevent rapid cooling. If finer crystals are desired, the hot saturated solution is stirred vigorously, and cooled rapidly—perhaps with the aid of cold water or an ice bath.

81. Special warning is given of the treacherous habits of carbon disulfide. Not only does this solvent have a very low boiling point (46°) but it may take fire without actual contact with a

flame. It may be ignited by a supposedly safe electric hot-plate, even when the incandescent wires are completely covered. Piped steam service is the safest source of heat, the steam being introduced into a water bath.

82. "Seeding" Methods. Occasionally a solution will not deposit crystals on cooling, despite the fact that the solution is already highly supersaturated. The presence of a protective colloid, perhaps a viscous substance, causes this trouble in many cases. If a so-called "seed-crystal" of the desired substance be introduced, crystallization sometimes starts, and continues until equilibrium is reached. Seeding is illustrated in the recrystallization of benzil (§ 292). In troublesome cases the seeding process may be combined to good advantage with refrigeration in an ice-salt bath at − 10° to − 15°. Cases have been known where a supersaturated solution, contaminated with "tar" which was acting as a protective colloid, required hours of refrigeration with ice and salt for the first crystallization. When the crystalline product was subjected to recrystallization, the time of crystallization was shortened to a few minutes.

83. Theory of Recrystallization. Ordinarily the molecules of impurities in a solid preparation will not readily fit into the geometrical design of the crystals of the principal substance itself. Accordingly, upon recrystallization the newly formed crystals emerge to the actual mechanical exclusion of the impure residual solution (the so-called "mother liquor"). Naturally the new crystals are comparatively pure, provided they are not allowed to grow so large and complex that they **occlude,** or box in, drops of mother liquor.

If the hot solution is cooled rapidly a multitude of fine crystals is likely to appear. Within limits this is a desirable outcome, as no single crystal is large enough to occlude impurities. On the other hand, it is possible to go too far. In cases where the desired substance is very insoluble in the cold solvent, its particles may be so numerous that they become colloidal. The colloidal particles not only tend to obstruct a filter, but also **adsorb** undue amounts of impurities on account of the excessive surface area exposed by the finely divided solid.

84. Choice of Solvent. Almost always the solubility of a preparation increases with rise in temperature. The accompanying figures illustrate common cases. Solubility is plotted against

temperature. As with vapor pressure, the solubility rises at an accelerated rate. Occasionally the slope of the curve is gentle, as in Fig. 2. This means that the solvent is less adapted to the process of recrystallization than the one represented in Fig. 1. The loss upon recrystallization in the second case is readily computed:

Suppose the solid in question were heated with just enough of the solvent (water) to dissolve the material at the boiling point.

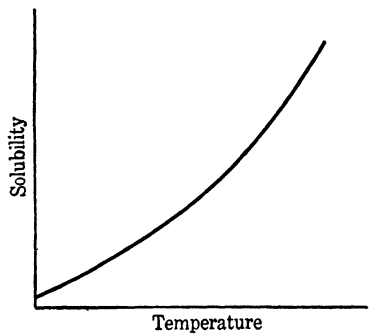


FIG. 1

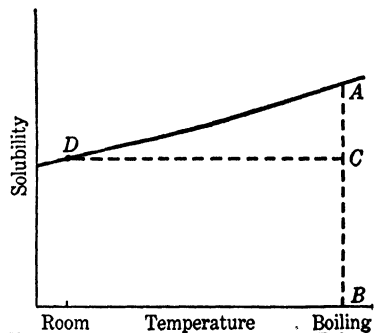


FIG. 2

SOLUBILITY-TEMPERATURE DIAGRAMS

The saturated, hot solution is now cooled to 20°. The content of the solution of the substance at 100° (boiling point) is represented by the line AB, or 30 grams. At 20° the content is represented by BC, which indicates 20 grams per hundred of solvent. Accordingly two-thirds of the original substance remains in solution, while but one-third, represented by AC, or 10 grams, is obtained as crystalline material.

On the other hand, the solubility of a substance may be 30, or even 50 times as much at the boiling point of the solvent as it is at 20°. Recrystallization may then be accomplished with a yield above 95%.

The selection of a solvent of the type shown in Fig. 1 usually means the choice of one not too closely resembling the substance to be recrystallized. Highly non-polar substances are often better recrystallized from ethyl alcohol than from ether or ligroin, for example. On the other hand, if the solvent and solute are too much unlike, as with water and dibromobenzene, it is impossible to dissolve enough under any circumstances for effective work.

Some compounds crystallize so rapidly that there is not time for the hot solution to pass through a filter. In such cases a steam- or hot water-jacketed funnel is prescribed, thus preventing crystallization in the wrong place.

List of Common Solvents

Solvent	Boiling Point	Solvent	Boiling Point
Diethyl ether	35°	Benzene	80°
Carbon disulfide	46°	Isopropyl alcohol	82°
Acetone	56°	Petroleum solvents (variable)	30° to 175°
Chloroform	61°	Water	100°
Methyl alcohol	65°	Toluene	111°
Di-isopropyl ether	68°	*n*-Butyl alcohol	118°
Carbon tetrachloride	76°	Glacial acetic acid	118°
Ethyl acetate	77°	*m*-Xylene	139°
Ethyl alcohol	78°		

85. Separation of an " Oil " from Solution. If a substance has a low melting point, the laboratory worker may have trouble with the separation of a second liquid phase, commonly called an oil, instead of the expected crystalline mass. Students very commonly get the impression that some strange foreign substance has put in an appearance, or that the preparation has decomposed. Actually there may be nothing but the known solute and solvent present. A clear understanding of this phenomenon depends upon a study of melting and solidification (Chap. XI). Accordingly the explanation is postponed, and taken up as a special topic in Chap. XII.

86. Unusual Solvents for Recrystallization. Low-boiling solvents like diethyl ether and petroleum ether are usually not well adapted to the process of recrystallization, unless one wishes to recover crystals by evaporation of the solvent—a method open to question. There is too small a difference between room temperature and the boiling point of ether. If however there is opportunity to chill an ethereal solution with an ice-salt mixture, or solid carbon dioxide, the disadvantage is avoided.

Occasionally a substance, likely one of great molecular weight, is not sufficiently soluble for practical purposes in any common solvent at moderate temperatures. This may necessitate the use of a high-boiling solvent such as nitrobenzene (b.pt. 210°). Unfortunately the crystals obtained with the use of such a solvent are wet with a liquid which will not readily evaporate. Care must

be taken to crush the crystals, and then to wash them first with pure nitrobenzene. Then wash away the residual nitrobenzene with some volatile solvent of suitable type, such as benzene.

87. Altering the Solvent to Promote Crystallization. In some cases there is no single solvent from which a preparation may be crystallized effectively. For example, alcohol may dissolve the material too freely, water not at all. Mixtures of the two may be employed to good effect; or it may be advisable to dissolve the material first in hot alcohol, add water cautiously until crystallization is about to take place, and then cool. The plan of adding water to alcohol must be used in moderation, however, as one may easily throw out a preparation in an impure, colloidal form if too much water be used. It is better to depend upon a long period of refrigeration for encouragement of crystallization rather than to add much water.

Clarification of Solutions

88. Laboratory Procedure. Discolored or turbid aqueous solutions of organic compounds are often clarified by treatment with a filter-aid, usually decolorizing carbon. The solution is boiled with a small quantity of the powdered carbon, perhaps a few grams per liter of solution. (Care is taken not to add carbon to a superheated solution, or the latter may foam excessively and boil over.) After five to ten minutes' boiling the mixture is rapidly filtered by one of the two following methods:

(*a*) In a Buechner funnel place neatly a piece of close-grained filter paper cut exactly to proper size. Wet the paper, press down firmly and apply suction, making certain that no space is left where carbon particles may slip under the paper and reach the filtrate. Now discard any water which may have accumulated in the filter flask, replace the funnel and resume suction. While suction is operating, carefully pour upon the center of the filter the solution containing the carbon to be removed.

(*b*) If the hot solution is not likely to produce crystals rapidly when slightly cooled, it may be filtered to advantage through a fluted filter, as described in § 76. Such technic is less likely to introduce fine particles of carbon into the filtrate. If crystallization in the filter is suspected, set aside whatever filtrate has already accumulated. After making a hole in the bottom of the filter, use the appropriate liquid—water or mother-liquor from a

first crystallization—to transfer the solid matter, carbon, crystals and all to flask or beaker for re-treatment.

89. Action of a Filter-Aid. The powdered solid used for clarification has at least two functions. It may collect viscous, tarry matter, holding it in a somewhat porous form upon the filter. Diatomaceous earth, which consists of minute needles, rosettes and irregular fragments of silica, is much favored for this purpose in chemical industry. Although inexpensive, this material is less useful in the ordinary laboratory, since pressure filtration is needed to make it really effective.

90. Adsorbents. Of much more importance in the laboratory is decolorizing carbon, which is capable of adsorbing finely dispersed colloids from suspension. This property of the carbon is of value not only in the handling of turbid solutions, but often in decolorizing certain transparent liquids which, although colored, look like true solutions. Actually these solutions contain undissolved matter, but in so fine a state of division that light is not greatly disturbed as it passes through the mass. Many of such colloidal solutions are brown in color.

Inasmuch as brown is not a recognized primary color, it is suspected that no pure organic compound exhibits such a color. Even the brown dyes (cf. Bismarck Brown) are probably mixtures of substances. It is therefore the custom to regard brown tints as evidence of impurity which is very likely to adhere to crystals which may later be produced in the solution.

Bone-black (animal charcoal) is the most widely-known decolorizing carbon, but by no means the best. It has limited adsorptive power, and moreover gives trouble at times from lime salts which are normally present in the commercial preparation. An acidic solution should never be treated with ordinary bone-black if the desired substance is to be obtained later by a process of neutralization. If such error were made, the calcium would be extracted as the soluble acid phosphate, and pass into solution. Later calcium phosphate would be precipitated along with the organic preparation when the solution was neutralized. This situation is avoided by the use of bone-black which is washed in advance with hydrochloric acid. Much better than bone-black, however, are some of the modern carbon preparations such as "Norit," made from birch wood, and "Darco."

At times an impurity may have so great a colloidal electric charge upon its particles that it is not readily adsorbed upon the surface of decolorizing carbon. A decided change in acidity of the solution may be of great benefit, suggesting that adsorbed hydrogen or hydroxyl ions were the cause of the difficulty.

If the appropriate reagent (alkali or acid, respectively) be added with the carbon, the offending adsorbed ion is removed, and the particles of impurity, thus discharged, go out with the carbon upon filtration. It is suspected that the efficacy of the alkaline purification of sulfanilic acid is explained in this way. (See § 274.)

Highly-colored soluble substances, especially dyes of great molecular weight, frequently are colloidal in character, although they seem to form perfect solutions. Such colors may often be removed in limited quantity with the aid of decolorizing carbon.

Occasionally decolorizing carbon will adsorb an undue amount of the substance undergoing purification. This possibility will serve as a warning against excessive quantities where preparations of high molecular weight are involved.

CHAPTER VIII

DRYING OF ORGANIC PREPARATIONS

91. Liquids. The "drying" of a liquid means the elimination of water from the preparation. Ordinarily the liquid is treated with some inorganic compound which has the capacity, for one reason or another, of taking water from other material. A conical (Erlenmeyer) flask of ample size is desirable as a vessel in which to conduct the process. Placed in such a container, the liquid spreads over a wide surface in a shallow stratum. If the drying agent is well scattered, every part of the liquid is near to some piece of the material. In chemical literature such a procedure is often called "drying over" the drying agent, e.g., "ether is dried over calcium chloride."

After the liquid is dry, it is usually either decanted or filtered to eliminate the spent drying agent. In exceptional cases, where the liquid is of very low boiling point, or where the hydrated drying agent happens to have adequate stability at the elevated temperature, the liquid is distilled directly from its mixture with the spent drying agent.

The least oxidized liquids, particularly the hydrocarbons and halides, dissolve water so sparingly that they are easily and rapidly dried. Kerosene, for example, is easily dried in a few seconds by agitation with anhydrous sodium sulfate. Usually in such a case most of the water whose removal is desired is not dissolved, but exists in fine globules, possibly emulsified. These globules are captured promptly even by a very ordinary drying agent, provided the latter is well dispersed in the liquid being dried. On the other hand such a substance as butyl alcohol, which dissolves considerable amounts of water, may not yield its aqueous content until some hours have elapsed. A compound of this type requires careful selection of drying agent.

92. Drying by Distillation. The distillation of a liquid organic preparation before the proper drying process has been conducted is ordinarily to be condemned as evidence of slovenly technic, and may cause definite chemical troubles. On the other hand,

where an ample supply of some stable liquid compound is available, and where the chemical action of hot water vapor is not to be feared, drying may be accomplished by the very process of distillation itself. Such technic is best applicable to unoxidized or slightly oxidized high-boiling liquids such as aniline and benzyl alcohol.

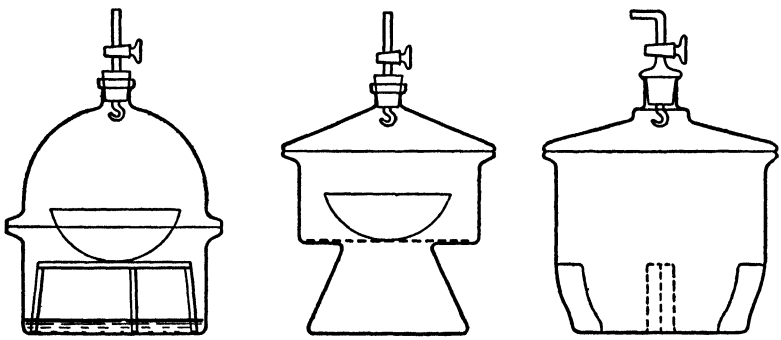
These liquids are so different from water in physical and chemical type that their aqueous mixtures do not obey Raoult's Law. The small and undesired water content may be expelled, in line with the process suggested in the last paragraph, virtually by a sort of a reversed steam-distillation, in which the rate of escape of water is rather large. This steam-distillation occurs at a low temperature (theoretically a trifle under 100°). At this temperature the vapor pressure of the high-boiling organic compound is not great, so that the quantity of the latter escaping with the small amount of water is not important in many cases. Following a change of receivers, the residual pure dry organic liquid is distilled. It is stated that even such volatile liquids as benzene and toluene may be effectively dried by such technic.

93. Solids. A freshly prepared solid, still wet, is ordinarily dried in the open air without the aid of drying agents or heat. In arid climates the simple exposure of wet crystals is usually satisfactory, and is often superior to drying in a simple desiccator of the type used in quantitative analysis. The crystals should be spread upon a large piece of filter paper, and the paper, thus laden, placed in an evaporating dish, which is then loosely covered with paper for protection from dust.

94. Use of an Oven. If the solid preparation will stand high temperatures in the presence of moisture, it may be dried in an oven, or in an open dish on the water bath. In doubtful cases one should test a small sample without risking the entire batch. It is not adequate merely to observe that the normal melting point of the preparation lies above the oven temperature. The substance may be hydrolyzed in such a procedure; or it may form a low-melting mixture with water which at least spoils the appearance of the ultimate crystalline product.

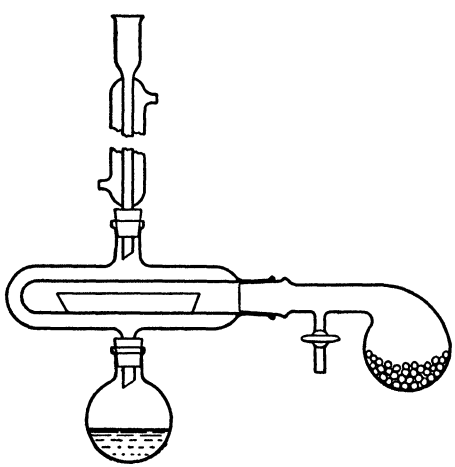
95. Drying under Reduced Pressure. Better than either of the above methods is that of drying in the vacuum desiccator. A suitable drying agent, usually concentrated sulfuric acid, is placed in the bottom of such a desiccator. A screen or perforated

porcelain plate supports the dish in which the preparation is placed for drying. Air is pumped out until the residual pressure falls to 30 or even 20 mm. Under these conditions the molecules of water vapor travel through the space between the crystals and the sulfuric acid in much shorter time than is possible when a



VACUUM DESICCATORS

blanket of relatively dense air intervenes. Some desiccators are not well designed mechanically, and may not safely be exhausted to low pressures. Consult the instructor as to safety limits in evacuation; or see the commercial catalog of the Fisher Scientific Company of Pittsburgh, Pa., which gives a critical appraisal of the hazards of different desiccators.



ABDERHALDEN DRYING APPARATUS

96. A vacuum oven is employed for drying a substance to the extreme degree required in precision analysis. One popular form of this is known as the Abderhalden drying apparatus. In this arrangement a preparation is enclosed in a glass-stoppered, evacuated

test tube surrounded by the hot vapors of a refluxing liquid. The water vapor coming from the crystals travels a short distance and meets a mass of calcium chloride or phosphorus pentoxide just outside of the heated zone.

97. Theory of a Drying Agent. Drying agents may be divided, though not always with clear lines of distinction, into two types: (*a*) those which react in a fundamental manner with water to produce an entirely new water-free substance, usually by a non-reversible reaction; and (*b*) those which take in water of hydration reversibly.

The drying of benzene with metallic sodium illustrates the first type of activity. The water is entirely broken up, and may not be recovered by an ordinary process. Calcium carbide is another reagent of similar type. When placed in aqueous alcohol or similar liquid, it converts the water into acetylene and calcium hydroxide. Phosphorus pentoxide, one of the most efficient, combines with water to yield one or another of the phosphoric acids. Calcium oxide, or quicklime, may be added to this class—or may be somewhat loosely treated as a substance of the (*b*) class which forms a hydrate reversibly.

98. Hydrate Formation. When one of the second class of drying agents comes into contact with water, it is said to bring into play its so-called "coordinate valences," by virtue of which it combines more or less firmly with the water. For example:

$$MgSO_4 + H_2O \rightleftharpoons MgSO_4.H_2O$$

The double arrow as usual indicates that the reaction is reversible, so that the conditions of equilibrium are of major consequence in this discussion.

If now more water is added, the hydrate $MgSO_4.H_2O$ yields in turn the dihydrate, tetrahydrate, pentahydrate, hexahydrate, and finally as the upper limit the heptahydrate, or "Epsom Salt," $MgSO_4.7H_2O$. Each of these compounds is a drying agent except the last one, which of course is already fully hydrated to the limit of its coordinate valences. Similarly other salts, such as calcium chloride and magnesium perchlorate, combine with water to form several hydrates. The number of molecules of water of hydration in other salts is not necessarily the same as in the cited example, however.

It is almost obvious that different salts have widely different efficiencies as drying agents. It is equally true that different lower hydrates of any one particular salt, such as magnesium sulfate, have widely variant values. From one theoretical standpoint the merit of a drying agent is shown by the **decomposition pressure** of the next hydrate above the substance in question. For example, the value of $MgSO_4.H_2O$ is measured by the decomposition pressure of $MgSO_4.2H_2O$. The following table gives approximate values for the decomposition pressures of the hydrates of magnesium sulfate at 25° C.:

$MgSO_4.7H_2O \rightarrow MgSO_4.6H_2O + H_2O$	13 mm.
$MgSO_4.6H_2O \rightarrow MgSO_4.5H_2O + H_2O$	10 mm.
$MgSO_4.5H_2O \rightarrow MgSO_4.4H_2O + H_2O$	9 mm.
$MgSO_4.4H_2O \rightarrow MgSO_4.2H_2O + 2H_2O$	5 mm.
$MgSO_4.2H_2O \rightarrow MgSO_4.H_2O + H_2O$	2 mm.
$MgSO_4.H_2O \rightarrow MgSO_4 + H_2O$	1 mm.

The meaning of the above table is illustrated simply by the ideal experiment of introducing an excess of any of the above hydrates into an evacuated vessel. For example, if the dihydrate were so introduced, some of its molecules would break up according to the appropriate equation above, yielding the monohydrate, until the newly produced water vapor was sufficient in quantity to exert a vapor pressure of 2 mm. Or, approaching the problem from the opposite extreme: if the monohydrate were admitted to a vessel containing water vapor at 10 or 15 mm., a reverse reaction would start, and the dihydrate would be produced until the pressure had fallen to 2 mm. It is the latter type of experiment which is of major significance in the problem at hand, viz., the drying of organic preparations.

By analogy from the last experiment, the monohydrate of magnesium sulfate will take water away from any surrounding fluid medium until the activity, or effective concentration of H_2O in that medium is cut down to a value equivalent to 2 mm. of ordinary water vapor.

Should an excess of the organic liquid (or other fluid medium) be now added, the monohydrate will continue to absorb water and maintain the 2 mm. maximum until it has all been converted into the dihydrate. Further addition of aqueous material at once offers opportunity for the formation of the next hydrate

$MgSO_4.4H_2O$. The vapor pressure limit is at once raised to 5 mm., however, and the drying from this point forward is not as thorough as before.

99. From this simple experiment two of the most important criteria of a good drying agent are at once revealed, as follows:

1. **Intensity** of drying.
2. Quantitative **capacity** for drying purposes.

Under caption No. (1) comes the major question—How low can the vapor pressure, and thus the water percentage, in a liquid preparation be taken by use of an ample supply of the given drying agent? Under (2) the question is—How much water can be absorbed by a given weight of the drying agent at a given intensity—that is, before it becomes necessary to go up to a still higher hydrate?

The answers to (1) come from the vapor pressure tables; those to (2) simply require a little supplementary chemical arithmetic. In both cases wide differences exist between the values for different salts. Magnesium perchlorate trihydrate, for example, is a much better drying agent than magnesium sulfate dihydrate, despite its larger molal water content. The merit of the perchlorate lies in its great intensity, and is a specific property of the particular magnesium compound.

Unfortunately the organic laboratory worker has no simple way of knowing the aqueous activity, or escaping tendency, of H_2O in his liquid preparations. He is thus unable to predict just the particular hydrate which will meet a given need. Furthermore, no certainty of hydrate composition exists in most common commercial preparations of drying agents, so that the exact behavior of a specific hydrate has little meaning in every-day laboratory practice.

100. A simple practical method of appraisal of commercial drying agents is that of using them to dry samples of air. The air, previously moistened, is allowed to come into contact with the drying agent, and is then analyzed for water content. The lower the final water content in the air sample, the better the drying agent from the intensity standpoint. The following table is taken mostly from a publication by Shepherd (reference at end of chapter). Similar data, taken at 30.5°, have been reported by the Bureau of Standards.

WT. OF H_2O LEFT IN ONE LITER OF GAS DRIED AT 25° C.

P_2O_5	less than	0.00002 mg.
$Mg(ClO_4)_2$	less than	0.0005
$Mg(ClO_4)_2.3H_2O$	less than	0.002
KOH fused		0.002
Al_2O_3		0.003
H_2SO_4		0.003
MgO		0.008
NaOH fused		0.16
$CaBr_2$		0.2
CaO		0.2
H_2SO_4 95%		0.3
$CaCl_2$ fused		0.36
$ZnCl_2$		0.8
$ZnBr_2$		1.1
$CuSO_4$		1.4
Na_2SO_4		12

Since one milligram of water contained in one liter of gas at 25° exerts approximately one millimeter of partial vapor pressure, mm. may be substituted for mg. in the foregoing table without error of significance in the phenomena under consideration.

COMMERCIAL DRYING AGENTS

101. Aluminum Oxide, Anhydrous. Al_2O_3. This preparation only recently has been commanding attention, but no great amount of data seems available describing its use in organic synthesis. It is marketed under the trade name "Hydralo."

102. Calcium Chloride. $CaCl_2$. Perhaps the best-known drying agent. It is marketed for drying purposes mainly in two forms, the "granular" and "fused." Granular calcium chloride consists of anhydrous $CaCl_2$ made by heating ordinary calcium chloride hexahydrate to red heat, but not to 806°, the melting point of $CaCl_2$. Four molecules of water disappear at 200°, and then two more at higher temperatures. By avoidance of melting the manufacturer is enabled to prepare a porous, chalky mass which is then crushed into coarse granules.

The granular calcium chloride acts not only by virtue of its transformation to the hydrate, but by colloidal adsorption, as would any porous material. It is thus difficult to measure the exact effectiveness of this type of preparation without consideration of the particular commercial product which happens to be at hand. Although the porous calcium chloride is more effective than a compact preparation, it is not favored in cases where a

small amount of a valuable liquid is to be dried. Loss of liquid by absorption is likely to occur. In such cases fused anhydrous calcium chloride is recommended in spite of its slower action.

Calcium chloride—either granular or fused— is not expensive. It has a low enough vapor pressure rating for ordinary drying of many liquids in organic chemistry, or for maintenance of a dry atmosphere in a desiccator used in quantitative analysis. On the other hand, calcium chloride is unsuited to the drying of alcohols, also some esters, which chemically combine with the salt. It is relatively unsuited for use in a desiccator whose purpose is to dry a solid; for such purpose concentrated sulfuric acid is much more efficient.

Calcium chloride is somewhat slow in action, therefore not as suitable for drying a hydrocarbon as sodium sulfate, which see below. This slowness of action is possibly due to the blanketing of each particle of the commercial product with a thin layer of solution formed out of the first small quantity of water received. If the wet pieces of calcium chloride be allowed to remain for a day or more in contact with the moist liquid, the moisture will strike into the mass, and a more permeable structure of solid will be produced—this time of a crystalline hydrate of low water content. The new hydrate itself is a good drying agent.

The industrial process of preparing anhydrous calcium chloride usually permits a slight amount of hydrolysis, yielding hydrogen chloride gas which escapes, and causing the product thus to be contaminated with calcium hydroxide. This is of importance in organic combustion analysis, where such calcium chloride must be treated with carbon dioxide before use in determining water vapor.

103. Calcium Oxide. CaO. This substance is very cheap, and is insoluble in alcohols. It is employed in drying ethyl alcohol. Its strongly basic character forbids its use with acidic preparations, or even with reactive materials such as aldehydes.

104. Calcium Sulfate. $CaSO_4$. Only recently (1933) has anhydrous calcium sulfate come to notice, through the researches of Hammond and Withrow. This substance rapidly and thoroughly dries not only hydrocarbons, but even alcohols and acids. Unfortunately it goes only to the hydrate $2CaSO_4.H_2O$, under the conditions of drying, and thus reacts with only 6.6% of its weight in water. It is excellent for final drying of liquids which were

nearly dry to start with. The porous commercial preparation of calcium sulfate (Drierite) is said to absorb as much as 12 to 14% of its weight in water during common operations of drying organic liquids.

105. Magnesium Perchlorate. $Mg(ClO_4)_2$. This excellent drying agent, known commercially as "Anhydrone," and in the form of its trihydrate as "Dehydrite," is also a somewhat recent discovery. (See Willard and Smith, reference at end of chapter.) It removes water very completely, and does not "channel" or run into a viscous mass in the manner of its rival, phosphorus pentoxide. It is used to absorb water vapor in organic quantitative analysis. Its high cost (several dollars per pound) has been its principal disadvantage. Laboratory workers are cautioned not to use magnesium perchlorate to dry organic acids, or aldehydes which may yield acids upon atmospheric oxidation. Mixtures of acid, perchlorate and combustible matter have been known to cause serious explosions.

106. Magnesium Sulfate. $MgSO_4$. Probably the best neutral, low-priced drying agent. Apparently no one has made a detailed specific study of this substance as a drying agent for organic liquids; but vapor pressure data, and general laboratory experience, indicate that magnesium sulfate is intermediate in drying capabilities between sodium sulfate and calcium chloride. Where calcium chloride is ruled out on account of addition compounds, as with certain esters, nitriles, etc., magnesium sulfate is valuable. It is insoluble in most organic liquids. Prepared by heating Epsom salt, $MgSO_4.7H_2O$.

107. Phosphorus Pentoxide. P_2O_5. The classical resource of the worker who wishes extreme efficiency. Serviceable for preparation of anhydrous ether, and for drying gases to a state of extreme desiccation. "Channels" badly; see magnesium perchlorate above. Being an acid anhydride, it is generally not suitable for most liquids, such as bases, alcohols, etc.

108. Potassium Carbonate. K_2CO_3. A moderately efficient drying agent which is useful with esters, nitriles, ketones, some alcohols and a few other substances which react with calcium chloride and are not thoroughly dried with sodium sulfate. A competitor of magnesium sulfate in such situations.

109. Potassium Hydroxide. KOH. The substance, available in stick and pellet form, is a remarkably thorough desiccant. Its

strongly basic character limits its use to basic or inert liquids and gases.

110. Sodium Hydroxide. NaOH. Somewhat inferior to potassium hydroxide, but sometimes substituted with fair success.

111. Sodium Sulfate. Na_2SO_4. This very inexpensive salt, while at the bottom of the merit list on thoroughness of desiccation, is rapid and neat in its action. It occurs in fine granules which are easily scattered throughout the liquid which is being dried. It is well adapted to the drying of non-polar, non-oxidized liquids in which water is almost insoluble. The sodium sulfate acts almost as a chemical sponge to take up water which is not actually in solution.

112. Sulfuric Acid. This extremely effective reagent is rarely used for drying of liquids, but is widely employed for drying of gases, and for desiccator service. Great care must be taken not to allow organic material to be spilled from a container into the sulfuric acid of a desiccator. Within a few hours the sulfuric acid reacts with the introduced material, generating sulfur dioxide and perhaps injuring the preparation being dried.

When used in a desiccator, sulfuric acid will absorb not only water, but alcohol as well. If alcohol be thus allowed to pass into the sulfuric acid, the acid should be changed before the desiccator is again used.

113. The **drying of the hydrochloride of a weak base** presents a special problem. Suppose such a preparation had just been separated from a strongly acid solution. The excess acid was necessary to prevent hydrolysis. The crystals are covered with residual mother liquor containing both water and hydrochloric acid. If they were placed in an ordinary sulfuric acid desiccator in the common way, so much hydrogen chloride gas would be liberated that there would soon be not even a partial vacuum. The drying process would be retarded. In such a case a dish containing a few pieces of solid sodium hydroxide is placed in the desiccator beside the vessel containing the preparation. The hydrogen chloride gas reacts with the sodium hydroxide forming common salt, which is harmless, and releasing water which is absorbed in the regular manner in the drying agent below.

114. Drying by Extraction. The partial drying of certain organic liquids may be accomplished by shaking them with a

highly concentrated aqueous solution of a very soluble salt such as calcium chloride. See § 71.

115. Drying by Hydrolysis. In hydrolysis water is consumed chemically. If therefore a sufficiently active reagent of appropriate type is placed in an organic solvent containing water, it may be hydrolyzed to such an extent that the solvent is almost completely rid of its aqueous content. This is exemplified in the method of Smith[1] for preparing absolute alcohol of extremely high grade from common, nearly anhydrous alcohol. In view of its usefulness in the preliminaries of certain syntheses described later (§§ 307, 308), laboratory directions are given below.

116. Extremely Dry Ethyl Alcohol. A two-liter flask, fitted to a fractionating column, is attached to a water-cooled condenser in such a manner that it may be used either for refluxing or ordinary distillation without the breaking of connections. In this flask place one liter of ethyl alcohol which contains not over 0.5% of water, and slowly introduce 7 g. of sliced sodium metal. After the sodium has dissolved, add 25 g. of diethyl succinate, and reflux for two hours on the water bath. Finally distil the alcohol (through the column) from the water bath. If the condenser is well protected from atmospheric moisture with a calcium chloride tube, the content of water in the product will be too low to be estimated by any ordinary method, such as that described in § 200. Note.—Diethyl phthalate may be substituted for the succinate specified by Smith.

Consideration of the above directions at once raises the question why sodium alone is not sufficient to eliminate the water, it being known that water is a much stronger acid than ethyl alcohol. At low concentrations of water, however, alcohol is enabled to compete. Sodium then reacts largely with alcohol, and thus does not finish the task of removing water.

$$2Na + 2C_2H_5OH \rightarrow H_2 + 2C_2H_5ONa$$

The introduction of an ethyl ester into the above situation makes possible a reaction consuming water, which presumably goes to completion:

$$C_2H_5OOC.R + C_2H_5ONa + H_2O \rightarrow 2C_2H_5OH + NaOOC.R$$

Distillation yields pure alcohol, the sodium salt being left as a nonvolatile residue.

[1] E. L. Smith, *Jour. Chem. Soc.*, 1927, 1288.

Ethyl succinate (or phthalate) is chosen for the purpose because of its high boiling point; any excess is left behind in the distillation. Although Smith makes no further claim for his particular choice of ester, it is probable that its dibasic character is of value here.

Suppose alcohol containing 0.3% of water were treated by the above method. 25 g. of diethyl succinate is about twice the ester equivalent of the 0.3% of water. Accordingly, each molecule of the ester will be only half-hydrolyzed:

$$C_2H_5OOC.CH_2.CH_2.COOC_2H_5 + C_2H_5ONa \rightarrow 2C_2H_5OH + NaOOC.CH_2.CH_2.COOC_2H_5$$

In this manner a quantity of the non-volatile ester-salt is present, thus ensuring completeness of reaction without danger of distillation of the needed excess of ester.

117. " Drying " with a Hydrocarbon. In cases where there is need to remove a hydrocarbon solvent, it is possible to accomplish the result by placing the crystalline mass, wet with hydrocarbon, in a desiccator containing a heavy, involatile hydrocarbon oil, or even paraffin itself. The solvent vapors are absorbed by the oil. The industrial extraction of gasoline from "wet" natural gas with the aid of oil involves similar principles.

QUESTIONS

1. What drying agent would you use to dry—
   (*a*) an ethereal solution of butyric acid,
   (*b*) a solution of *p*-dibromobenzene in benzene,
   (*c*) an ethereal solution of tributylamine,
   (*d*) methyl cyanide,
   (*e*) methanol,
   (*f*) ortho-nitrotoluene,
   (*g*) meta-xylene,
   (*h*) acetic acid containing only 0.5% of water?
2. Why is an extract of an organic compound dried before instead of after evaporation of the ether?
3. What scientific information do you need in order to decide the following question—Should the calcium chloride, used to dry ethyl iodide (§ 206) be removed before the iodide is finally distilled?
4. How can it be possible by mere distillation to dry a liquid like benzene, whose boiling point is almost twenty degrees below the boiling point of water, the liquid which is to be expelled?
5. What does temperature have to do with the efficiency of a drying agent?

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CHAPTER IX

SOLUBILITY OF ORGANIC COMPOUNDS

118. For the promotion of a reaction between two or more substances a good solvent is often favored. For recrystallization, it is preferable to employ a solvent which is not too good; while for washing a crystalline preparation it is of course best to choose a solvent which will not dissolve the solid appreciably. Accordingly, solubility data are much in demand.

Since there are thousands of possible solvents, and hundreds of thousands of organic compounds which might be solutes, one can hardly expect to find solubility tables to cover each combination of solvent and solute. It is thus desirable to formulate rules to help in predicting the solubility of any given organic compound in any given solvent.

In predicting solubility most organic chemists use a sort of intuition based on the fundamental rule colloquially known as "Like dissolves like." Stated more formally, this principle may be expressed as follows:

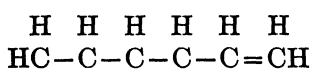
A substance is likely to be soluble in a solvent which it closely resembles in chemical constitution and physical characteristics. For example, hexane is very soluble in heptane; butyl alcohol in amyl alcohol; formic acid in acetic acid; propylene dibromide in ethylene dibromide. The likenesses here are obvious. On the other hand, butyl alcohol is very soluble in chloroform, whereas aniline hydrochloride is not. Questions naturally arise: Wherein lies the similarity of the alcohol and chloroform? And why are aniline hydrochloride and chloroform particularly unlike?

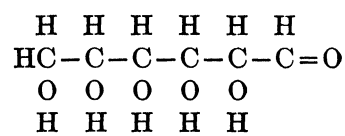
Several kinds of "likeness" influence solubility. If the solute resembles the solvent in most of these characteristics, it is likely to dissolve freely in that solvent. If unlike at many points, it will be relatively insoluble.

(*a*) *Degree of Oxidation by Oxygen.* The percentage of oxygen in a compound is perhaps the greatest single factor readily applicable in judging likeness of an organic solute and solvent. Substances containing little or no oxygen tend to be very soluble in

solvents containing no oxygen. Substances of high oxygen content dissolve freely in solvents containing much oxygen. The unoxidized solutes, on the other hand, do not dissolve appreciably in solvents containing much oxygen, and vice versa.

For example, the molecules of hexene and glucose are both built upon the same carbon skeleton, and thus at first glance seem to be alike. Each contains six carbon atoms and twelve hydrogen atoms.





Glucose, however, contains much oxygen. Suppose benzene, C_6H_6, is the solvent. Hexene proves to be very soluble, glucose almost insoluble. With water, a completely oxidized solvent, the results are reversed. Glucose is dissolved freely and hexene scarcely at all.

(*b*) A substance of low **dielectric constant** is likely to be most soluble in a solvent of low dielectric, insoluble in one of high constant, and vice versa. For example, bromobenzene, dielectric constant 5.2, is miscible with carbon tetrachloride, d.c. 2.25; but it is almost insoluble in water, d.c. 81. This rule is little used, because many dielectric constants are not known. It is closely related to rule (*c*) given below.

(*c*) A polar substance is more soluble in polar solvents, less soluble in non-polar solvents. Non-polar solutes have corresponding solubility relations. Polar compounds are those exhibiting in some way electropositive and negative parts. Some of these are of the type called a "dipole," in which the center of positive charges in the molecule is not the same as that of the negative electrons; e.g., methanol. Other polar compounds have such distinct positive and negative parts that the molecule actually dissociates into separate positive and negative fragments, which are of course the ions. Salts are thus the most strongly polar organic compounds.

Water, although but slightly ionized, is highly polar. Accordingly various organic salts, such as aniline hydrochloride and sodium benzoate are usually more soluble in water than their parent bases and acids, such as aniline and benzoic acid. These

salts are of course very insoluble in non-polar solvents such as pentane.

Two rules additional to those exemplifying the likeness principle are also important:

(*a*) A solute of low **molecular weight** is generally more soluble in a solvent than one of high molecular weight. Kerosene is less soluble than gasoline in ethyl alcohol, for example, Furthermore, since both solute and solvent may be liquids, this rule may be reversed—solvents of low molecular weight have relatively high efficiency.

(*b*) A solute of low **melting point** tends to be more soluble in solvents than one of high melting-point. For example, phenol, melting-point 43°, is far more soluble in water than is benzoic acid, a compound of somewhat similar structure and with more oxygen, but which melts at 121°. Similarly, solids are ordinarily less soluble than similar liquids in a given solvent. Even a given solid substance is less soluble in a solvent than the liquid form of that same substance.

119. Reaction Solvents. A substance tends to "dissolve" in a solvent with which it chemically combines. This is really another example of the likeness rule, but under a disguise. For example: benzaldehyde, C_6H_5CHO, an almost non-polar substance with little oxygen and fairly large molecular weight, is but slightly soluble in water, as one might expect (1 g. to 300 g. of water). It might be expected to be less soluble in aqueous sodium bisulfite solution, a highly polar medium. It reacts with the bisulfite, however, to form a new compound,—

$$C_6H_5CHO + NaHSO_3 \rightarrow C_6H_5CHOH-SO_3Na$$

The new compound is obviously in part like sodium bisulfite in structure. Therefore it dissolves freely.

Similarly: β-naphthol ($C_{10}H_8O$), a substance with only a small percentage of oxygen, is but slightly soluble in water. It dissolves freely in aqueous sodium hydroxide, however, since the polar salt is formed.

Likewise: amylene is almost insoluble in water, but very soluble in fuming sulfuric acid, a highly polar liquid. It forms an alkyl-sulfuric acid compound, $C_5H_{11}HSO_4$.

The great solvent power of acetone is thought to be due in part to the ability of that compound to combine loosely with many

solutes. No clear-cut, defined compound is produced, but the solute may be described as "solvated," just as many inorganic compounds are "hydrated" when crystallized from water. Acetone thus dissolves resins, pitches, dried paint, varnish, lacquer, as well as a host of pure organic compounds containing more or less oxygen.

120. Halogens. A chlorine atom, substituted for hydrogen in an organic compound, usually gives a solubility effect much like adding two or three carbon atoms to the original molecule. For example, ethyl chloride in solubility relations is much like butane. With bromine and iodine the weight effect is accentuated, though not in any proportion subject to exact prediction. Ethyl bromide is much like pentane, and ethyl iodide like hexane. These halides are therefore almost insoluble in water, but are miscible with ether, gasoline and such non-polar solvents.

When three chlorine atoms are concentrated on one carbon atom, as in chloroform, a very slight tendency toward the polar character is observed. This solvent accordingly dissolves to some extent certain slightly polar compounds, such as alkaloids, waxes, etc.

121. Sulfur, Nitrogen. These elements give no striking solubility effect of themselves unless they cause the formation of some polar substance such as an acid, base or salt. Ethyl mercaptan (C_2H_5SH) for example, although a substance of low molecular weight, is soluble only to the extent of 1.5 g. in 100 cc. of water. Benzene sulfonic acid, on the other hand, is soluble in water, not because of the specific influence of the sulfur atoms, but because of the oxygen content, the hydroxyl group and the polar acid character. Diethylamine, while devoid of oxygen, dissolves freely in water because it reacts with that solvent to form the diethylammonium ion $(C_2H_5)_2NH_2^+$, a polar substance. (See Chap. XV.)

122. Double Bonds. Unsaturated hydrocarbons are very slightly polar. They are thus slightly more soluble than paraffins in water. Gasoline, for example, is miscible with 95% alcohol, an aqueous solution, if the gasoline contains a high fraction of olefines and aromatics. Paraffin gasoline, however, is not miscible with 95% alcohol. This fact is of interest in certain foreign countries where there is demand for such mixtures as motor fuel.

123. The Hydroxyl Group. Being a structural component of water, the hydroxyl group has a profound influence favoring aqueous solution. A great liking for water is seen in such hydroxyl derivatives as glycol, glycerol, pyrogallol, glucose. Even a substance of such great molecular weight as cane sugar (sucrose) is very soluble in water. Its molecule contains eight hydroxyl groups.

124. Solubility of Solids. Most of the foregoing set of rules applies much more consistently to liquid solutes than to crystalline substances. In the solid state the forces holding molecules together are so great, and yet so widely variant, that remarkable differences in solubility occur between very similar solutes. For example, the solubility of maleic acid at 25° is 78 g. in 100 g. of water. That of fumaric acid, its (trans-) geometric isomer, is only 0.7 g. The mere difference between the "cis" and "trans" structure seems to be responsible for this unexpected contrast.

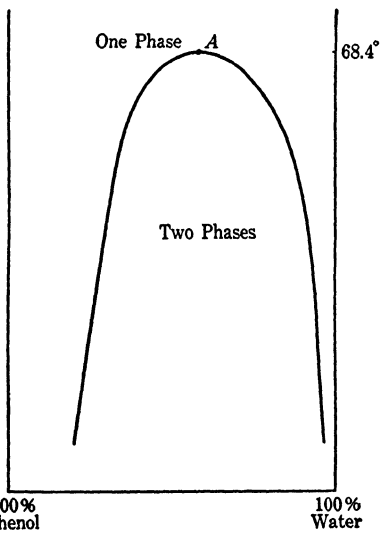
125. Intermediate Solvents. Ethyl alcohol is the most important example of the intermediate type of solvent. Its value lies very largely in the fact that it frequently dissolves both polar and non-polar substances, thus permitting their intermixture and possible speedy reaction. For example; benzyl cyanide is ordinarily prepared by the interaction of benzyl chloride, a non-polar oil, with sodium cyanide, a polar, water-soluble salt. The addition of ethyl alcohol to the proposed mixture creates a liquid phase in which substantial amounts of both reactants may dissolve. The reaction is then completed in a comparatively short time.

126. Slightly Polar Solvents. Ordinary diethyl ether is a more useful solvent in the organic laboratory than pentane or hexane, although the latter two can be furnished in isomeric mixtures from oil refineries at a much lower price. Much of the superiority of ether lies in its oxygen content, which presumably enables the substance to dissolve a small amount of water (about 1 gram in 75 grams of ether). For example:

Suppose an amine, $R-NH_2$, is to be precipitated from solution in the form of its hydrochloride salt ($R-NH_3Cl$). Since the R group is of the hydrocarbon type, the amine is best dissolved in a non-polar solvent. Hydrogen chloride gas is passed into the solution, and the polar salt precipitated. If such an operation were conducted in pentane, or its equivalent petroleum ether, the newly-formed salt would carry with it any water which might

have entered during the admixture of reagents. The pentane would repel the water. If dry ether were used, on the contrary, a dry, crystalline salt would be obtained, and the small amount of water would stay in the solvent. A much neater preparation may thus be obtained.

127. Solubility of Liquids in Liquids. If two liquids are similar, and their mixture obeys Raoult's Law, they will necessarily be miscible in all proportions. Extremely unlike liquids, such as decane and water, deviating positively to the highest degree from Raoult's Law, are practically insoluble in each other. Other combinations of intermediate character, such as phenol and water, or hexane and methyl alcohol, form two liquid phases, one of which is a saturated solution of the first component in the second, the other a saturated solution of the second in the first. A change either in temperature or in composition may cause the two phases to become alike, and thus actually produce one phase. This is the equivalent of saying that an emulsion (intimate mixture of globules of one liquid in another), which is by nature turbid, may clear up if heated, or if the proper amount of one of the components is added. The figure shows the limits of temperature and composition within which phenol and water may not produce a single liquid phase.



THE SYSTEM PHENOL-WATER

128. Test for Water in Alcohol. In the experiment on absolute alcohol (§ 197), a special petroleum product is mixed with alcohol in order to locate the point *A* (as of the figure). The more water present, the larger is the two-phase zone. Point *A* rises regularly with each added percentage of water. The temperature value of each of the successive points *A* is then plotted against composition of the alcohol, resulting in the graph shown in § 201.

129. Questions. A series of questions is added to illustrate the application of the solubility rules. The first of these, Nos. 1 to 7, are straightforward queries dealing with cases in which the rules operate in agreement, or where but one rule has obvious significance. The second series, Nos. 8 to 17, refers to situations where the rules may seem to conflict. The answer to this type of question is likely to point out the fact that one rule, perhaps not the most obvious, is exerting such great influence that it completely reverses the prediction which some other rule invites.

Series 1

1. Why is acetaldehyde more soluble than butyraldehyde in water?
2. Why is ethyl iodide less soluble in water than in ethyl alcohol?
3. Why is bromobenzoic acid less soluble than benzoic acid in water?
4. Why is butyl alcohol more soluble than its isomer diethyl ether in water?
5. When a 25% (saturated) aqueous solution of methyl acetate is treated with solid sodium chloride, methyl acetate is partially thrown out of solution. Why should this happen?
6. Why is phenol more soluble than phenolphthalein in alcohol?
7. How do we account for the fact that only the first three members of the series of normal aliphatic alcohols are miscible with water, whereas the first four normal aliphatic acids are miscible with the same solvent?

Series 2

8. Why is naphthalene more soluble in ethyl alcohol than in methyl alcohol, a solvent of less molecular weight?
9. Why is aniline, C_6H_7N, much less soluble than dipropylamine, $C_6H_{15}N$, in water?
10. Why is amyl alcohol less soluble in water than in concentrated sulfuric acid?
11. Why is methylamine hydrochloride, CH_6NCl, less soluble in propyl chloride, C_3H_7Cl, than in ethyl alcohol, C_2H_6O?
12. Why is starch, which contains at least half as many hydroxyl group as carbon atoms, insoluble in alcohol?
13. Why is phenylene diamine more soluble than dinitrobenzene in water?
14. Why is water more soluble in propyl alcohol than in valeric acid, a more highly ionized solvent?
15. Why is it necessary to convert the metal lead into such an unusual and expensive compound as tetra-ethyl lead before applying it to the preparation of non-detonating ("Ethyl") gasoline?

16. Why is *p*-dibromobenzene less soluble in acetone than in diethyl ether, a solvent of greater molecular weight?

17. Why is ether more soluble in concentrated sulfuric acid than in water, a less ionized solvent?

18. Show how the very fact that *n*-butyl alcohol and water form a two-liquid-phase system proves that the mixture does not obey Raoult's Law.

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Kamm, Oliver, "Qualitative Organic Analysis" (Wiley, 1932), Chap. 2.

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CHAPTER X

SUBLIMATION

130. Purification by vaporization and recondensation may be carried out with solids as well as liquids. If a substance is vaporized and the vapor made to pass directly into the solid state without intermediate passage through the liquid state, the process is known in practical chemistry as **sublimation.**

In the formal literature of physics and physical chemistry sublimation is defined more narrowly as the mere passage of a substance directly from the solid to the vapor state. No restoration of the solid is considered. In practical chemistry, however, the mode of vaporization in the operation of sublimation is of secondary importance. The outstanding feature of the process is the shortcut from vapor to solid.

In the laboratory sublimation is often carried out by the heating of a preparation between two watch glasses or two beakers placed mouth to mouth. The vapors expelled from the lower of the two glasses or beakers reach the upper, on whose cool glass surface they form sublimed crystals. This procedure is simple and effective for very small amounts of product, but is tedious where a considerable yield is required. In the preparation of pure anthracene and anthraquinone (§ 296) the process is expedited with the aid of a current of air.

Comparatively few substances are adapted to the process of sublimation. Among these are certain quinones; indigo; benzoic acid; camphor; iodine; phthalic anhydride. For illustration, three substances of widely variant behavior are contrasted:

Hexachloroethane, almost ideally adapted to sublimation; naphthalene, capable of being sublimed, but only with special technic and precautions; *p*-nitrobenzaldehyde, which practically speaking cannot be sublimed at all. With adoption of these as practical illustrations, the process of vaporization and recondensation may now be examined more critically with the aid of Figs. 1 and 2.

(*a*) *Hexachloroethane.* Starting with the cold solid at temperature 0, a surprisingly rapid increase of vapor pressure occurs as

the temperature rises, represented by the curve approaching *P*. The pressure of 760 mm. is reached before the melting point *P* is attained. This is a truly remarkable situation. Rarely does any organic compound have so high a vapor pressure in the solid state. At the point on *OB* representing 760 mm. and 185°, the whole mass of solid hexachloroethane goes into the vapor state. Without mechanical aid there can be no further increase in pressure, assuming the usual external atmospheric pressure of 760 mm. There may, however, be a slight superheating of the vapor, yielding a product whose temperature and pressure are marked as *A*.

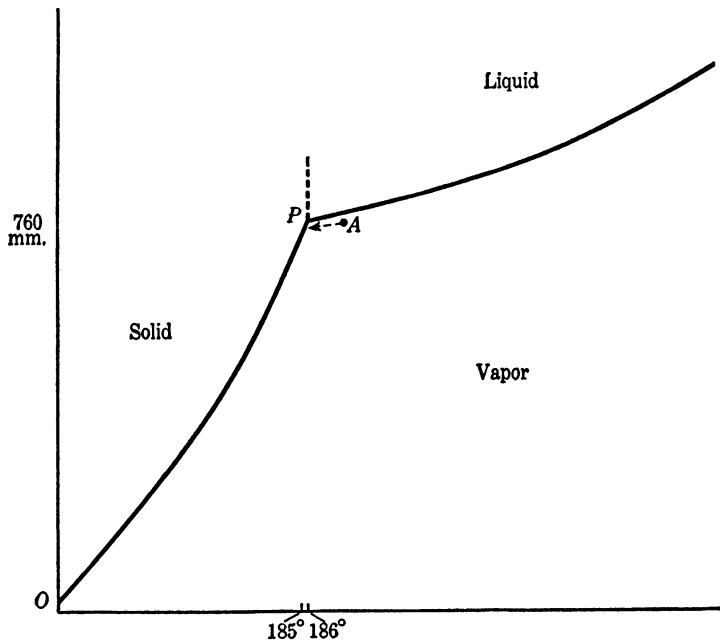


FIG. 1. SUBLIMATION OF HEXACHLOROETHANE

Let the vapor *A* now be cooled. Speaking in graphic terms, *A* will immediately shift in the direction of the arrow. This shift will of course be decidedly to the left—also downward, representing a slight drop in (partial) pressure with possible entry of a little air. Contact with curve *OP* means that the solid phase again begins to appear. Sublimation is thus easily accomplished as the dwindling mass of vapor approaches the state *O*. For practical directions, see § 295.

(*b*) *Naphthalene.* When this substance is heated in a manner similar to case (*a*), the whole distance *OP* (Fig. 2) is traversed with a climb in vapor pressure to the value of only 7 mm. The compound melts, and not until the distant point of 218° is reached does the whole mass go over into vapor. Slight superheating again occurs, yielding a vapor *B* analogous to *A* in Fig. 1. When vapor *B* is cooled, the *liquid-vapor* equilibrium line *PR* will be encountered this time. Condensation to the liquid state occurs

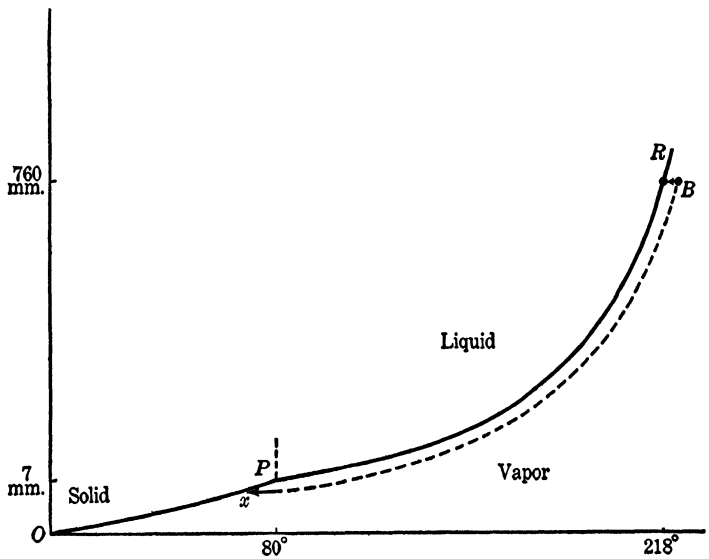


FIG. 2. SUBLIMATION OF NAPHTHALENE

until the temperature has fallen to 80.09° (the freezing point) and the partial pressure to about 7 mm. Any further lowering of the temperature will now cause sublimation of the type illustrated with hexachloroethane. Most of the product has already been distilled, however, and the yield of sublimate is relatively small.

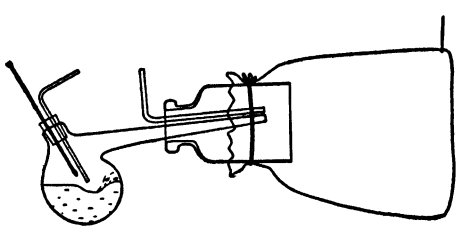
If the operator insists on really subliming the whole mass of naphthalene, he may reduce the pressure by mechanical means, and then reduce the temperature. Both pressure and temperature may be reduced simultaneously as long as the former is kept constantly below the value required to form a liquid phase. The dotted line *BX*, diverted so as to escape contact with the liquid-vapor equilibrium curve, shows the course by which liquid conden-

sation is avoided. It may approach as closely as possible, without harm, provided it does not touch the boundary of the liquid field.

The above result may be accomplished without evacuation of apparatus by mixing of the vapor of the desired substance with air or other relatively inert gas. Such dilution lowers the partial pressure of the substance and also cools the material. As a result a deposit of sublimed crystals accumulates in the cooling chamber, perhaps falling like snow. Such preparations as zinc dust and flowers of sulfur can be made in such a manner.

(*c*) *p-Nitrobenzaldehyde* has a vapor pressure of 0.009 mm. at 100°, a temperature slightly below its melting point. It is impracticable to produce a useful quantity of solid crystals from so rare a vapor. Many substances of common use have vapor pressures much under 1 mm. at their melting points, and thus are not well adapted to sublimation.

131. A sublimed product is usually purer than a distilled product because there is no liquid to extract impurities from the gases in the cooling chamber. The newly-deposited crystals do not dissolve the gaseous impurities appreciably, if at all. Furthermore, the partial gaseous pressures of the impurities, while sufficient to cause them to dissolve in a ready-made liquid, are insufficient to cause them to condense alone as a new independent phase, either solid or liquid. Accordingly the volatile impurities escape from among the subliming crystals and are eliminated.



PSEUDO-SUBLIMATION

132. Genuine sublimation of an ordinary organic compound, whose vapor pressure in the solid state seldom reaches 10 mm., is bound to be slow. One may then resort to the "frozen mist" process, which may be called pseudo-sublimation. For example, benzoic acid is melted in a retort, and heated to about 170°. Air is blown through the liquid, carrying quantities of benzoic acid vapors to the cooling chamber, which is a cloth bag, attached much like the bag of a vacuum cleaner. As the diluted vapor reaches the bag and is slightly cooled, it condenses to a liquid,

being above its melting point (121°) and below its boiling point (249°). This liquid first occurs as a fine mist, or suspension of minute droplets of liquid in the air. Before the mist has a chance to coalesce into large drops of distilled liquid, it meets a current of refrigerated air blown into the bag. The fine droplets immediately solidify. Any impurities of a volatile nature which might for the moment have been dissolved in the droplet are squeezed out in the crystallization and blow away. Accordingly the "pseudo-sublimate" may be just as pure in the end as a genuine sublimate which did not pass through the liquid state. It is likely that some of the commercial "sublimed" products actually come from such a pseudo-process.

133. In research operations sublimation is sometimes conducted under reduced pressure, perhaps under 1 mm. Again the yield is but slowly obtained, largely because of the rarity of the vapors traveling to the cooling chamber.

134. The accompanying table shows how great the differences are in the vapor pressures of various substances at their melting points:

Substance	Vapor Pressure at Melting Point	Melting Point
Carbon dioxide	3900 mm.	−57°
Hexachloroethane	780 mm.	186°
Phos. pentachloride	760 mm.	166°
Camphor	370 mm.	179°
Nitrogen	96 mm.	−210°
Iodine	90 mm.	114°
Ammonia	45 mm.	−78°
Benzene	36 mm.	5.5°
Naphthalene	7 mm.	80°
Benzoic acid	6 mm.	121°
Water	4.58 mm.	0°
Bromine	0.44 mm.	−7°
Zinc	0.15 mm.	419°
Sulfur	0.03 mm.	119°
p-Nitrobenzaldehyde	0.009 mm.	106°
Toluene	0.001 mm.	−95°
Mercury	0.000001 mm.	−39°

QUESTIONS

1. Describe the procedure you would expect to use if you were required to purify the following substances by sublimation:
   (a) camphor
   (b) sulfur
   (c) benzene

2. Suppose the iodobenzene cited in the steam-distillation experiment of § 63 were replaced by camphor. Describe the probable behavior of the system when the attempt is made to conduct the steam-distillation.

3. What advantage might there be in "steam sublimation" as contrasted with ordinary sublimation in air? (See § 299.)

4. At least three of the substances mentioned in the *upper part* of the foregoing vapor-pressure table are used for killing or repelling insects. What relation might this fact have to the subject under discussion in this chapter?

5. On the basis of principles discussed in this chapter explain the peculiar behavior of liquid carbon dioxide when released in quantity from a cylinder into a cloth bag.

CHAPTER XI

THE PHENOMENA OF MELTING AND FREEZING

135. Changes from the solid to the liquid state, and vice-versa, are of fundamental importance in many operations with organic compounds, particularly in methods of crystallization. Incidentally the well-known method of identifying a compound by determination of its melting point offers a satisfactory basis for discussion of the underlying theory. After consideration of such theory, broader applications follow, as suggested in the next chapter.

The crystalline substance of which the melting point is to be determined is placed in a specially prepared melting-point tube, which is virtually a miniature test tube. The tube together with a thermometer is placed in a bath of non-volatile liquid. Slow heating of the liquid enables one to note the temperature at which the crystals melt. Details of the laboratory procedure are given in § 189 ("Melting Point of an Unknown Substance").

136. Liquid for the Heating Bath. Concentrated sulfuric acid is often employed as the bath liquid, although olive and cottonseed oils, and glycerol are also serviceable, and are much safer. The vegetable oils gradually darken so much as to become useless for this purpose. Sulfuric acid may also darken, particularly if organic matter falls into the liquid. Such dark coloration may be eliminated by adding a few cg. (avoid excess!) of solid potassium or sodium nitrate and heating until the contamination is cleared up by oxidation. Sulfuric acid fumes offensively at temperatures much above 150°.

If the melting points to be determined are all considerably above 60°, hard-hydrogenated cottonseed oil is very suitable for this purpose. This preparation has the advantage of solidifying promptly upon cooling, and thus is readily stored and kept clean. Its high flash point (over 300° C.) stands in its favor. A single portion may be used several times before it darkens too much to be useful. When it finally becomes too dark to permit ready observation of the melting point tube, it may then be set aside for serv-

ice in common oil-baths (see § 23). For the latter application it is still as useful as ever.

137. One of the neatest methods of melting-point determination is that wherein the thermometer and tube are slipped down into narrow holes in a heavy copper block, mounted over a burner. A horizontal cross-hole is drilled so that one may watch the behavior of the crystals being tested. The copper conducts heat so freely that the thermometer and tube quickly come to the same temperature. (See Shriner and Fuson, *The Systematic Identification of Organic Compounds*, John Wiley and Sons.)

138. Theory of Melting-Point Determination. If an organic compound is pure and stable, the melting process all takes place at constant temperature, and the melting point is said to be "sharp." If the substance is impure, no single melting point is obtainable. Upon being heated the substance gradually becomes liquid over a range of rising temperature, which usually lies below the known correct melting point of the pure substance. For example, pure naphthalene melts sharply at 80.09°; a sample containing a very few per cent of another substance, on the other hand, might begin to melt at 60° or 70°, and become entirely liquid at 75 to 80°.

Not only is the melting point determination a test of purity, but it is equally valuable as a means of telling which of the hundreds of thousands of organic compounds is the one being examined. If the melting point can be estimated within one degree, the determination eliminates over 99% of possible substances from further consideration. One leading company dealing in organic chemicals advertises in its catalog the melting points and melting ranges of its merchandise and thus conveys much more useful information than by following the hackneyed custom of printing "C.P.," "Purified" or "Refined" after the listed items.

139. The Relation of Vapor Pressure to Melting Point. It has already been observed that both the liquid and solid forms of a substance exert vapor pressure, which rises with increase of temperature. The vapor pressure of a solid, however, rises faster than that of the corresponding liquid, as suggested in Figs. 1 and 2, showing the behavior of camphor.

For simplicity suppose that a vessel is completely filled with a mixture of the above solid and liquid, maintained at constant temperature. Under such conditions molecules of the liquid, at-

tempting to leave as though by distillation, can escape to no other place then to the solid. The solid, attempting to evaporate, can go only into the liquid. If the first process should be more rapid than the second, the material would all *solidify*. If the latter is more rapid, the solid is said to *melt*. To decide which phenomenon is likely to occur at any given temperature, superimpose Fig. 1 upon Fig. 2, obtaining Fig. 3. Since the two curves are

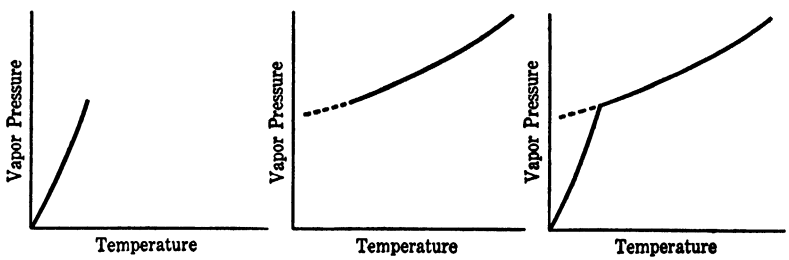


FIG. 1 FIG. 2 FIG. 3

VAPOR PRESSURES OF SOLID AND LIQUID FORMS OF THE SAME SUBSTANCE

necessarily not parallel, they must intersect at a point. This is the melting-point, which is an absolute constant if no extraneous pressure is involved.

The transformation of liquid camphor to solid will always be faster than that from solid to liquid provided the temperature lies below 179°. At temperatures above 179° the solid, having the greater vapor pressure, will be transformed more rapidly into the liquid phase. Only at the temperature of 179° are both vapor pressures alike, since two non-parallel curves of such simple character can intersect at only one point. Thus both rates of transfer are alike. Equilibrium is attained. Solid and liquid may remain together indefinitely as long as the system is neither heated nor cooled.

140. Comparison of Practical Methods. The common "micro" method of determination of melting point, while rapid and convenient, is not ideal from the standpoint of precision in location of the desired temperature value. If a considerable quantity of a substance is available, a more elegant and precise method may be employed. 25 grams or more of the crystalline substance is partially melted, and the mixture of solid and liquid stirred together in the form of a thin slush. If a thermometer is used as

the stirring rod, with complete immersion, the equilibrium temperature may be read off directly after a few minutes, provided there is an appreciable fraction of both phases continuously present. The whole outfit may be placed in a bath which is maintained at a fairly constant temperature one or two degrees above or below the true melting point. Inside the inner vessel a constant temperature reading should be obtained in either case. The method is particularly good where the substance has a high heat of fusion, as with polar compounds.

Parts of the curves of Fig. 3 are dotted. These sections represent unstable conditions where the phase in question theoretically cannot exist. The upper curve would refer to a solid above its melting point, a condition which does not exist, theoretically or practically.

141. Metastable Condition. The lower dotted curve represents the vapor pressures of a liquid below its freezing point. While theoretically impossible, this condition in practice may actually exist for an extended time. The liquid is then said to be "undercooled" (in England "supercooled"). Undercooling sometimes deceives a beginner when he attempts to locate the melting point of a substance by cooling the liquid until it actually solidifies.

For example, pure acetic acid is supposed to solidify at 16.67°. When the substance is cooled, however, the temperature may reach 15° or even 10° before crystallization takes place. Finally the excessive cooling seems to force the crystallizing process, and the liquid suddenly and rapidly becomes solid. The temperature rises, but before it attains the correct equilibrium value the whole mass may become solid and no significant thermometer reading can be made. The new solid will, however, melt promptly and sharply at 16.67°.

142. Behavior of Impure Substances. Suppose a small amount of a second substance, naphthalene, is introduced into the equilibrium mixture of pure solid and liquid camphor—all at the temperature of 179°.

The naphthalene immediately dissolves in the liquid camphor, but not in the solid. Following Raoult's Law, the vapor pressure of the camphor in the liquid phase is at once lowered in correspondence with the change in mole-fraction. Camphor will now pass less rapidly from liquid to solid than from solid to liquid. In

common language, the solid melts faster than the liquid solidifies. But melting uses up heat; and as no heat is being added, the temperature falls.

The phenomenon may be represented as in Fig. 4, which is merely an extension of Fig. 3. The solid camphor at the outset had the vapor pressure and temperature (179°) marked as the point P. The impure liquid at this temperature would have the vapor pressure (i.e., the partial vapor pressure of the camphor component only) marked as the depressed value X. Obviously a phase with pressure P cannot exist in the same vessel side by side

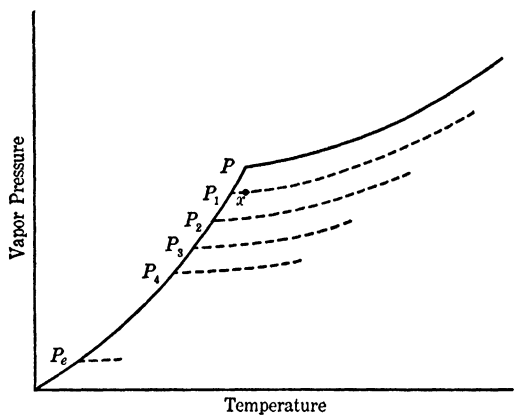


FIG. 4. EFFECT OF IMPURITY UPON MELTING POINT

with a phase of the same substance in which the pressure is X. The solid represented at P would melt at once and go into the condition X.

But the melting of a solid requires heat. None is supplied from the outside, therefore the temperature of the mixture falls. The vapor pressure of the solid P, and of the impure liquid X, both fall at the rate marked by their respective curves until they meet at P_1. Here equilibrium ensues, and no further change is seen. Solid camphor and the solution of naphthalene in camphor may remain together indefinitely at the temperature P_1 which is below the normal melting point of camphor.

Other points, still lower in temperature, such as P_2, P_3 and P_4, may be located, showing the equilibrium temperatures of solid camphor in contact with solutions of increasing naphthalene con-

tent. Within reasonable limits Raoult's Law now has a new application, viz., that the molecular percentage, and thus the molecular weight, of a compound may be measured by determining depression of melting point.

If the melting point of camphor can be depressed to P_1, P_2, P_3, P_4, a question naturally arises—How far may it fall? The answer is P_e, the **eutectic** point, which in this case is reached when the fraction of naphthalene reaches 42 mole per cent. It is the temperature below which not even the impure liquid can persist; further refrigeration simply causes both components to solidify completely and the experiment is done. The eutectic point is better understood from a diagram plotted in a different way.

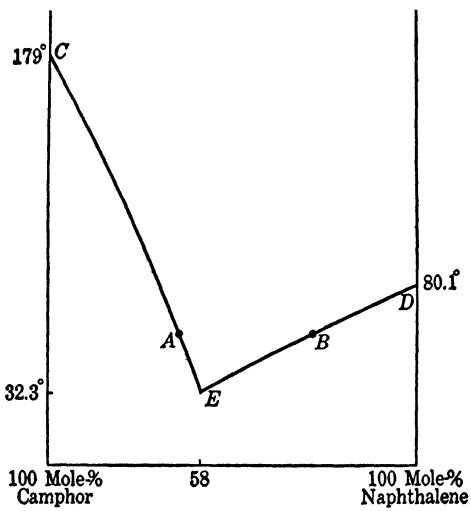


FIG. 5. MELTING POINT—COMPOSITION DIAGRAM

Melting point is plotted against composition throughout the whole range of possible mixtures of camphor and naphthalene. The curve CE indicates the successively lower melting points of camphor as naphthalene is added up to the maximum of 42 mole per cent impurity. The curve ED shows the melting points of naphthalene with camphor considered as an impurity, up to 58 mole per cent. Of course the 42% solution of naphthalene in camphor and the 58% solution of camphor in naphthalene are identical. Therefore the curves must intersect as at E, the eutectic point, which happens to be 32.3°.

143. Melting Range. On the basis of the foregoing discussion it may now be easier to understand the successive phenomena in the conventional micro method of determining melting range of such a preparation as the impure camphor above cited. Figure 6 represents, ideally, a single crystal of camphor with a few small crystals of naphthalene (the "impurity") scattered over its sur-

face. Nothing significant happens while the mixture is being heated up to the eutectic temperature. As soon as the eutectic temperature is reached, and further heating is attempted, the appropriate numbers of molecules (in the ratio of 58 to 42 in this case), already in contact at the interface, join to form a new liquid phase, which for the moment is the eutectic solution.

A sharp observer may now notice a moist appearance on the surface of the camphor crystal. However, the melting process does not seem to continue without further rise in temperature. Actually the cessation of melting is due to the exhaustion of solid naphthalene, which was originally present only in scant quantity anyway.

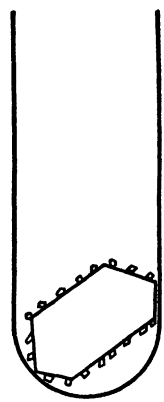


FIG. 6. MELTING POINT TUBE

Solid camphor is now in equilibrium with the small superficial coating of eutectic liquid. Let the temperature be now raised by one degree. The activity (or vapor pressure) of the solid is increased more than that of the liquid; therefore the solid now proceeds to melt faster than the liquid solidifies. But the melting dilutes the eutectic liquid with camphor, promptly raising the partial pressure of that component in conformity with Raoult's Law. This promptly counteracts the melting process, and a new equilibrium is reached at the higher temperature. Further increases in temperature will cause more and more melting until finally the solid camphor is exhausted; that is, until the material is all in the liquid state. Obviously the final melting point—the only really significant melting point of the mixture in question—cannot be as high as 179°, but it may approach that figure if the original fraction of impurity was small.

The melting range thus really extends from the eutectic temperature up to the point of disappearance of the last crystal. In actual practice, with small amounts of impurity, it is usually impossible to detect the initial melting or eutectic condition. The crystals may not be arranged over the surface of a conspicuous crystal as in the ideal illustration proposed above. Thus the temperature may rise many degrees above the eutectic temperature before an appreciable accumulation of liquid occurs. In the case of camphor contaminated with much naphthalene, one might detect initial melting at 80° or 100°, and would then expect a pro-

tracted range of melting. On the other hand, if the initial melting seemed to occur at 177°, the whole process would be complete within a few tenths of a degree, and the preparation adjudged to be nearly pure. If two workers tested the same impure preparation, one might find a higher *initial* melting temperature, but they should both find the same *final* melting point.

On the melting point-composition diagram of naphthalene and camphor are represented two mixtures, *A* and *B*, which ostensibly have the same melting point, introducing possible confusion. These are readily distinguished by mixing pure naphthalene with each. In case *A* the melting point is lowered; in *B* it is raised.

144. The practical summary of the above discussion is this: a relatively pure preparation has a *short* and *high* melting range; an impure preparation has a *long* and *low* range.

Due to its small molecular weight, water has the tendency to depress the melting points of preparations greatly. Efficient drying is thus desirable.

145. Some substances undergo an abnormally great depression of melting point with addition of the second component. Camphor is of such character. It is accordingly used to advantage as a solvent in the well-known Rast method of molecular weight de-

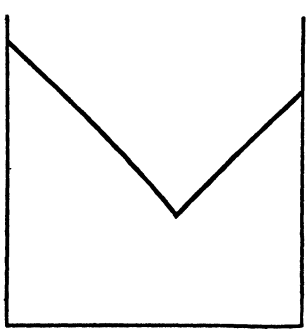


FIG. 7

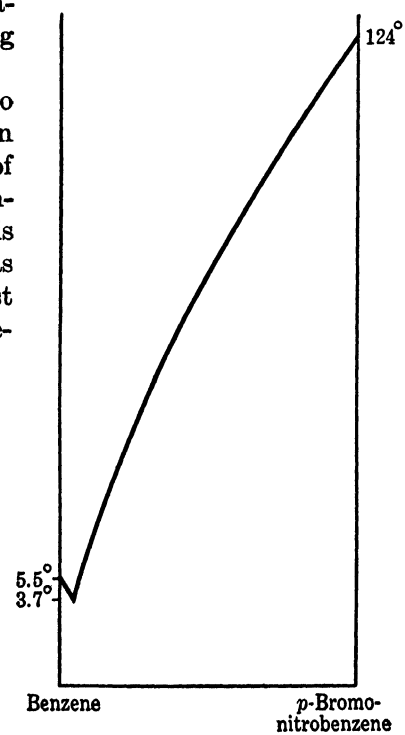


FIG. 8

COMMON MELTING POINT DIAGRAMS

termination, recently improved by J. H. C. Smith and W. G. Young (Ref. below). See also § 196.

146. In Fig. 7 a melting-point diagram of conventional type is shown, with the eutectic point distant from both axes. Where a great difference in melting point occurs, the eutectic point may be displaced to an extreme position at one side, as in Fig. 8.

The whole foregoing discussion is based on the relatively simple assumption that the two compounds in a given mixture are not mutually soluble in the solid state; further that they do not react with each other. Unfortunately many substances do not strictly follow the ideal curves pictured. Many of these enter into loose, unstable compounds whose presence causes more or less elevation of melting temperature. Such abnormalities do not, after all, interfere with the general principle of melting-point depression. Further details are described in special works of the type of Findlay's Phase Rule.

QUESTIONS

1. How might you find the molecular weight of a substance by determination of melting point?

2. How could you use a known pure preparation of benzoic acid in an experiment to prove that a certain white powder of unknown composition is benzoic acid?

3. Explain with the aid of a diagram how you might use the melting point determination to prove that two substances chemically combine with each other,

(*a*) quantitatively, (*b*) slightly, running to equilibrium.

4. Suppose you heated a quantity of a pure crystalline substance at a steady rate, introducing just one calorie per minute, until the melting point was passed. If the various temperatures attained were plotted against the number of minutes' time elapsed, what would be the general appearance of the curve so drawn? Of what use might such a curve be?

5. Which would have the lower melting point, a 1% solution of ethyl alcohol in acetic acid, or a 1% solution of water in acetic acid?

6. Devise a scheme for determining the melting point of a substance which is so unstable at elevated temperatures that it decomposes before the melting point can be reached in the regular micro procedure.

REFERENCE

Smith, J. H. C., and Young, W. G., *J. Biol. Chem.*, **75**, 289 (1927). Modification of Rast micro-melting-point method.

CHAPTER XII

RECRYSTALLIZATION FROM SOLUTION

147. In Chap. VII is described the simple process of preparing crystals by the cooling of a hot, relatively concentrated solution. Troubles occasionally arise, however, from a lack of knowledge of the melting point-composition relations of the materials involved. This special supplementary discussion is therefore added herewith, following the explanation of melting and freezing phenomena given in Chap. XI.

When a crystalline preparation is dissolved in a solvent, the process is merely a special case of the melting of a substance in the presence of a specific "impurity." The solvent of course plays the role of impurity, which true to rule lowers the melting point of the solute. Pure benzoic acid, for example, melts at 121.7°; but in the presence of a suitable excess of water it melts—that is dissolves—at 80°, 60° or other relatively low temperature.

148. The possibility of blunders in this type of work is illustrated in the recrystallization of acetic acid from aqueous solution. Figure 1 shows the melting points of all mixtures of acetic acid and water. The eutectic point in this case is at −27°.

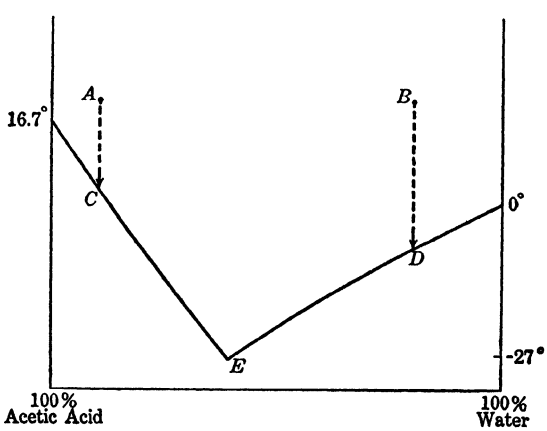


FIG. 1. MELTING POINTS OF ACETIC ACID-WATER MIXTURES

As a first experiment let a 90% solution of acetic acid in water (marked as *A*, at 20°) be cooled, presumably with the aid of an effective freezing mixture. At *C* (3°) crystals should appear. Actually a slight undercooling is required before crystallization starts. A substantial yield of pure crystalline acetic acid now accumulates as the temperature falls to values approaching −27°. A rapid filtration on the Buechner filter permits isolation of the desired preparation.

The second experiment shows faulty technic. A 20% solution of acetic acid (*B*) is cooled from 20° to −7°. At this point (*D*) crystals appear, and a large crop of beautiful material is collected and possibly admired. Unfortunately the crystalline product is ice, not acetic acid, and the principles involved in its appearance are quite like those given above in the *A*–*C* case. One should note, therefore, that crystallization of a given compound may not be successfully accomplished unless the experimenter chooses a solution in which the concentration of the desired substance is in excess of the eutectic concentration. Otherwise he gets either crystals of the solidified solvent, a solid eutectic mixture, or no solid matter at all, as the case may be.

In the case of acetic acid and water the process of crystallization is simple because the two components are miscible in the liquid state in all proportions even at low temperatures. When the mutual solubility of the solute and solvent is limited, a new trouble enters. Acetanilide (see § 364) gives a good example of this situation.

149. Separation of an "Oil." When the attempt is made to recrystallize acetanilide from water, frequently only a part of the crystal mass dissolves. The remainder melts and forms a relatively dense liquid phase which settles to the bottom of the container, and is often called the "oil." This new phase is really a saturated solution of water in acetanilide. Unfortunately the oil tends to retain impurities. If the whole mixture be merely cooled at this point, not only will the usual yield of purified crystals be obtained from the solution, but along with the desired crystals will appear an unattractive, and possibly impure, cake of solid acetanilide which came from the oil phase. This difficulty, and its remedy, are illustrated in Fig. 2.

In Fig. 2 the melting-point curve starts as usual with the normal melting point of the pure solvent (water) as marked at *A*, or 0°.

As usual it drops to the eutectic E, which in this case happens to be very close to the left vertical axis of the graph. The right branch of the curve rises from E, and normally would proceed to B, the melting point of pure acetanilide. This curve is broken, however, into two disconnected sections EC and DB. The intruding intermediate zone $CDGHF$ is a field in which acetanilide and water are not miscible. It is impossible to prepare a solution of these two components with any temperature and corresponding

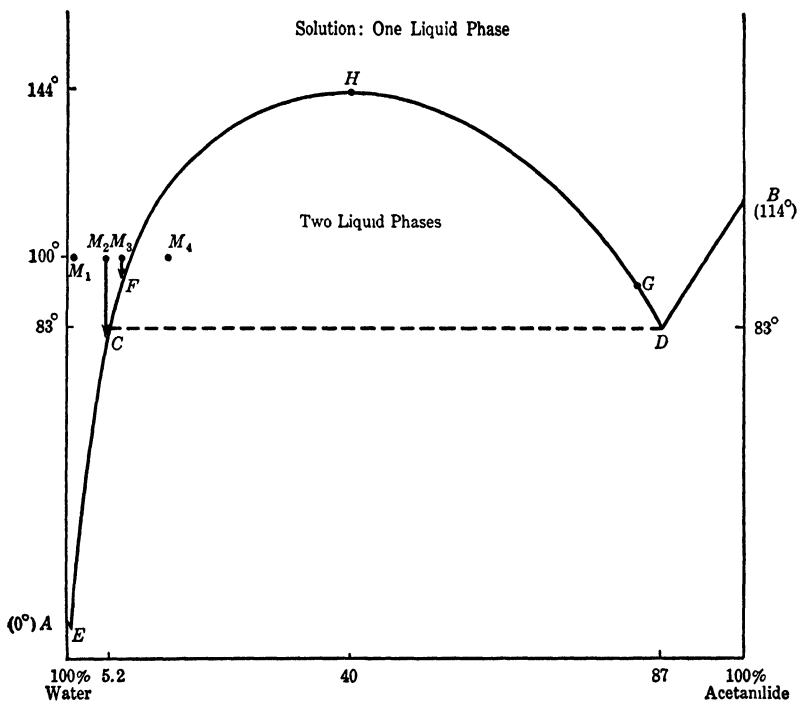


FIG. 2. THE SYSTEM ACETANILIDE-WATER

concentration falling within that zone. This fact is likely to disturb the process of recrystallization seriously.

Suppose several mixtures M_1, M_2, M_3, M_4, be made of solid acetanilide with boiling water, with the purpose of finding a suitable solution from which crystals may be obtained upon cooling. Not all of these mixtures are satisfactory.

M_1 is too dilute. Like mixture B in Fig. 1, it will yield ice upon extreme cooling.

M_2, a 5% solution, in many respects is ideal for recrystallization. As the solution is cooled, a point just below C is soon reached, and from thence to E a continuous crystallization of the one substance acetanilide will occur. In actual practice such a procedure gives beautiful snow-like crystals, especially if the cooling be done rapidly.

Suppose the worker is dissatisfied with the relatively dilute and possibly voluminous solution M_2, and increases the concentration to 7%, as at M_3. Since M_3 is in the "solution" field, there is still but one phase present in the boiling mixture. M_3 is now cooled to F, and threatens to pass into the forbidden zone. At this point a second liquid phase G, much richer in acetanilide, separates out, first in an emulsified mixture. Soon the droplets of G coalesce into a pool of the "oil" previously mentioned.

As the mixture of solution F and oil G is cooled, each phase becomes supersaturated with the component which is present in the smaller proportion. F then releases some of its acetanilide, and G gives up some of its water. F becomes C—cooler and less rich in acetanilide; G becomes D—cooler and richer in acetanilide.

At 83°, the temperature of C and D, the zone of crystallization is just reached. C now begins to produce crystalline acetanilide instead of the oil. Being thus stripped of acetanilide, it withdraws a new supply from the oil D. Theoretically this double process should now go on until the oil has all disappeared; that is, D dissolves in C, and then pure acetanilide drops from C.

In practice, however, D usually lies as a compact pool of liquid, and does not get a chance to go through the two theoretical paths. Actually it seems to solidify just as it lies, forming a cake of more or less crystalline material from which the dissolved impurities did not have a good opportunity to escape.

M_4 is worse. Since a solution of M_4 specifications is impossible without operation under pressure, the laboratory worker notices as he boils the M_4 mixture (at about 100°) that the oil is present from the start. Cooling of this mixture gives results just as described for M_3.

The simplest remedy for the difficulties of M_3 and M_4 is of course to dilute the mixture to such a value as M_2, which upon cooling will be certain to miss the line CF. Such a plan may be used in the first acetanilide experiment (§ 364).

The dilution plan of course has one drawback. The increase in amount of water involved in the shift from M_3 or M_4 to M_2 means a definite additional loss of acetanilide in the ultimate mother liquor.

To avoid this loss, let solution M_3 be cooled directly without dilution. The oil G of course appears when the main solution reaches the state F; but at this point the mixture is vigorously agitated. When states C and D are reached by the solution and oil, respectively, the emulsion of the two starts to solidify. As before C yields crystals, and D in turn dissolves in C. Since no pool of oil is allowed to accumulate, the formation of crystals may take place freely out in the open. Impurities are easily squeezed out of the separate tiny droplets as they disappear. As soon as the oil D is exhausted, so that only crystals and solution remain, the temperature may now fall. Crystals continue to accumulate, but the agitation is of course no longer necessary.

The agitation method is illustrated in our experiment with *p*-toluidine—see § 265. *p*-Toluidine melts at 44°, and requires special care if one would obtain pure loose crystals. Other troublesome examples are *o*-nitrophenol, and *m*-dinitrobenzene. Benzoic acid, on the other hand, is easily handled, since its C–D temperature is much higher — 98°, and is thus practically out of the way of the ordinary range of temperature change in laboratory manipulation.

For further explanation of this type of behavior, particularly of the temperature changes, see any text on the phase rule. Schreinemakers, *Zeitschr. physikal. Chem.*, **23**, 429 (1897), has given an elaborate report on the behavior of succinonitrile, $NC-CH_2-CH_2-CN$, which beautifully illustrates the phenomena described here for acetanilide. Findlay (*Phase Rule*, several editions, Longmans) and Taylor (*Treatise on Physical Chemistry*, Vol. 1, p. 542, D. Van Nostrand Co.) give good summaries of the paper on succinonitrile, using it as their illustration of the phenomena described in Fig. 2.

CHAPTER XIII

MASS ACTION—EQUILIBRIUM

150. The formation of an ester from an alcohol and an acid affords an excellent example of chemical equilibrium. Historically, it happens that the preparation of ethyl acetate was used in the original exposition of the law of mass action, as presented by Guldberg and Waage.

When ethyl alcohol and acetic acid are mixed, a slow reaction starts according to the following equation:

$$\underset{\text{Alcohol}}{C_2H_5OH} + \underset{\text{acid}}{CH_3COOH} \rightarrow \underset{\text{Ester}}{C_2H_5O.CO.CH_3} + \underset{\text{water}}{H_2O}$$

This reaction, slow in the absence of a catalyst, apparently becomes slower as time passes and finally seems to stop at a point where 2/3 of the molecules of alcohol and acid have reacted, 1/3 failing to produce the desired ester. Actually there is reason to believe that the reaction has not stopped at all; rather that a new and opposing reaction, that of hydrolysis, has appeared, and has increased to such an extent that the steady transformation of alcohol and acid into ester and water is exactly compensated by the reaction of ester and water to form alcohol and acid. No net change is possible from this point forward. This is chemical equilibrium, represented simply by including a double arrow in the original equation:

$$\underset{\text{Esterification}}{C_2H_5OH + CH_3COOH} \rightleftharpoons \underset{\text{Hydrolysis}}{C_2H_5O.CO.CH_3 + H_2O}$$

Fundamental chemical principles indicate that the velocity of a bimolecular reaction, such as that of esterification, varies as the product of the effective[1] concentrations of the alcohol and the acid. That is,

V_1 varies as $C_{Al} \times C_{Ac}$ where V_1 is velocity.

[1] The term "effective" applied to concentration suggests that a numerical correction, called the activity coefficient, may be applied to simple molal concentration where results of greater precision are desired. For simplicity the activity correction is ignored, without serious error, both here and in § 159.

C_{Al} is the concentration of alcohol, and C_{Ac} the concentration of the acid. Similarly, an expression for the opposite reaction of hydrolysis may be given—

$$V_2 \quad \text{varies as} \quad C_E \times C_{H_2O} \quad \text{where} \quad V_2$$

is the velocity of the reverse reaction, and C_E and C_{H_2O} are the concentrations of ester and water, respectively. These two expressions of variation may of course be stated as equations by the insertion of constants, K_1 and K_2:

$$V_1 = C_{Al} \times C_{Ac} \times K_1 \tag{1}$$

$$V_2 = C_E \times C_{H_2O} \times K_2 \tag{2}$$

At equilibrium these two velocities must necessarily be equal; and since

$$V_1 = V_2,$$

therefore

$$C_{Al} \times C_{Ac} \times K_1 = C_E \times C_{H_2O} \times K_2$$

If we rearrange the terms, we have

$$\frac{C_E \times C_{H_2O}}{C_{Al} \times C_{Ac}} = \frac{K_1}{K_2} = K, \tag{3}$$

where K is now defined as the **equilibrium constant,** which has a definite numerical value for the specific case at the temperature chosen. In the case of ethyl acetate, it has already been noted that at equilibrium 2/3 of the molar quantity is in the form of ester and water, 1/3 as unreacted alcohol and acid. Substituting these values in equation (3)—

$$\frac{\frac{2}{3} \times \frac{2}{3}}{\frac{1}{3} \times \frac{1}{3}} = K = 4, \tag{4}$$

the equilibrium constant of this reaction.

151. A two-thirds yield as a theoretical maximum is of course unsatisfactory. Accordingly methods are sought for displacing the equilibrium in the direction of higher ester yield. In one method the alcohol is added a little at a time, and the ester expelled as fast as produced. This permits a large displacement of equilibrium over the reaction period as a whole. Actually this process resolves itself into two significant parts, as follows:

(*a*) At first a large concentration of acetic acid is present with a small concentration of alcohol. By influence of **mass action,** a relatively high yield of ester is now produced—high with respect to alcohol so far added. To illustrate the situation, suppose only one mole of alcohol has been added to a mass of 16 moles of acid. This mixture has a volume of about one liter. Therefore the approximate molal concentrations at the outset, before reaction, are

$$C_{Al} = 1$$
$$C_{Ac} = 16.$$

The alcohol and acid are now allowed to react and attain equilibrium. At this new equilibrium, ester and water appear as new components. Their molal concentrations, as yet unknown, are represented as C_E and C_{H_2O}. For simplicity, assume that the volume of one liter is unchanged. Every mole of "E" or "H_2O" produced of course means just one mole less of alcohol, and one less of acid. Therefore the concentrations of alcohol and acid at equilibrium will be just C_E moles less, in each case, than before; that is:

$$\text{Alcohol, } C = (1 - C_E)$$
$$\text{Acid, } C = (16 - C_E)$$

If we substitute these values in equation (3), we have

$$\frac{C_E \times C_{H_2O}}{(1 - C_E)(16 - C_E)} = K = 4$$

But

$$C_E = C_{H_2O};$$

therefore

$$\frac{(C_E)^2}{(1 - C_E)(16 - C_E)} = 4,$$

from which $C_E = 0.981\ M$, which means a production of 0.981 mole of ester from the original 1.000 mole of alcohol added. This means 98.1% as a theoretical maximum yield—an excellent conversion.

There are now only about 15 moles of acetic acid left. Should one merely add another mole of alcohol, the yield of ester this time would not be quite so favorable. Further additions (14 moles more of alcohol) would of course eventually set back the efficiency of the total process to the 66 2/3% limit previously cited. To avoid this, advantage is taken of the second feature of the process.

(*b*) *Removal of the Product by Distillation.* Since ethyl acetate is volatile, the original yield is expelled before addition of the next portion of alcohol. This leaves only acetic acid and water behind. Reversal of reaction is largely prevented, and much more complete conversion assured. (See § 234.)

With many esters, for example methyl salicylate (b.pt. 223°), it is not possible to expel the ester as it is produced. In such a case it is better to use only the method of (*a*) above, choosing the less expensive component (in this case methyl alcohol) for use in excess. It should also be observed that the equilibrium constants of different esters have different numerical values.

152. Use of an Acid. A strong inorganic acid, generally sulfuric or hydrochloric, is usually added to the alcohol-acid reacting mixture. It serves as a catalyst, increasing the velocity of both forward and backward reactions to the same degree, and thus not affecting the equilibrium constant. Where the oxidizing power of sulfuric acid is to be avoided, hydrogen chloride gas often serves as a substitute. Being volatile, the hydrogen chloride is readily expelled, or may be removed by washing.

CHAPTER XIV

CALCULATION OF QUANTITIES OF MATERIALS

153. In devising exact directions for preparing an organic compound, one should first write a complete balanced equation showing the transformation of the starting materials into the product. For example, when phthalic anhydride is heated with resorcinol (see § 347), fluorescein is produced:

$$\underset{\text{Phthalic anhydride}}{C_6H_4(CO)_2O} + 2\underset{\text{resorcinol}}{C_6H_4(OH)_2} \rightarrow \underset{\text{fluorescein}}{C_{20}H_{12}O_5} + 2H_2O$$

This reaction proceeds smoothly to completion. There is presumably no concern about loss by evaporation, or formation of by-product. Accordingly convenient quantities are chosen in agreement with the equation; that is, 15 grams of the anhydride (0.1 mole) and 22 grams of resorcinol (0.2 mole).

154. Altering of Proportions. Frequently a reaction does not proceed in as simple a manner as indicated above. Reasons arise for choosing other than the theoretical proportions of raw materials. For example:

(*a*) One of the reagents may be of such character that it is likely to be partially wasted during the process, in spite of careful technic. Perhaps the reagent is slowly oxidized in an undesired side-reaction. In other cases the reagent may be a volatile liquid, like methyl alcohol (b.pt. 65°) which is inexpensive as well as prone to escape by evaporation. An excess of such a reagent is then prescribed.

(*b*) The reaction employed in the synthesis may be one which runs to equilibrium. It is desirable to drive it more nearly to completion than normal conditions permit; wherefore an excess of one reagent is used. The substance used in excess is usually either one which is inexpensive, or one of which the superfluous residue is easily removed, and perhaps reclaimed, at the end of the reaction period. Usually the excess reagent is eliminated by distillation, or by washing.

(*c*) Occasionally one of the reagents is of a type difficult to remove from a reaction mixture in which it might survive, in part,

as a residue. It is thus desirable to use an excess of the second reagent to make certain that the consumption of the first will be complete.

In some cases there is uncertainty of the purity of a reagent. Such diverse materials as isopropyl alcohol, sodium dichromate, hydrochloric acid, glycerol, etc., have varying amounts of water in their common commercial forms. An excess may thus be desirable.

155. Calculation of Yield. The theoretical yield in an organic synthesis is that quantity of product called for by ordinary chemical arithmetic under the particular directions employed. In the simple case of fluorescein the equation shows directly that one mole of fluorescein is produced from one mole of phthalic anhydride and two moles of resorcinol. Applying this observation to the above case, 0.1 mole, or 33.2 grams, of fluorescein is the largest amount which could possibly come from the quantities of reagents actually used in the experiment. 33.2 g. is thus the theoretical yield.

Usually, however, deviations from theoretical proportions in the quantities specified make it necessary to decide which reagent is to serve as the basis of calculation:

Example. 60 g. of *n*-butyl bromide was heated with 15 g. of metallic sodium (Wurtz reaction), and 20 g. of *n*-octane obtained as a product.

$2C_4H_9Br$	+	2Na	→	C_8H_{18}	(+ 2NaBr)
2 moles	+	2 gram atoms	→	one mole	
274 g.	+	45 g.	yields	114 g.	(Theory)
60 g.	+	15 g.	yields	20 g.	(Practice)

It is apparent from an inspection of the theoretical and practical figures that 15 g. of sodium is an excessive amount to use with 60 g. of butyl bromide. Part of the sodium will be left over, and thus its full original quantity has no place in the calculation. Butyl bromide is the limiting factor—the substance of which the supply is short. The problem is thus simplified—How much octane can be made from 60 g. of butyl bromide?

60 g. of butyl bromide is 60/137 mole. Since two moles of the bromide yield, by theory, one mole of octane, 60/137 mole of bromide will yield $1/2 \times 60/137$ mole, or 30/137 mole (25 g.) of *n*-octane. Only 20 g. of octane, however, was actually obtained. The "percentage yield" is therefore 20/25 or 80%.

156. Three or More Starting Materials. Where three or more starting materials are used, any two are taken at random for consideration. The theoretical and practical proportions of these two are first examined, as in the octane example given above. At once one of the two reagents is eliminated from consideration. Next the third reagent is compared with the surviving material, and a decision thus made as to which of the three is present in scant supply, and thus is the basis for calculation.

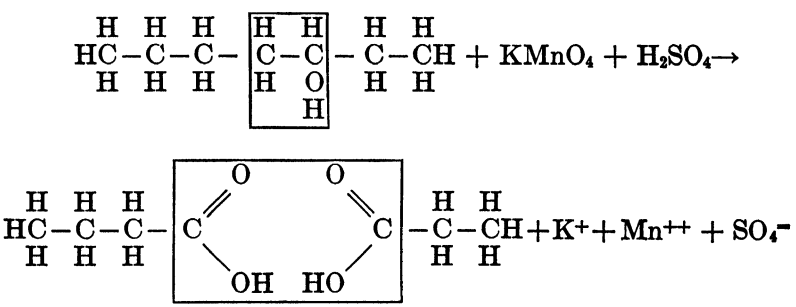
Example. Suppose *A*, *B*, and *C* are starting materials in the synthesis of *D* (and a worthless by-product *E*):

A	+	*B*	+	*C*	→	*D*	+	*E*
70 g.	+	10 g.	+	30 g.	→	95 g.		(Theory)
55 g.	+	20 g.	+	20 g.	yields	50 g.		(Practice)

First consider *A* and *B*, noting gross excess of *B* in the practical specifications. Reject *B*. Next compare *A*, still under consideration, with *C*. Evidently the supply of *C* is scant. Reject *A*, and base calculation on *C*.

157. Calculation of Quantities Used in an Oxidation Reaction. The method of balancing an equation by valence changes, familiar to many students in inorganic chemistry, may be applied with slight modification to organic compounds. For example: What quantity of potassium permanganate is theoretically required—in the presence of sulfuric acid—to convert 58 g. of ethyl butyl carbinol into propionic and butyric acids?

First represent graphically the exact changes which take place, preserving similar positions (on paper) for each carbon atom, before and after reaction:



As illustrated above, draw enclosing lines about those carbon atoms which are said to be oxidized. The total valence of the

carbon atoms in the upper enclosure reaches the algebraic sum of -2, meaning that these carbon atoms have three negative valences (holding hydrogen) and one positive (holding hydroxyl). Valences between carbon atoms have no significance in this sense, positive or negative, and may be overlooked as of zero value. In the product, however, the algebraic sum of valences for those same carbon atoms is $+6$, all holding oxygen.

Since the reacting carbon atoms change in valence from -2 to $+6$, eight electrons must have been given up, and thus eight equivalents of oxidizing agent are required per mole of alcohol. Permanganate ion, on the other hand, in changing to manganous ion, has an oxidizing equivalent of five, the manganese gaining five electrons and changing from a valence of $+7$ to $+2$. It is thus necessary to use eight moles of permanganate to oxidize just five moles of the alcohol. To complete the equation, add the sulfuric acid needed to produce the salts of potassium and manganese:

$$5C_7H_{15}OH + 8KMnO_4 + 12H_2SO_4 \rightarrow 5C_3H_7COOH + 5C_2H_5COOH + 8K^+ + 8Mn^{++} + 12SO_4^{=} + 17H_2O$$

Only 58 g., or 0.5 mole, of the carbinol was given, however. 0.8 mole of permanganate and 1.2 mole of sulfuric acid are thus required.

Similar methods of calculation may be carried out for reductions of organic compounds; for example, in the conversion of nitrobenzene to aniline, where nitrogen is involved instead of carbon.

QUESTIONS

1. If four reagents were required in a mixture used for organic synthesis, how would you decide which of the four should serve as a basis for calculation of theoretical yield?

2. Benzene (780 g.) was chlorinated, yielding chlorobenzene (562 g.) and *p*-dichlorobenzene (294 g.). Calculate the percentage yield.

3. What quantity of potassium dichromate is required in the presence of sulfuric acid to convert 37 g. of sec.-butyl alcohol

(*a*) into the ketone? (*b*) into acetic acid?

4. In the presence of acid, how many gram-atoms of zinc are required by theory to convert one mole of nitrobenzene into aniline?

5. If the reduction of nitrobenzene is conducted in alkaline solution, zincate ion ($ZnO_2^{=}$) and hydrazobenzene, $C_6H_5.NH.NH.C_6H_5$ are produced. What quantity of zinc would be required in this case to reduce one mole of nitrobenzene?

CHAPTER XV

ORGANIC ACIDS AND BASES

158. Many operations of organic synthesis, particularly those used in Chap. 17, depend upon the conversion of organic acids or bases into salts, or the reverse. Unfortunately the time-honored definitions of acids and bases are not satisfactory in the organic field, and thus certain newer conceptions are in order:

An acid is a compound which is capable of giving up protons (positively charged atoms of hydrogen) *to a base which it may encounter.* No free circulation of isolated "hydrogen ions" is recognized.

A base is a compound which is capable of accepting protons from an acid. No necessity of hydroxyl ions is recognized. Hydroxyl ion is merely a special case of a base in the inorganic domain, and there are thousands of other bases, of entirely different constitution, among organic compounds.

Probably the most important single characteristic of either an acid or a base is its **strength.** Since knowledge of relative strengths of various organic acids comes from the behavior of these acids with bases, it is perhaps best to examine first the chemistry of basic substances.

159. Bases. Hydroxyl ion, OH^-, is the commonest and most important base. The fact that some metallic or metal-like constituent is usually associated with hydroxyl leads to the common habit of calling the two together a base—for example, sodium hydroxide. Actually the real base is the hydroxyl part alone, with only secondary influence from the sodium. Its chemical reactions require no "hydrogen ion," but are rather illustrated as follows:

$$\underset{\text{Hydroxyl ion}}{OH^-} + \underset{\text{acetic acid}}{CH_3COOH} \rightarrow \underset{\text{water}}{H_2O} + \underset{\text{acetate ion}}{CH_3COO^-}$$

As usual with a base, hydroxyl takes a proton from the acid. Similarly, other ionic bases, such as carbonate, $CO_3^=$, phosphate, $PO_4^=$, and borate, $BO_3^=$, could be used with varying degrees of efficiency in place of hydroxyl.

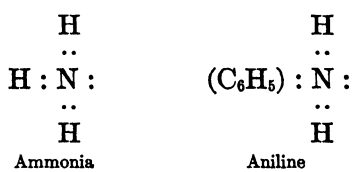
In organic chemistry, however, most of the well-recognized bases are not negative ions, but electrically neutral substances in complete molecular form. The most important of these are structurally similar to ammonia. Ammonia itself, for years awkwardly called a "base-former," is simply a base, as illustrated in the following well-known reaction, conducted in the absence of water:

$$NH_3 + HCl \rightarrow NH_4^+ + Cl^-(\rightarrow NH_4Cl)$$

Organic amines play a similar role, such as that of aniline when treated with hydrogen chloride:

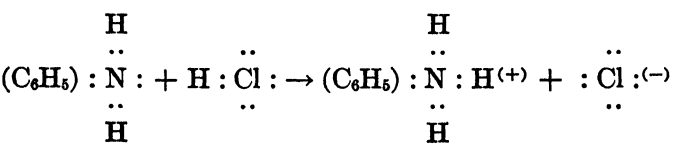
$$\underset{\text{Aniline}}{C_6H_5NH_2} + \underset{\text{Hydrogen chloride}}{HCl} \rightarrow \underset{\text{"Aniline hydrochloride"}}{C_6H_5NH_3^+} + Cl^-$$

The laws of simple valence give no clear explanation of the above reactions. If the Lewis electronic formulas are used, however, the procedure seems to be more logical.



ELECTRONIC FORMULAS (according to Lewis' theory)

In such a formula a single bond is assumed to be a pair of electrons serving the purpose of holding together the various positive nuclei N, C, H, which would otherwise repel each other. In the molecule of aniline, as well as that of ammonia, there is an extra pair of electrons not shared by hydrogen. Apparently every amine base has such an unshared pair of electrons. Plainly there exists an opportunity for the base to attract a proton, which may thus be drawn out of an acid and brought over to share the extra electron pair. Rewriting the last equation in the Lewis form:



In common writing or printing the resulting aniline hydro-

chloride may well be represented by the expression

$$C_6H_5NH_3^+ \cdots\cdots Cl^-,$$

in which the dotted line shows a polar attraction and not a true chemical bond.

The requirements of a base are two: First an unshared pair of electrons; second, an inherent tendency to attract protons at the expense of an adjoining acid. If that tendency of attraction is great, the base is considered strong. If the attraction is slight, the base is weak.

Similar adjectives are applied to acids. If, however, the acid gives up its protons with relative ease, it is called a strong acid; if it holds protons tightly it is weak.

Actual measurement of the strength of an acid requires the use of a standard weak base as a reference reagent. Similarly the strength of a base is found by testing the compound with some standard weak acid. Water, which is both a weak base and a weak acid, is used for both kinds of measurement. For example, the strength of ethylamine could be found by testing the ability of this organic base to take protons from water:

$$\underset{\text{Ethylamine}}{C_2H_5NH_2} + H_2O \rightleftharpoons \underset{\text{Ethylammonium ion}}{C_2H_5NH_3^+} + OH^-$$

It is important to notice that this reaction runs to equilibrium, and does so almost instantaneously. At equilibrium only a limited fraction of the organic base is found combined with protons in the ethylammonium form. The strength of the base is denoted by the extent to which the transfer to the $C_2H_5NH_3^+$ form has occurred at equilibrium.

Ignoring the concentration of water in this equilibrium, which is practically constant, an equation may be set up in conformity with the principles discussed in Chapter XIII (Mass Action and Equilibrium). In this equation brackets refer to concentration; for example, $[OH^-]$ means "concentration of hydroxyl ion":

$$\frac{[C_2H_5NH_3^+] \times [OH^-]}{[C_2H_5NH_2]} = K_B,$$

which is known as the **ionization constant** of the base.

160. In the table given in § 161 a few representative bases are listed. Bases like ethylamine, with constants in the vicinity of

10^{-3} to 10^{-4}, would be regarded as rather weak in inorganic chemistry, by contrast with hydroxyl ion, a powerful base. Only one to five per cent. of the base accepts protons in common water solutions. In the organic field, however, a constant of 10^{-3} indicates a relatively strong base. Aniline, with a K_B of 4.6×10^{-10}, is typical of a weak base. In a saturated aqueous solution of aniline only a very small fraction of one per cent. of the aniline molecules accept protons from water.

161. Acids. With acetic acid as an example, water is again drafted into service as a substance for reference—this time to play the role of a **base**:

$$H_2O + CH_3COOH \rightleftharpoons H_3O^+ + CH_3COO^-$$

Again discarding the concentration of water as a useless constant, an equation may be set up:

$$\frac{[H_3O^+] \times [CH_3COO^-]}{[CH_3COOH]} = K_A,$$

known as the **ionization constant** of the acid.

In this case the constant is recorded (see following table) as 1.8×10^{-5}. This is a median value in organic chemistry, and indicates that acetic acid is an acid of moderate strength. Hundreds of ordinary carboxylic acids are found in this class, with constants from 10^{-4} to 10^{-5}. Those acids whose K_A value is in

IONIZATION CONSTANTS

ACIDS		BASES	
Trichloroacetic acid	2×10^{-1}	Guanidine	3×10^{-1}
Dichloroacetic	5×10^{-2}	Dipropylamine	1.02×10^{-3}
Oxalic (first H^+)	3.8×10^{-2}	Diethylamine	1.26×10^{-3}
Chloroacetic	1.6×10^{-3}	Ethylamine	5.6×10^{-4}
Lactic	1.4×10^{-4}	Triethylamine	5.3×10^{-4}
Benzoic	6.6×10^{-5}	Ammonia	1.8×10^{-5}
Acetic	1.8×10^{-5}	Strychnine	1×10^{-7}
Carbonic (first H^+)	3×10^{-7}	Pyridine	2.3×10^{-9}
Phenol	1.3×10^{-10}	Aniline	4.6×10^{-10}
Sucrose	1.8×10^{-13}	Dimethylaniline	2.4×10^{-10}
Water	10^{-16}	α-Naphthylamine	9.9×10^{-11}
Ethyl alcohol	10^{-18}	o-Chloroaniline	9.2×10^{-13}
Phenylacetylene	10^{-21}	Urea	1.5×10^{-14}
Triphenylmethane—not over	10^{-23}	Water	—
Diphenylmethane—not over	10^{-25}	Acetamide	—
Phenylmethane (toluene)	—	Triphenylamine	—
Methane	—	Acetone	—

the range of 10^{-1} to 10^{-3} are rated as strong. This statement infers that a large fraction of the molecules of such strong acid are found to have reacted with water in their equilibrium mixture with that solvent. Those acids with constants of 10^{-10} or thereabouts, exist largely in their original molecular form in the water equilibrium, and are called weak.

Hydrogen chloride is so strong an acid that it yields its protons to water completely—at least in ordinary solutions:

$$\begin{array}{ccccccc} H_2O & + & HCl & \rightarrow & H_3O^+ & + & Cl^- \\ H & & & & H & & \\ \vdots & & \vdots & & \vdots & & \vdots \\ H:\ddot{O}: & + & H:\ddot{Cl}: & \rightarrow & H:\ddot{O}:H^{(+)} & + & :\ddot{Cl}:^{(-)} \\ \vdots & & \vdots & & \vdots & & \vdots \end{array}$$

The resulting ionic pair $H_3O^+Cl^-$ is known as an **oxonium salt,** analogous to ammonium salts, although the laboratory label probably reads "Hydrochloric Acid, HCl, Dilute." The H_3O^+ ion itself is sometimes called "hydronium ion," again with analogy to the ammonium ion.

Neutralization of an organic base by a strong acid in water solution calls for consideration of the H_3O^+ ion. For example, suppose aniline is allowed to react with dilute aqueous hydrochloric acid instead of pure hydrogen chloride. H_3O^+ now serves as the acid:

$$C_6H_5NH_2 + H_3O^+Cl^- \rightarrow C_6H_5NH_3^+ + Cl^- + H_2O$$

This equation simply means that the nitrogen base, like most of its kind, is stronger than an oxygen base like water. Therefore it almost completely strips the oxonium ions of their extra protons, releasing ordinary water molecules.

162. Extremely Weak Bases. An organic base which is weaker than water cannot be detected as a base in water solution. For illustration, suppose aqueous hydrochloric acid were used in an attempt to react with triphenylamine, an extremely weak base. Unfortunately this amine, being weaker than water, will therefore be unable to take protons from H_3O^+. It thus appears to be inert and neutral. In this manner literally thousands of very weak organic bases often escape identification as bases. These include ethers, which do not react appreciably with dilute hydro-

chloric acid, but react readily with anhydrous HCl:

$$R:\ddot{O}:+H:\ddot{Cl}:\rightarrow R:\ddot{O}:H^{(+)}+:\ddot{Cl}:^{(-)}$$

Sometimes these "ether-oxonium salts" may even be recrystallized.

163. Extremely Weak Acids. An organic acid which is weaker than water cannot be "neutralized" in water solution. Water simply gives up its protons more readily than the weak acid, leaving the latter untouched in spite of the possible addition of large amounts of bases. Practical applications of this principle will appear later.

164. Practical Applications. From the above numerical data and theory a number of practical applications are derived, as follows:

(1) *Ordinary carboxylic acids*, containing carbon, hydrogen and oxygen only, are so much weaker than the common strong inorganic acids such as hydrochloric and sulfuric that they may readily be produced from their salts by mere admixture of the latter with the strong acid. Water does not appreciably interfere with this process, since the oxonium ion H_3O^+, which holds the acidic protons in aqueous solutions of strong acids, is itself a stronger acid than the carboxylic acids which are to be formed. If the desired carboxylic acid is to be isolated by distillation, sulfuric acid, a non-volatile reagent, is employed, so that any excess of the reagent will not be distilled. On the other hand if the organic acid is to be isolated by crystallization, hydrochloric acid is employed, so that any excess will easily be dissipated by simple evaporation.

(2) *Phenols* are so much weaker than carboxylic acids that separations of the former from the latter are occasionally based upon this fact. The mixture of phenol and carboxylic acid is treated with sodium bicarbonate. The carboxylic acid yields its proton to the bicarbonate ion, producing carbonic acid, a weaker acid; while the phenol does not react, since it is weaker than carbonic acid. The unreacted phenol is then isolated by ether-extraction, distillation or other process to which the carboxylic acid, now in the form of its salt, does not respond.

(3) The fact that acids weaker than water may not be neutralized with aqueous bases is turned to advantage in the purification of ethyl alcohol contaminated with acids. The addition of sodium hydroxide converts all carboxylic acids, phenols and of course all strong inorganic acids into non-volatile salts. Barring the presence of neutral or basic volatile substances, a distillate containing only alcohol and water may easily be obtained from the mixture.

(4) Closely connected with the foregoing principle is the rule that salts of acids weaker than water must be carefully protected from moisture. Water, the stronger acid, would of course react with such compounds as sodium ethylate, calcium carbide (acetylide) and zinc diethyl. Even salts of acids slightly stronger than water, such as sodium acetoacetic ester, react with water so extensively as to upset synthetic procedures involving those salts. Naturally all such salts are prepared with complete avoidance of water.

(5) Compounds of the type of toluene and ethane are so low in acidic strength that their sodium salts are prepared only with elaborate precautions. Furthermore these salts are so reactive that the admixture of moisture or even ordinary air to them causes violent decomposition and spontaneous combustion. Accordingly they find no application in common organic synthesis.

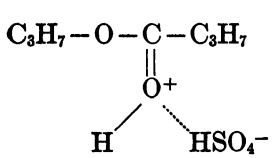
(6) Somewhat analogous to (1) above, it becomes evident that a weak organic base may be expelled from its salt by admixture of a stronger base. For example, aniline hydrochloride (§ 266) is converted into free aniline base by the addition of hydroxyl ion (sodium hydroxide):

$$C_6H_5NH_3^+ + OH^- \rightarrow C_6H_5NH_2 + H_2O$$

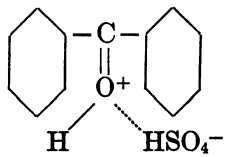
(7) Many organic compounds not commonly recognized as bases will form salts with anhydrous acids. Such compounds are too weak to react even with the relatively strong H_3O^+ acid. Given a strong anhydrous acid, like concentrated sulfuric acid, a reaction takes place, and the base dissolves. Advantage is taken of this situation in qualitative organic analysis (see § 386-B-3). Here cold concentrated sulfuric acid is used to identify oxygen and nitrogen derivatives by observing its power to yield protons to these compounds, thus forming salts which dissolve in the acid. It is probable that concentrated sulfuric acid plays the same role in the well-known acid treatment of petroleum widely employed

in refineries. To be sure, such concentrated sulfuric acid is not 100% pure. It may be reported to contain five to eight per cent. of water. Such water is of course not free (basic) H_2O, but is in the form of H_3O^+ or similar co-ordinated hydrate. The residual acid therefore serves virtually as a non-aqueous reagent, and can form salts of ethers, aldehydes, ketones, esters, nitriles, etc.

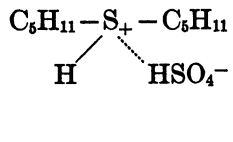
Structural formulas of these salts offer no fundamental novelty in arrangement. For example:



Propyl butyrate acid-sulfate

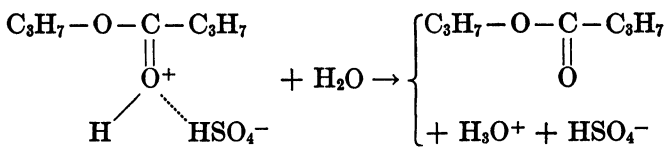


Benzophenone acid-sulfate



Diamyl sulfide acid-sulfate (a "sulfonium" salt)

When a compound such as one of the above is poured upon ice (thus avoiding high temperatures in dilution) the aqueous base H_2O, furnished by the ice, immediately reacts with the oxonium or sulfonium salt, expelling the weak organic base, which then separates in liquid or solid form. For example:



Concentrated sulfuric acid, particularly the anhydrous and fuming grades of the reagent, are known to be excellent for dissolving organic matter which adheres to soiled glassware. It is likely that the largest part of this powerful solvent effect is due to the ability of the anhydrous reagent to convert oxidized matter in the organic stains or tars into salts which are of course very soluble in the sulfuric acid.

(8) Salts of extremely weak amine bases may be prepared with the aid of similar principles, but with the use of a convenient diluent. For example, in the molecule of dinitroaminobenzoic acid the basic character of the amine group is suppressed by the accumulated force of three radicals of somewhat acidic character. Anhydrous alcohol, ether, or mixtures of the two are then used as solvents instead of water. Gaseous hydrogen chloride then causes the precipitation of the desired hydrochloride in an effective manner.

CHAPTER XVI

SEPARATION OF SUBSTANCES FROM MIXTURES

165. Evidence of experience and intelligence in practical organic chemistry is found in one's ability to use a combination of physical and chemical means to separate individual compounds from mixtures. A simple case is illustrated in the following problem: How may one isolate pure aniline and pure nitrobenzene from a mixture of the two?

The mixture is first shaken with an excess of dilute hydrochloric acid. Two distinct liquid phases remain; an aqueous solution of aniline hydrochloride, and under this a layer of unchanged nitrobenzene. The nitrobenzene is separated, washed free of traces of acid, dried and distilled, with promise of high percentage of recovery. The aniline hydrochloride solution is treated as described elsewhere (§ 266); that is, it is made alkaline, steam-distilled, extracted with ether; the extract is dried, ether expelled and residue of aniline distilled.

166. The separation of acetic acid and benzene from a mixture of the two illustrates corresponding methods where acidic material is involved:

The mixture is shaken with an excess of aqueous sodium hydroxide. This completely extracts the acetic acid, converting it into the polar salt. The residual benzene may then be separated, filtered if necessary, dried, and distilled.

The solution of sodium acetate is evaporated to dryness, and the water of hydration expelled by cautious heating of the crystalline residue. Anhydrous (100%) sulfuric acid is now added. Upon distillation, pure "glacial" acetic acid is obtained.

Problems such as those illustrated above depend largely upon principles discussed in Chap. XV, which should be read in advance. For further practice, two lists of mixtures are given below. The first (§ 167) deals with the problem of separating and purifying two substances, while the second involves merely the purification of the one main component, with rejection of accompanying material. A significant test of proficiency comes from the writing

of complete, exact directions for any given separation, suitable for the guidance of a novice. In such directions there should be not only correct application of chemical reactions, but proper choice of apparatus and physical methods.

167. Separation of Two Substances. How would you prepare the individual components, each in a pure state, from each of the following mixtures?

(1) Benzoic acid and naphthalene.
(2) *p*-Toluidine and *o*-nitrotoluene.
(3) Benzoic acid and phenol. (Note that the dissociation constant of benzoic acid is very much greater than that of phenol.)
(4) Aniline sulfate and sulfanilic acid. (Change one component into volatile form.)
(5) Hexyl alcohol and cresol. (The alcohol is a weaker acid than water.)
(6) *n*-Butylamine and *n*-hexane.
(7) Benzaldehyde and benzyl chloride. (Convert one component into water-soluble form, from which it is easily reclaimed.)
(8) Aniline and dimethylaniline. (Use the fact that dimethylaniline has no N—H chemical bond.)
(9) Diamylamine and diphenylamine. (Aromatic bases are weaker than aliphatic.)
(10) *tert*-Butyl alcohol and ethyl alcohol. (Note differences in ease of esterification.)
(11) Aminobenzoic acid and benzoic acid. (Aminobenzoic acid is amphoteric.)
(12) Aminobenzoic acid and aniline.

168. Purification. Frequently but one of the two or more organic substances in a mixture is desired. The problem then permits the virtual destruction or loss of the others, and allows of greater variety of treatment.

How would you purify each of the following without concern about the loss of the accompanying materials?

(1) Pentane (containing amylene).
(2) Methyl aniline (containing aniline).
(3) *n*-Amyl butyrate (containing *n*-amyl alcohol).
(4) Ethyl acetate (containing ethyl alcohol and acetic acid).

(5) Quinoline, a tertiary amine (containing aniline and phenol; all three substances slightly volatile at 100°).
(6) Methyl ethyl ketone (containing ethyl alcohol).
(7) Diethyl ether (containing amylamine, as in "recovered ether" which had been used in an extraction and distilled without thorough purification).
(8) Hexyl chloride (containing hexyl alcohol).
(9) Ethyl alcohol (containing acetic acid and aniline).
(10) Benzyl alcohol (containing valeric acid).
(11) *n*-Octane (containing dibutyl ether).
(12) Benzene (containing benzaldehyde).

CHAPTER XVII

USE OF THE LITERATURE OF PRACTICAL ORGANIC CHEMISTRY

169. If there is need for practical directions for preparation of any well-known organic compound not described in this volume, it is advisable to consult other manuals, of which a score or more have appeared in recent years, principally in Germany, Great Britain and the United States. These are mostly laboratory guides for courses of university instruction. One entitled *Organic Syntheses* (John Wiley and Sons, 1921–), deserves special notice. Appearing in small volumes, this work is designed as an aid to research workers who wish to prepare their own organic reagents. It is probably the best source of laboratory directions in print. Each section has been tested by workers in two or more laboratories, and a revised collective volume covering the first nine annual volumes is available.

If the laboratory worker is concerned with research in laboratory synthesis, however, a more serious library investigation is requisite. Anyone who would attempt to find better methods of laboratory procedure without a search of the literature down to date lays himself open to ultimate ridicule when a critic points out the fact that someone else has already made the same discoveries.

First among the books useful in a search of the literature is Beilstein's great *Handbuch der organischen Chemie* (fourth edition). The Beilstein handbook is virtually an encyclopedia which aims to give at least a brief account of all definitely-known organic compounds described in original papers prior to 1910. Parallel with Beilstein is Richter's *Lexikon*, a formula-index, covering the same period of time. This work lists a large number of compounds, including a few not found in the Handbuch. A continuation of the Lexikon, under the editorship of Stelzner, appeared until 1921. A few supplementary volumes of Beilstein have also appeared. Students should of course make use of the numerous references given in Beilstein, Richter and Stelzner to

original articles in chemical journals, which are the real archives of chemistry.

For information of date later than 1921, journals are the usual resource. Abstract journals, international in scope, serve as necessary guides to such information. For many years the German *Chemisches Zentralblatt* and the British abstracts were the only adequate material of this type available. Since the World War, however, the annual production of chemical literature has become so vast that only the newer *Chemical Abstracts*, published by the American Chemical Society, is now able to cope with the huge problem of abstracting every article on chemistry published in the whole world. Both the *Decennial Indexes* (to *Chemical Abstracts*) for 1907–1916 and 1917–1926, and the annual indexes for years after 1926, should be consulted. A colossal new index for 1927–1936 is promised for 1938.

For more detailed advice on literature search, see *Introduction to Organic Research*, by Reid (Van Nostrand), *A Guide to the Literature of Chemistry*, by Crane and Patterson (John Wiley and Sons) and *Chemical Publications*, by Mellon (McGraw-Hill).

170. Check-List of Laboratory Manuals of Organic Chemistry. (Cited elsewhere by number.)

1–16. Adams and associates, *Organic Syntheses*, John Wiley and Sons. (Accompanying reference numbers also indicate the volume numbers in the Organic Syntheses series.)

17. Adams and Johnson, *Laboratory Experiments in Organic Chemistry*, second edition, Macmillan Co.

18. Adkins and McElvain, *Practice of Organic Chemistry*, second edition, McGraw-Hill Co.

19. Coghill and Sturtevant, *Introduction to the Preparation and Identification of Organic Compounds*, McGraw-Hill Co.

20. Cohen, Julius, *Practical Organic Chemistry*, Macmillan and Co.

21. Coleman and Arnall, *Synthetic Organic Chemistry*, Blakiston's.

22. Colbert, J. C., *Laboratory Technique of Organic Chemistry*, Century Co.

23. Cumming, Hopper and Wheeler, *Systematic Organic Chemistry*, revised edition, Constable.

24. Fieser, L. F., *Experiments in Organic Chemistry*, Heath & Co.
25. Fischer, Emil, *Preparation of Organic Compounds* (translation from the German), D. Van Nostrand Co.
26. Fisher, Harry, *Laboratory Manual of Organic Chemistry*, third edition, John Wiley and Sons.
27. Gattermann, L., *Practical Methods of Organic Chemistry* (translation from an early German edition), Macmillan Co.
28. Gattermann-Wieland, *Laboratory Methods of Organic Chemistry* (translation of a recent revised and enlarged German edition), Macmillan and Co.
29. Heidelberger, M., *Advanced Laboratory Manual of Organic Chemistry*, Chemical Catalog Co.
30. Norris, J. F., *Experimental Organic Chemistry*, revised edition, McGraw-Hill Co.
31. Noyes, W. A., *Organic Chemistry*, Chemical Publishing Co.
32. Porter, Stewart and Branch, *Methods of Organic Chemistry*, Ginn and Co.
33. Sudborough and James, *Practical Organic Chemistry*, Blackie and Son.
34. Vanino, L., *Präparative Chemie*, Vol. II, Enke.

PART II

LABORATORY EXPERIMENTS

(NOTE.—*Numbers marked "Ref.," in connection with various optional experiments described below, refer to the laboratory manuals listed in § 170, page 141.*)

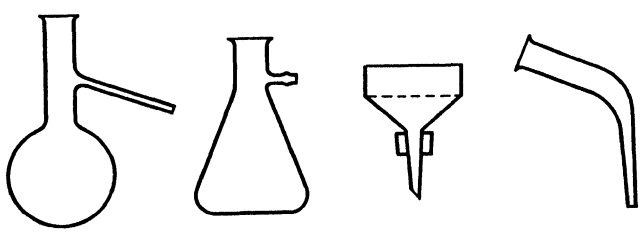
PRELIMINARY LABORATORY WORK

NOTE. *Of the following introductory operations, perform only those specified by the instructor, according to the arrangements of your laboratory.*

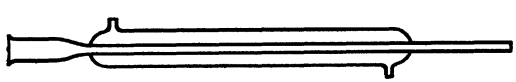
171. Inspection of Desk Equipment. First make sure that laboratory desk contains all of the apparatus specified on the ficial list. A copy of the list may be obtained from the storeroom if one is not found in the desk. Return defective pieces to the storeroom, and obtain any missing articles *on the first day of laboratory work.* Note particularly the possibility of inconspicuous defects in those of the following pieces which may be on your list:

Water-cooled (Liebig) condenser; watch for concealed cracks in the inner tube at points where the outer tube is attached with rubber.

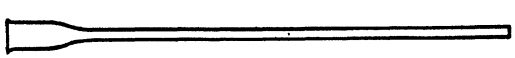
Thermometer; if it has been abused by careless cooling in faucet water, it may have inconspicuous cracks near the mercury well.



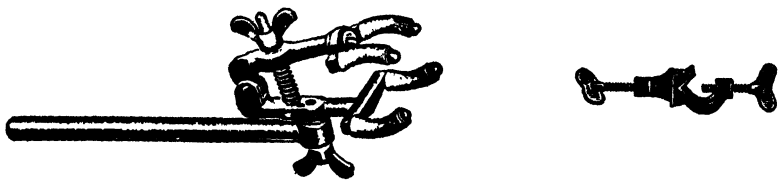
Distilling flask | Filter flask | Buechner funnel | Adapter



Liebig (water-cooled) condenser



Air-cooled condenser



CONDENSER CLAMP AND CLAMP HOLDER

Gas hose; if used tubing is furnished, beware of rubber which is cracked or has weak spots due to fire damage.

Separatory or dropping funnel; see that the glass stoppers are the ones which belong to the funnel, and which thus fit properly.

172. Broken Glassware. If the services of a glassblower are available, do not discard broken glassware in cases where the pieces may be satisfactorily repaired. Consult the storekeeper, who will receive the damaged ware for exchange, or advise you of arrangements for repair service. For example, distilling flasks and dropping funnels with broken delivery stems are often readily mended.

173. Preparation of Apparatus for the First Experiments. Examine the directions for the first two experiments assigned by the instructor and prepare the necessary glass, rubber and cork parts for assembly as needed later. Before boring corks for this purpose, read § 7 carefully. If one of the first assignments is the preparation of absolute alcohol, time may be saved by carrying out the directions of § 174 next following.

174. Absolute Alcohol. Start this experiment at once—before assembling equipment for distillation—as described in § 197, and proceed to the point where a delay of two or more days is required. Next read the discussion of the use of a reflux condenser (§ 24), and fit the water-cooled condenser in the proper manner to the flask holding the quicklime and alcohol, ready for prompt use on a subsequent day.

175. Preparation of Boiling Stones. Read § 33. Break up in an iron mortar 25 to 50 grams of clean, dry unglazed crockery, and pass the granular product through suitable sieves. Crush all of the material to a size not exceeding 5 mm. in diameter, and discard the dust and fine grains under 2 mm. Preserve the pieces of 2 to 5 mm. size as boiling stones, and keep them clean and dry in a bottle. In any case where a liquid "bumps" during distillation

or refluxing, interrupt the heating for two or three minutes and then place three or four stones in the boiler. It is well to develop the habit of adding these stones to all mixtures undergoing distillation, save only in the case of reduced-pressure operations. Note the last part of § 33, dealing with a fire hazard in the use of boiling stones.

176. Preparation of Cleaning Solution. Select a Pyrex beaker of 250 to 400 cc. size, and make special note that the vessel does not have the slightest crack. In this beaker, mounted over wire gauze, heat about 100 cc. of technical concentrated sulfuric acid to about 100°. With the aid of a glass rod stir in about 3 g. of finely granulated sodium or potassium dichromate. Continuous stirring is essential to prevent the agglomeration of the resulting chromic acid into large masses. Allow the mixture to cool to 50° or below, and pour both the orange-red solution and the precipitated chromic acid into a dry *bottle* (of glass stoppered type) of about 125 to 250 cc. capacity. Do not use a flask or other thin-walled vessel for storage of cleaning solution. The reagent is capable of setting fire to woodwork, and no risk of breakage should be incurred. The use of this solution is described in § 10.

177. Preparation of Anhydrous Magnesium Sulfate. Spread about 35 g. of Epsom salt ($MgSO_4.7H_2O$) in a thin layer in a 4 or 5 inch evaporating dish and heat the dish over wire gauze with a Bunsen burner. The material will partially melt, and nearly half of its mass will be expelled in the form of steam. A dull white, chalky mass should remain as a residue. Crush this into coarse granules and preserve the whole product (granules and powder) in a well-corked wide-mouthed bottle.

This preparation should be used particularly where a neutral non-reactive drying agent is required. See §§ 98 and 106 for further details.

CALIBRATION OF A THERMOMETER

178. Determine the accuracy of your high-range thermometer at the 0°, 100° and 218° points as described below, and test the low-range thermometer at the 0° and 100°. Read §§ 16–18.

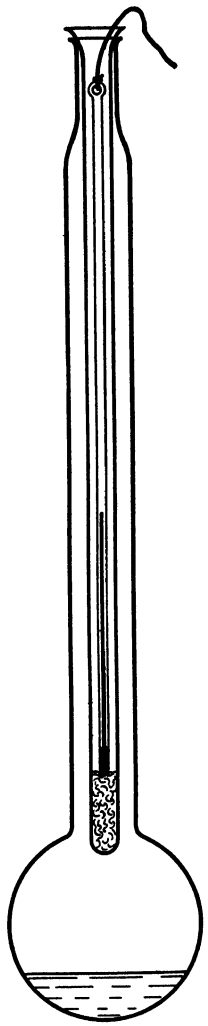
179. Correction at 0° C. Place the thermometers in finely crushed ice to which has been added enough distilled water to produce a thin slushy mass. If the entire mercury column is immersed for five minutes or more, the temperature of 0° should be indicated if the thermometer is correctly calibrated. Record the facts in the notebook.

180. Correction at 100° C. Assemble the apparatus pictured in Fig. 3, § 25, using a distilling flask of any size from 250 to 500 cc., but omitting the adapter. Instead of the wire gauze shown in the figure, use a piece of asbestos board in the center of which a hole 3 or 4 cm. in diameter has been cut. Place 100 cc. of pure distilled water in the flask, add two or three boiling stones, and distil the liquid over the Bunsen flame at a moderate rate. When the temperature reading has become constant, record the readings both of the thermometer and of the laboratory barometer. Determine the length of the mercury column which protrudes from the heated zone, and consult § 18. Note boiling-point data given in § 407, Appendix, and determine the correction, if any.

If the asbestos board is omitted, heated air creeps up along the upper walls of the flask, and superheats the escaping steam. The resulting temperature record may rise to 101° or 102°, and thus be worse than useless.

181. Correction at 218° C. By replacing the water with pure naphthalene, and using the apparatus of Fig. 2, § 25 instead of Fig. 3, the 218° point may be examined, but care must be taken to warm the condenser tube so that the distillate will not solidify and close the condenser passage.

It is somewhat simpler to boil naphthalene in a special Pyrex flask with a neck about 50 cm. long. As illustrated in the accompanying figure, a slender test tube of thin Pyrex glass, holding a small wad of glass wool as a cushion, receives the whole length



NAPHTHALENE APPARATUS FOR CALIBRATION

of the thermometer. With ordinary care, naphthalene may be boiled actively enough to keep the entire mercury column surrounded by the stream of refluxing condensate, and still without appreciable loss of vapors. In about ten minutes the thermometric reading should be constant, and should register the boiling point of naphthalene (218.1° at 760 mm. pressure). For values at other barometric pressures, see the Appendix, § 407.

DISTILLATION OF PETROLEUM

182. When a mixture of two or more substances is distilled, the boiling temperature is usually not constant. The components pass over into the condenser in new and constantly changing proportions. A boiling range is thus recorded instead of the boiling point observed in the previous experiment. See § 42 for theory of this phenomenon. In commercial practice, mixed products are often sold on specification of boiling range.

In a 100 or 125 cc. distilling flask, fitted with a high-range (0°–360°) thermometer and an air-cooled condenser, as shown in Fig. 2, § 25, place a few boiling stones, and add 50 cc. of kerosene or other suitable petroleum through a funnel. Provide a dry flask as a receiver. Using wire gauze to protect the distilling flask, heat the latter with the Bunsen flame, and record in the notebook the temperature when the first drop of distillate falls into the receiver. Continue the distillation until about half of the oil has passed over, place a new empty receiver under the condenser, and record the temperature at the moment of change. Continue the distillation, with removal of the wire gauze if necessary, until the boiler just runs dry, and record the final boiling point, sometimes technically known as the "dry point." (If petroleum heavier than kerosene is used, be careful not to over-run the maximum allowable height of the mercury column in the thermometer.)

After both fractions of the distillate are cool, hold one up before the light and pour the second fraction into it. Notice the temporary distortion of light as the two liquids are first mixed. This disturbance roughly indicates the variation in refractive index, which in more precise operations could be used as a test of the character of the oil.

QUESTIONS

1. How does the boiling range of your product differ in general from that of gasoline?

2. Where many components are present in one mixture, would a mere specification of boiling range alone be completely satisfactory as a commercial requirement? Why?

PURIFICATION OF A TECHNICAL ORGANIC PRODUCT BY RECRYSTALLIZATION

183. Read Chapter VII, describing the general method of isolation of a solid preparation. For the purposes of this assignment §§ 73 to 77, inclusive, correspond to the operations performed by the manufacturer before delivery to the laboratory of the crude product which is handled as described below. §§ 78 to 90 apply directly to the problem at hand. In the following directions, technical sulfanilic acid is taken as an illustration.

Weigh out 10 g. of the crude product and place it in a beaker or conical flask. Add 75 cc. of water, stir well, and heat to boiling. Add water until the boiling solution completely dissolves the crude preparation, but do not try to dissolve dust, trash, etc., which is obviously not the crystalline substance desired. Treat the solution as described in §§ 78 ff., and dry the resulting purified crystals as described in § 93. Weigh the dried product and calculate the percentage of recovery of crystalline material.

MELTING POINT OF AN UNKNOWN SUBSTANCE

SHORTER EXPERIMENT

184. Obtain a sample of a pure organic compound of identity unknown to you, and also a few milligrams of the purest benzoic acid available—the latter for use as a reference in practice. Next prepare melting point tubes, and apparatus for the determination, as described in §§ 189 ff. Find the melting-points of both substances under examination, as described in §§ 195 ff.

LONGER EXPERIMENT

185. Material for Test. In this experiment each student receives a sample of an impure organic preparation. This material is nominally a single substance, but may be either a commercial product of "technical" grade, or a crude laboratory preparation. Before identification from melting point is practicable the material must be purified. Read Chap. VII on the "Isolation and Purification of a Solid Product." Proceed as follows:

186. Recrystallization. Using small test tubes, try various plans for recrystallization of the impure material, testing first water, and then if necessary alcohol and benzene as solvents. Other factors being equal, water or alcohol is favored over benzene. First try to dissolve a few crystals in about 0.5 cc. (10 to 15 drops) of the *unheated* solvent. If the substance dissolves freely in the cold, the solvent is plainly unsuited to the standard process of recrystallization (§ 78) for this case. Try another solvent, or even a mixture of solvents.

If the solid does not dissolve freely in the cool solvent, heat the mixture almost to the boiling point. If necessary, add more solvent until the organic compound is completely dissolved at the boiling temperature. Keep a record of the approximate amounts of materials used. Do not try to dissolve minute particles of dust, cork, or other trash which may happen to accompany the preparation and which are obviously not the desired organic compound. Without attempt to remove impurities, cool the resulting solution, if necessary with the aid of an ice bath, to encourage crystallization. The ideal outcome of this experiment

is described in § 187 below. On the other hand, certain troubles may arise, and these are handled according to § 188(*a*), (*b*), (*c*).

187. Ideal Conditions. Under favorable circumstances the solution slowly deposits a moderately small yield of beautiful, distinctly separate crystals, with enough accompanying liquid so that the mixture is easily poured upon a filter. Such an experiment may then be considered as a model for repetition on a larger scale. Now decide what vessels, quantity of solvent, fire precautions etc. are necessary to effect the purification of about half of the sample at hand, and proceed. Note that no attempt is made to obtain a maximum or even a large yield. Frequently the production of a restricted yield of crystals from a relatively dilute solution facilitates filtration and permits the most effective elimination of dissolved impurities. In any case do not use more than 50 cc. of a solvent of appreciable cost, such as alcohol or benzene, with appropriate limitation of amount of substance recrystallized.

If the solution prepared in the preliminary test-tube experiment was turbid, filtration of the main quantity is thus suggested. If it is tarry, or discolored, use a small amount (0.5 g. or less) of decolorizing carbon as described in § 88. Brown, olive, purplish-gray and other dull composite tints indicate impurities which may escape an ordinary filter. Pure organic compounds are usually white (colorless in solution). Others are of simple primary colors, such as yellow and orange; comparatively few are red, green, blue, or violet. Many are yellowish white.

When the final yield of purified crystalline material has separated from solution, collect it on a filter, wash it *cautiously* (!) with a few cc. of cold solvent of the kind you have been using, and dry between filter papers.

If you suspect that the product is still impure, set aside a few milligrams of the crystals as a reference for test of melting point, and immediately recrystallize the remainder. This process may be repeated once or twice, and the ultimate array of successively recrystallized samples tested in the melting point experiment to follow. If the last two recrystallizations give products which not only melt sharply, but also agree exactly in melting point, there is assurance that you have really purified the preparation, and thus may make a critical comparison with melting point data given in the literature.

188. Difficulties. If the program of § 187 (above) does not go forward smoothly, one of the following options may fit your situation:

(*a*) The small test-tube sample of solution, upon cooling, may suddenly "set" to an apparently solid crystalline cake which is not readily handled on a filter. In such a case carefully add more solvent, drop by drop, frequently reheating and cooling, until the solution is so dilute that some time is required—perhaps five minutes or more—to obtain loosely crystalline material upon cooling. Now proceed as already described in § 187.

(*b*) The sample of solution upon cooling becomes turbid. Numerous droplets of a so-called "oil" separate out, run together, and either sink or float according to density. For purposes of this experiment, where a large yield is of no consequence, the following method is useful: Cool the mixture slowly until the oil solidifies. At once decant or otherwise separate the residual solution from the solidified oil. Allow this isolated solution to cool still further. Only crystals are now obtained; these are likely to be of high purity, and they are handled as described in § 187.

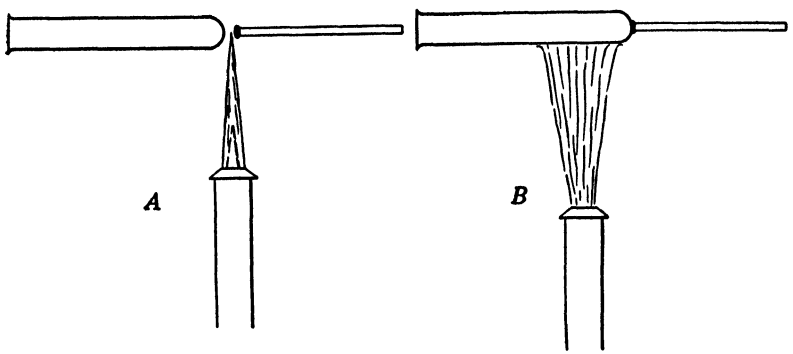
The difficulty from separation of oil may also be handled by diluting the hot, clear solution until no separation occurs before the falling temperature reaches the point where only crystals separate. Still another method of forestalling the production of oil from aqueous solutions is to add drop by drop enough ethyl alcohol to hold the material in solution at the higher temperatures. This is the equivalent of saying that many preparations of low melting point may be recrystallized from 20, 40 or perhaps 60% alcohol, but not from pure water without the formation of oil at any stage. Further discussion of the oil problem is given in § 149.

(*c*) If no crystals can be obtained even from extremely concentrated solutions cooled in an ice bath, try "seeding" the solution with a minute crystal of the original preparation. If this doesn't work, try a change of solvents, or a mixture of solvents. For example, should ethyl alcohol be too effective a solvent, try adding water drop by drop. If benzene is too effective, try diluting it with a solvent which is more highly oxidized (e.g. alcohol) or one more reduced (e.g. light petroleum).

DETERMINATION OF MELTING POINT

189. Preparation of the Tube. Thin-walled glass tubing is required as material from which the tubes are made. Ordinarily a 12 to 18 mm. test-tube is the best form in which such glass may be procured from an ordinary commercial supply or storeroom.

Using a small blast flame, heat the closed end of the test tube with continuous rotation, as shown at *A* in the illustration. Simultaneously heat the end of a piece of glass rod or tubing in like manner. When the tips of both pieces of glass are bright red hot and plastic, firmly seal them together with as little crumpling or twisting of the plastic joint as possible. Now hold the joined tube in a straight line until the seal is just rigid enough so that no bending will take place.



At once shift the test-tube with its convenient handle to position *B*, where it is now to be strongly heated, with continuous rotation, at the *tip* of a large brush flame. A little practice enables the beginner to rotate the tube without twisting the softened portion, until a stretch of 3 to 5 cm. of the tube is very soft but has not yet collapsed.

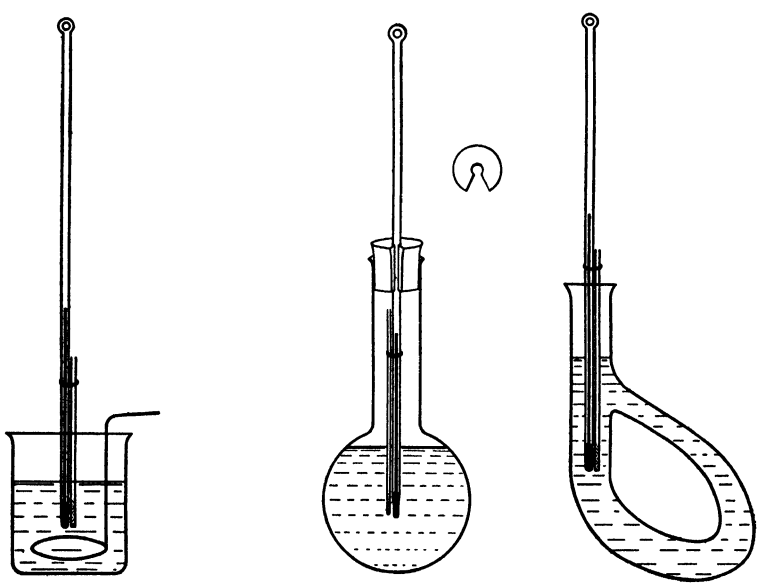
At this point remove the tube from the flame, and immediately draw it out to the full expanse of your outstretched arms; then pause a few seconds in this position to ensure the solidification of the fine tube while it is still unbent.

If the work is properly done, a considerable length of thin-walled tubing is produced. This should be about 1 to 2 mm. in diameter. Using the needle-pointed flame, cut this tube into 15 cm. lengths. In this manner each length will be sealed air-tight from the start, and may be preserved indefinitely free from dust and moisture on its inner surface. When a melting point tube is needed, cut one of these double-sealed tubes in half, thus obtaining two melting point tubes of convenient size.

190. Introduction of Material. Obtain a few milligrams of pure crystalline benzoic acid for preliminary practice in the deter-

mination. Introduce a milligram or more of this compound into a melting point tube. If the closed end of the tube is bounced on a wooden table, the solid may be encouraged to fall into place at the bottom. If the preparation is coarsely crystalline, crush it, but do not powder it finely before introducing it into the tube, lest there be a slight change in melting point.

191. Manipulation. Fasten the tube with its enclosed sample of crystals to a thermometer (0° to 360° range) so that the organic compound lies close to the mercury well. If sulfuric acid is used as the bath liquid, experienced workers take advantage of its surface tension, and merely lay the tube along the thermometer, which has been wetted with the acid in advance. It is safer to attach the tube to the thermometer with the aid of a slender rubber band cut with scissors from the end of a piece of fresh, soft, 3/16-inch rubber tubing. Care is taken to keep the rubber band well up out of the bath.



APPARATUS FOR DETERMINATION OF MELTING POINT

Now assemble apparatus suitable for the heating of the tube, with use of an approved bath liquid, according to the directions given by the instructor. Three commonly used arrangements are

shown in the accompanying figure; see § 136 for discussion of relative merits of bath liquids.

192. Beaker Method. With the aid of a Bunsen or blast flame bend a piece of 4 or 5 mm. glass rod into the form of a loop with handle as shown. Use this bent rod as a stirrer, which may be raised and lowered without interference with the thermometer or melting point tube, thus ensuring uniform temperature.

193. Flask Method. Use a Pyrex flask of about 200 cc. capacity. Do not fill it to a level higher than that shown in the diagram, lest the bath liquid eventually overflow, due to expansion at high temperatures. No wire gauze is used. Heat the flask at the *bottom only* with a *very small flame.* Such an outfit is particularly favored where there are determinations made from day to day, and thus where it would be undesirable to expose a bath liquid in an open vessel continuously. Somewhat more experience is required to ensure uniformity of temperature and accurate results in such a method where no stirring is performed. The third, or modified Thiele apparatus, facilitates circulation of bath liquid.

194. Practice in Determination. Heat the vessel steadily at first until the temperature is within 6 or 8 degrees of the probable melting point—that is, to about 115° in the case of benzoic acid. Now heat slowly—at a rate not exceeding two degrees per minute. The acid should melt sharply at 121.7° (corr.). Repeat the determination, each time with a new melting point tube, until you can reproduce with confidence this known value. It will of course be necessary to correct the direct reading for emergent stem, and possibly for error in the graduation of the thermometer. See § 18.

195. Melting Point of "Unknown" Substance. Heat a melting point tube containing a sample of your purified unknown substance rapidly in order to determine approximately its melting temperature. Discarding this first tube, make a final accurate determination on a new tube, noting whether the product melts sharply, or over a range. Record in the notebook the temperature when melting started, and that when the last crystal disappeared. If this melting range is more than one degree, an excessive amount of impurity is suspected, and the process of purification of the material should be continued. The usual

corrections should of course not be overlooked. Read Chap. XI, dealing with the theory of this determination.

QUESTIONS

1. Suppose every one of the solvents available for the recrystallization either dissolved the material too well, or not well enough; what may then be done?
2. Why are we particular not to permit moisture (as from the blast lamp flame) to get into a melting point tube?
3. Picric acid and benzoic acid have almost exactly the same melting point. How could you use the procedures of this experiment to distinguish the two acids?

DETERMINATION OF EMPIRICAL FORMULA

Molecular Weight from Melting Point

196. The determination of the empirical formula of an organic compound normally calls for two quantitative experiments, namely:

(*a*) Elementary analysis, leading to the simplest formula. For example, octane yields the simplest formula C_4H_9.

(*b*) Determination of molecular weight, which shows whether it is necessary to multiply the coefficients determined in (*a*). In the example of octane, the factor of two is required, yielding the final formula C_8H_{18}.

Obtain a sample of an "unknown" organic compound, together with the figures for weight of carbon dioxide and water found in the quantitative combustion analysis of a specified weight of the compound. (The actual determination of such figures requires special apparatus and training not called for in this course.)

Using a quantitative balance, weigh out to the accuracy of 1 mg. not less than 0.190 nor more than 0.210 g. of the unknown compound into a dry test tube, and record the weight in the notebook. Add to this a sample of pure camphor, weighed to like accuracy, ranging from 1.950 to 2.050 g. Heat the mixture gently over the Bunsen flame until it has entirely melted and immediately cool, stirring with a dry glass rod until the mixture has solidified. Place a milligram or more of this mixture in a melting-point tube, and determine its melting point, as described in § 191. Record the temperature where the last crystals disappear as the melting point of the mixture. Determine also the melting point of pure camphor. Since only the

lowering in melting point is important in this experiment, a possible calibration error of the thermometer is scarcely worth considering.

Calculate the simplest formula of the compound from the combustion data furnished. Next calculate the molecular weight, using the value 39.7 as the so-called cryoscopic constant. The following statement is approximately true, provided mixtures of nearly 1 : 10 ratio are considered: One mole of a solute normally lowers the freezing (or melting) point of 1000 grams of camphor by 39.7 Centigrade degrees. Incidentally, compounds of a type where the lowering is abnormal will not be issued in this experiment unless notice to the contrary is given. See also reference at the end of Chap. XI.

Finally, from the simplest formula and the determination of molecular weight, calculate the empirical formula of the compound.

Combustion analysis is conducted by either of the following standard methods, which differ fundamentally only in size of the samples weighed. Especially good descriptions of these methods are given by the authors cited below:

Macro (large scale) method: Fisher (Ref. 26).
Semimicro (intermediate) method: Fieser (Ref. 24).
Micro (small scale) method: Pregl-Roth-Daw, *Quantitative Organic Microanalysis*, 1936, or Pregl-Fyleman, same title, 1930, P. Blakiston's Son and Company.

ABSOLUTE ALCOHOL

197. Many laboratory and industrial processes require the use of nearly pure ethyl alcohol, in which the content of water is much below one per cent, and preferably not over 0.2%. Such alcohol mixes with certain oils freely whereas 95% alcohol does not. Unfortunately this dry, or "absolute" alcohol is not readily prepared by ordinary fractional distillation (see § 47). One solution of the problem is obtained by mixing quicklime (calcium oxide) with commercial aqueous ethyl alcohol. The quicklime combines with the water to form calcium hydroxide, leaving the alcohol behind practically free from water (see § 103).

198. Calculate the quantity of quicklime which is required by theory to react with the water present in 150 cc. of commercial ethyl alcohol. The commercial product supplied to the author's laboratory as this is written contains approximately 92% by weight of ethyl alcohol, the balance being almost all water. (It is commonly called "95% alcohol," the percentage being figured by volume, as customary in distillery practice.) Use the *weight-per cent value only*, inasmuch as calculations " by volume" involve unnecessary arithmetical labor. If the laboratory alcohol differs from the standard above mentioned, the instructor will give notice of the deviation.

Inasmuch as technical quicklime is not pure, weigh out on a rough balance double the amount calculated above. Select only hard pieces varying from about 4 to 15 mm. in diameter, rejecting all powdered material, much of which may already be slaked.

In a 700 or 1000 cc. flask place the alcohol and quicklime, and warm the mixture by placing the flask in a pan of hot water for a few moments. As soon as the temperature of the alcohol has reached 60° stopper the flask tightly and set it away for two to seven days. Read § 24 before resuming operations.

After the proper time interval attach a water-jacketed reflux condenser to the flask and place the flask in a water bath. A calcium chloride tube may be mounted on the top of the reflux condenser. If the experiment is being conducted in very dry summer or fall weather, with the relative humidity below 30%, the calcium chloride tube is of little use, and may be omitted.

In such case a piece of cotton is used instead, to hinder atmospheric diffusion.

Heat the water bath until the alcohol in the flask boils quietly, and continue the refluxing process for one hour or more. Now rearrange the outfit for ordinary distillation, using the set-up shown in Fig. 1, § 25, including a thermometer (0 to 100° size). On the extremely dry days above cited a simple flask may be substituted for the suction flask and calcium chloride tube; but in such a case be sure that there is no stopper connecting the receiver with the condenser. Even in dry weather the filter flask and calcium chloride tube are used if one desires a preparation over 99.8% pure. In rainy weather their omission may reduce the purity of the final product even below 99%.

If the laboratory is provided with the special paraffin oil for water test, proceed as described in § 199 below. If such oil is not available, follow directions of § 202.

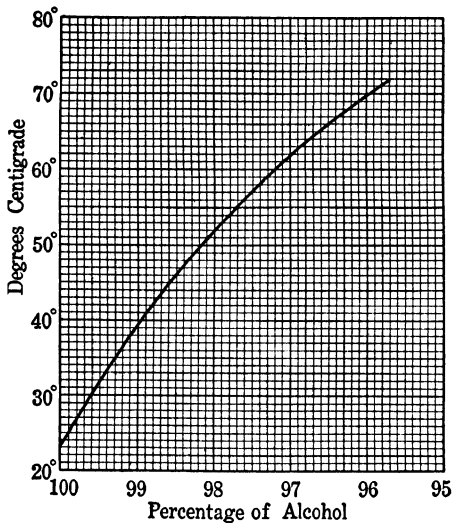
199. Distillation; with Estimation of Water Content. Distil the alcohol, collecting the first four or five cc. of product in a small dry test-tube, and the next three cc. in a small dry graduated cylinder. Now connect the condenser to its regular receiver, and proceed with the distillation. Finally as the distillation nears completion, collect another 3 cc. sample in the dry graduated cylinder. Cork the tubes containing these samples unless they are tested at once; and do not delay the tests more than an hour.

While the main distillation is in progress, determine the percentage of water in each of the three small samples above mentioned, using the (quantitative) paraffin oil method described below. Finally shake the receiver containing the principal yield of absolute alcohol, to ensure uniform mixing. Now withdraw a 3 cc. sample of this main product, and determine its water content. Report this as the test on your preparation as submitted to the instructor or assistant.

200. Procedure of Test. Measure just 3 cc. of the alcohol to be tested from a dry graduate into a dry 6-inch test-tube. Add just 4 cc. of "Standard Paraffin Oil Mixture" and stir with a dry thermometer.

Heat the liquid until it becomes clear—that is, until it goes into one phase. Alternately cool and heat the tube, with constant stirring, until you are able to determine to a nicety the temperature at which the clear liquid just begins to show turbidity.

Consult a graph or table which shows directly the corresponding percentage of alcohol. The accompanying graph applies to the particular oil used in the author's laboratory at the time these directions were written.



MISCIBILITY TEMPERATURES OF OIL WITH ETHYL ALCOHOL CONTAINING SMALL AMOUNTS OF WATER

If the process of dehydration has been conducted carefully, the percentage of alcohol will be above 99, and often exceeds 99.6. See §§ 127–128 for a discussion of the theory of this test.

201. This table shows the maximum temperature at which a mixture of four volumes of "Standard Paraffin Oil No. 4A" and three volumes of aqueous or absolute alcohol exists in two phases, i.e., is turbid when stirred. It is assumed that no other impurity than water is present in the alcohol.

202. Distillation; with Qualitative Test. If the special paraffin oil called for in § 198 is not available, simply distil the whole quantity of alcohol in two fractions. Collect the first four or five cc. in a small dry test-tube, and the balance in the regular receiver normally provided. Divide the first sample of distillate into two approximately equal parts. To one add a few particles of anhydrous copper sulfate, and to the other a crystal or two of potassium permanganate. Test in a similar manner very small samples of the main alcohol distillate. The appearance of a coloration in any case indicates the presence of more or less water. On the other hand, these salts are practically insoluble in really absolute alcohol. These tests are admittedly inferior, and not comparable with the oil method of § 200 above.

Determine the theoretical, actual and percentage yields (including the quantities set aside for test). Note the density data given below:

203. Density of Alcohol at Various Temperatures.

Percentage by Weight	15°	Density 20°	25° C.
90%	.822	.818	.813
91	.820	.815	.811
92	.817	.813	.808
93	.814	.810	.805
94	.811	.807	.803
95	.809	.804	.800
96	.806	.801	.797
97	.803	.798	.794
98	.800	.795	.791
99	.797	.792	.788
100	.794	.789	.785

204. Note. The "Standard Paraffin Oil Mixture" is composed of highly purified paraffin and cycloparaffin oils obtained by special refining of petroleum. It is easily prepared by mixing a small amount of intestinal lubricant, or of confectioners' oil, with a very highly refined kerosene. The particular oil "No. 4A" which yields the data given in the accompanying graph was made by mixing 70 volumes of "Oronite Crystal Oil" and 524 volumes of "Elaine" kerosene, both products of the Standard Oil Company of California. While there is no assurance that future specimens of these oils will give exactly the same results, it may be noted that they seem to be well standardized products. No difficulty was experienced in preparing from commercial stock of 1934 an oil of the 4A characteristics which matched the oil of five years before.

The mixed oil, such as the #4A above cited, is calibrated by test with a number of samples of ethyl alcohol whose water content is known from density determinations at 25°.

OPTIONAL EXPERIMENTS

205. Other alcohols. Methyl alcohol may be dehydrated in a manner similar to that given above. On account of its lower boiling point, methyl alcohol should be handled with greater precaution against fire. (See § 26 (b).) In this case *n*-hexane is substituted for the special paraffin oil, as described by M. M. Rising, *J. Am. Chem. Soc.*, 48, 1929 (1926).

Alcohols with more than two carbon atoms per molecule are more easily dehydrated. When one of these is shaken with solid potassium hydroxide, two liquid phases are formed, the lower of which contains

the larger part of both the water and caustic alkali, and which is discarded before distillation of the alcohol.

For preparation of extremely dry alcohol, see § 115.

QUESTIONS

1. What is the chemistry of the action of the calcium oxide?
2. Why is a water bath used here?
3. Is there any objection to the use of another drying agent? E.g., calcium chloride, sulfuric acid, phosphorus pentoxide, sodium sulfate.
4. Is there any objection, aside from expense, to the use of sodium metal as a dehydrating agent?
5. Why is the process of fractional distillation not adequate to rid the alcohol of water?
6. Why do the earlier fractions of the distillate have a different water content from that distilled later? Explain with the use of a boiling-point diagram.

ALKYL HALIDES

ETHYL IODIDE

$$3C_2H_5OH + PI_3 \rightarrow 3C_2H_5I + P(OH)_3$$

206. This experiment illustrates the general reaction in which hydroxyl is replaced by halogen from the appropriate phosphorus halide. Since ready-made phosphorus iodide is usually not obtainable, a reacting mixture of the less costly free elemental products, phosphorus and iodine, is used here. Red phosphorus is preferred to the extremely active yellow form both for safety and convenience in control of the reaction.

In a 200 cc. round-bottomed flask place 30 cc. of ethyl alcohol and 2.5 g. of red phosphorus. Absolute alcohol is preferable, but 95% alcohol will do. Add gradually, in small portions, 25 g. of iodine crystals. Shake the mixture frequently during the addition, and dip the flask into cold water at times to remove the heat of the reaction and prevent loss of the volatile product by evaporation. As soon as there seems to be no further evolution of heat, stopper the flask tightly and set it away for a day or more.

At the next laboratory hour attach a water-jacketed reflux condenser to the flask, place the outfit over the wire gauze and boil the solution gently for two hours. Now rearrange the apparatus for ordinary distillation, using wire gauze. Use a small flask as receiver and place the vessel in an ice-water bath. Be sure to include a thermometer, since otherwise it will be impossible to tell accurately when the desired product has all been distilled.

Using a small, quiet blue flame, distil the reaction mixture until the rate of distillation slackens and nearly ceases. A slight additional yield of distillate is obtainable if the flame be now played gently over the unprotected bulb for a few seconds. Do not heat the flask strongly, lest trouble be incurred from dark-colored products of decomposition, including iodine, which go over into the receiver and cause difficulties in purification later.

With the aid of a common iron ring, mount a small separatory funnel on a stand, and see that all paper strips are removed from ground glass stoppers and stopcock plug. Treat the latter with a

small quantity of stopcock lubricant. In this funnel place the crude ethyl iodide, and add about 20 to 30 cc. of approximately 1 N NaOH solution. Stopper the funnel, shake a few moments and then allow the two liquids to be separated from each other. Run out the ethyl iodide layer into a small flask, taking care not to let the aqueous wash liquid follow. Now pour out the sodium hydroxide layer from the top of the funnel. Repeat the washing process, using water alone this time. Further details of such processes are given in § 67.

Transfer the colorless product, free as possible from excess of water, to a small conical flask, and add one gram of granular anhydrous calcium chloride. Stopper the flask tightly and allow the preparation to stand until it is dry. (See § 91.)

Place a piece of cotton about the size of a pea in a common funnel. Using this cotton as protection against particles of calcium chloride which might otherwise fall through, pass the dry ethyl iodide into a dry 50 or 100 cc. distilling flask. (Question—Why is it desirable to remove the calcium chloride in this way before final distillation?)

Mount the flask over a water bath, and distil through a water-jacketed condenser into a small flask which rests in an ice-water bath. Preserve the distillate in a tightly stoppered bottle. Boiling point of ethyl iodide, 72°. Upon standing the substance soon turns pink, then amber or brown, due to separation of iodine. A minute globule of mercury kept in the preparation absorbs this iodine and prevents the discoloration.

NOTE. If the fingers should become stained with iodine, wash with sodium thiosulfate solution, which is kept on the laboratory shelf for such purpose. Failure to follow this advice promptly may result in serious irritation of the skin.

OPTIONAL EXPERIMENT

207. Methyl iodide; an extremely volatile liquid (Refs. 13, 19, 20, 23, 30).

QUESTIONS

1. Why should absolute alcohol be preferred in this experiment? What inorganic side-reaction might be promoted if 95% alcohol were used?

2. Why is the side-reaction not considered to be of serious importance?

3. Explain how ether might appear as a by-product in this experiment.

4. Suppose you substituted the very active yellow phosphorus for red phosphorus in order to profit by the greater speed of reaction possible with the former. How would you change the technic, and the apparatus, so as to keep the reaction under control? (See Adams and Voorhees, *Jour. Am. Chem. Soc.*, 41, 789 (1919).)

5. What chemistry is involved in the use of sodium hydroxide to remove free iodine from the crude product?

6. What is the nature of the reaction of iodine with the sodium thiosulfate used to wash stained fingers in this experiment?

7. How do you decide whether phosphorus, iodine or alcohol is the factor upon which to base your calculation of theoretical yield? (See § 156.)

n-BUTYL BROMIDE

$$C_4H_9OH + NaBr + H_2SO_4 \rightarrow C_4H_9Br + NaHSO_4 + H_2O$$

208. When a primary alcohol is heated with hydrogen bromide, the corresponding normal alkyl bromide and water are produced. Concentrated aqueous hydrobromic acid meets the technical requirements in such a reaction, but is expensive. A mixture of sodium or potassium bromide and sulfuric acid serves as an acceptable and economical substitute.

Add 0.6 mole of sodium or potassium bromide and 70 cc. of water to 0.5 mole of *n*-butyl alcohol contained in a 500 cc. round-bottomed flask (or if Pyrex, a Florence flask will do). Attach a water-jacketed reflux condenser as shown in § 24, using a simple wire gauze instead of a water bath as support. Clamp the condenser somewhat loosely so that the flask can be shaken. Introduce in small portions 70 cc. of concentrated sulfuric acid through the top of the condenser. After each addition shake the flask until the portion last added is well mixed with the alcohol and bromide. Carelessness in delaying the actual effective mixing of reagents may precipitate violent boiling later, with possible blow-out of material through the top of the condenser. If the experiment is not conducted in a hood connect the upper end of the condenser by means of a short tube to an inverted funnel whose mouth is placed near but not actually in a quantity of water in a large bottle or beaker like that shown in the figure of § 228. The mixture is now heated gently under reflux for two hours, after which the apparatus is rearranged for ordinary distillation. A ther-

mometer is included, and the mixture distilled over the wire gauze through a water-jacketed condenser. Note the peculiar behavior of the thermometer, and compare its reading with the boiling points of the components of the reaction mixture. (See discussion in § 63.) Distillation is now carried out until only a water-soluble phase seems to be coming over; i.e., no further globules of "oil" are apparent in the condenser. This result is attained usually by the time the temperature has reached 110°.

With the aid of a common iron ring mount a separatory funnel on a ringstand. After seeing that all paper slips are removed from ground glass parts, treat the dry stopcock with a small amount of stopcock lubricant. With the aid of the funnel, separate the crude reaction product, or oil, from the watery portion of the distillate. Which is the butyl bromide layer, upper or lower? Wash the crude butyl bromide successively with dilute (about N) sodium hydroxide, cold concentrated sulfuric acid (25 cc.) and finally with water. The washing operation is conducted by shaking the distillate in each case with the wash liquid in the separatory funnel. (See § 67 for discussion of method of washing.) After each shaking a separation is made and the wash liquid discarded.

Finally shake the product with a few cc. of saturated sodium bicarbonate solution, and run the bromide layer, with careful separation, into a small conical flask where it is to be dried. Add about 3 g. of granular anhydrous calcium chloride, and shake the mixture until the liquid seems to be clear and free from emulsified water. If convenient the mixture may be allowed to stand for several hours or days, during which time it will become clear without the necessity of shaking (see § 91). Now strain the liquid through a piece of cotton about the size of a pea, mounted in a funnel, allowing the liquid to pass into a small distilling flask. Mount this flask upon a wire gauze, attach a water-jacketed condenser and distil.

The liquid boiling between 99° and 103° is substantially *n*-butyl bromide. Boiling point of pure *n*-butyl bromide, 101.6°.

OPTIONAL SYNTHESES

209. Methyl bromide, b. pt. 4.6°. Illustrating preparation of an extremely volatile liquid, condensable in ice-salt mixture, and preserved in a stout-walled sealed vial, which should be tested after com-

pletion under safety precautions; consult the instructor. Methyl bromide may also be used directly as a gas in standard synthetic procedures (Ref. 34).

Ethyl bromide, b. pt. 38°. Readily obtained by the rapid reaction of ethyl alcohol with the bromide-sulfuric acid mixture (Refs. 1, 16, 18, 19, 20, 23, 27, 28, 30, 31, 32, 33).

Amyl bromides—method similar to butyl bromide.

QUESTIONS

1. What is the purpose of the sulfuric acid in this experiment?
2. What difference in method would you think advisable if ethyl bromide were to be made instead of the butyl derivative? If methyl bromide were required?
3. How could you reverse the main reaction of this experiment; i.e., recover *n*-butyl alcohol from the bromide? Devise apparatus for accomplishing this, keeping in mind the physical and chemical properties of the substances involved.
4. What is the purpose of the sulfuric acid used as a washing liquid? Of the sodium hydroxide?
5. Why is the boiling point of the mixture of crude butyl bromide and aqueous residue below 100°, although water (b. pt. 100°) is the lowest-boiling ingredient in the mixture?

tert-BUTYL CHLORIDE

$$(CH_3)_3COH + HCl \rightarrow (CH_3)_3CCl + H_2O$$

210. Replacement of the hydroxyl group is much easier to accomplish in a tertiary aliphatic alcohol than in primary or secondary alcohols. No zinc or phosphorus halides, and not even boiling temperature are required. The halogen acid must however be of high concentration.

In a 200 or 250 cc. separatory funnel place 0.5 mole of *tert*-butyl alcohol of any grade from anhydrous to the 88% constant-boiling aqueous mixture. To this add 1.5 moles (about 130 cc.) of C.P. concentrated hydrochloric acid (sp. gr. 1.19), and at intervals shake the mixture well. After twenty minutes discard the aqueous layer, and wash the remaining layer of crude *tert*-butyl chloride with a 5% solution of sodium bicarbonate. After all acid seems to have been eliminated, wash the product with water until it is neutral to moist litmus paper. Dry the preparation over calcium chloride (about 8 g.) and distil through an effective water-cooled condenser into a receiver cooled with ice. Collect

the fraction boiling at 49° to 52° and preserve in a bottle containing two or three small pieces of anhydrous calcium chloride. Yield, 78–88%.

QUESTIONS

1. What change in technic would be necessary if the *tert*-butyl alcohol were replaced with

   (*a*) *sec*-butyl alcohol?
   (*b*) *n*-butyl alcohol?
   (*c*) methyl alcohol?

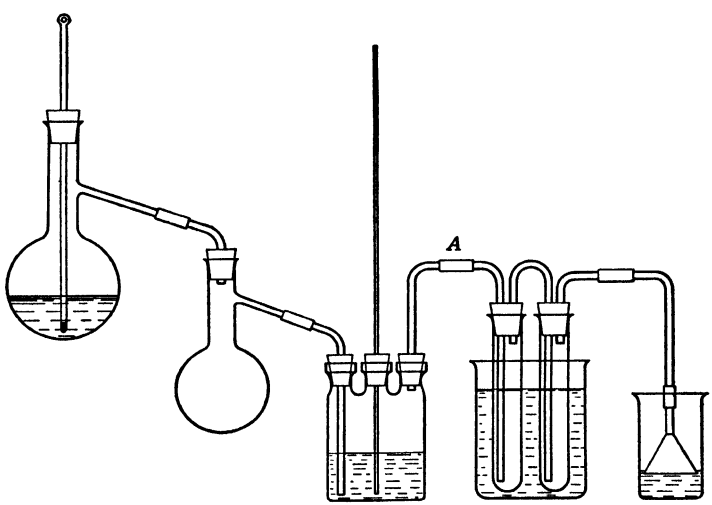
2. Which of three isomeric butyl chlorides would be most easily preserved pure in a moist atmosphere, the primary, secondary or tertiary?

UNSATURATED HYDROCARBONS

ETHYLENE AND ETHYLENE DIBROMIDE

$$C_2H_5OH + H_2SO_4 \rightarrow C_2H_5HSO_4 + H_2O$$
$$C_2H_5HSO_4 \rightarrow C_2H_4 + H_2SO_4$$
$$C_2H_4 + Br_2 \rightarrow C_2H_4Br_2$$

211. The transformation of a simple aliphatic alcohol into its acid-ester (ethyl sulfuric acid) proceeds smoothly with either primary, secondary, or tertiary alcohols. The second reaction, yielding the olefine hydrocarbon, proceeds with greater difficulty in the first case than with either secondary or tertiary alcohols. At the rather high temperature required in the present case, side reactions of oxidation and charring occur, so that the resulting ethylene is not pure. The gas is therefore washed with alkali before it is allowed to react in characteristic manner with bromine.



Arrange the apparatus represented in the above diagram. In this assembly a 1-liter distilling flask delivers its gaseous product, ethylene, into a safety flask of about 500 cc. capacity. Note the unusual position of the thermometer; this is not arranged for a

distillation, but a reaction in which a non-condensing gas is evolved. Interest lies in the temperature of reaction in the liquid phase, not that of a condensation.

The bent inlet tube for the 500 cc. flask should be of a size near to that of the sidestem of the generator flask. The three-necked Woulff bottle is equipped with a small open safety tube about 75 cm. long. If a Woulff bottle is not available, substitute a filter flask with a two-holed rubber stopper fitted to the inlet and safety tubes, or even a 500 cc. conical flask with three-holed stopper. The two 8-inch-test-tubes stand in cold water. Note particularly that the inlet tube in each test-tube reaches almost to the bottom of the vessel. If this precaution be not observed, difficulty will be experienced in getting the dense liquid bromine to diffuse up into the zone of the absorption reaction. A small supply of crushed ice is kept at hand so that the water surrounding the test-tubes may be kept at temperatures in the vicinity of 5° to 15°. It is equally important that the bromine be neither cold nor warm (above 20°). If too cold, it does not react readily and may solidify. Much ethylene is then lost. If too warm, bromine evaporates excessively, causing loss of yield and offensive fumes in the laboratory.

The small amount of noxious vapors which escapes from the last test-tube is caught in a beaker. The funnel should *just touch* the surface of the liquid in the containing vessel. Under such circumstances it will be impossible for the liquid to be sucked back into the bromine tubes in case of reversal of pressure. The addition of ice to the beaker at the right helps in controlling bromine fumes.

Add 150 cc. of concentrated sulfuric acid to 75 cc. of 95% ethyl alcohol in the generator flask, and mix the two thoroughly. Now add 25 to 50 boiling stones (pieces of unglazed clay plate about the size of small wheat grains; see § 175). Place about 100 cc. of 6-normal sodium hydroxide in the Woulff bottle, and 100 cc. of approx. 1-normal sodium hydroxide, or sodium thiosulfate, in the flask or bottle containing the inverted funnel. Connect the whole apparatus tightly, using rubber stoppers and avoiding the use of paraffin sometimes recommended. Now test the apparatus with air or gas to see that there are no leaks.

Go outdoors, or to a hood, place 10 cc. of bromine and about 5 cc. of water in each of the two test-tubes, and connect all parts

again ready for the passage of ethylene gas. (***Warning.***—Bromine is a dangerous reagent, attacking the skin vigorously. If it should be spilled upon the hands, wash the hands at once under the faucet, and treat the wound promptly with sodium thiosulfate (see inside back cover). *Do not take bromine from stock for this experiment unless you are prepared to go ahead with the work at this time.* If bromine be left in the student's locker, there will be evaporation, corrosion of equipment, and an odor nuisance in the laboratory. If the bromine is chilled in ice, or taken just when needed from the refrigerator, it is handled with less discomfort.)

Temporarily disconnect the rubber tube at the point where the ethylene is led into the first bromine tube, as at *A* in the figure. Now heat the generator rapidly until the temperature of the reaction mixture reaches 155°. An active flow of ethylene should now ensue. Keep the temperature between 155° and 175° for three or four minutes, or until the air in the large vessels has largely been replaced by ethylene. This expelled air escapes through the disconnected tube. By not permitting the air to bubble through the bromine unnecessary volatilization of the latter is avoided.

Now reconnect the tube at *A* securely and proceed with the generation of ethylene at 155°–175° as before. Do not delay this proceeding, lest excessive decomposition take place in the generator, but heat effectively, keeping a lively current of ethylene flowing. It may also be observed that the ethylene dissolves in the bromine more freely after the reaction is well started than at the outset. If the evolution of gas ceases, or if you interrupt the heating, disconnect the generator from the safety flask.

After sufficient ethylene has passed to decolorize the bromine in both tubes, stop the generation of gas and transfer the contents of both test-tubes to a separatory funnel which has a properly lubricated stopcock. Wash the crude dibromide first with water. If it is thought that any bromine persists, wash with a few cc. of N/2 sodium bisulfite. Next wash with sodium hydroxide (about N/2) and finally with water again. Separate the product carefully, transfer to a small conical flask, dry over granular anhydrous calcium chloride and distil over the wire gauze. A product of satisfactory quality is distilled over the range of about 127° to 132°. Boiling point of pure ethylene dibromide, 131.7°.

OPTIONAL SYNTHESES

212. Propylene and propylene dibromide. Substitution of isopropyl alcohol for the ethyl alcohol specified above affords interesting advantages and disadvantages. With a secondary alcohol the reaction is more easily carried out, permitting use of 75% sulfuric acid instead of the conc. reagent. Charring is eliminated, and the sodium hydroxide wash (Woulff bottle) is unnecessary. Apparently a very small amount of acetone is produced, however. If unchecked, this compound may react with bromine, yielding the offensive lachrymator bromo-acetone. The sodium hydroxide used in the Woulff bottle is accordingly replaced with sodium bisulfite solution, which dissolves acetone. See the acetone experiment (§ 224) for notes on the purity of commercial isopropyl alcohol.

Ethylene dibromide. A small-scale experiment, economical of time and materials, is given by E. F. Degering, *Jour. Chem. Education*, 13, 377 (1936).

Ethylene glycol (1,2-dihydroxyethane), used in recent years as an anti-freeze for radiators, may be prepared by hydrolysis of ethylene dibromide. (Ref. 23, 25, 31.)

QUESTIONS

1. How do we avoid the production of ether instead of the desired ethylene?
2. What is the purpose of the sodium hydroxide in the Woulff bottle?
3. What undesirable reaction might take place further on if we did not use the sodium hydroxide?
4. What is the nature of the reaction of the ethylene with the bromine?
5. How could you tell that the reaction was not one of substitution?
6. What chemistry is involved in the use of the sodium hydroxide at the end of the apparatus where the waste vapors escape?
7. What other methods could be used to produce the ethylene?
8. What is the purpose of the long "safety" tube?
9. Suppose you desired to prepare hexene instead of ethylene. What changes would you expect to make in the directions?
10. Suppose you substituted a tertiary alcohol for the ethyl alcohol. Would this substitution have any effect on the readiness with which the reaction would take place? What change in the directions would you make?
11. Why does the ethylene dissolve in the bromine more freely after the reaction has proceeded for some time? (See § 118.)

AMYLENE AND ACETYLENE

213. Advantage is taken of the comparative ease with which a tertiary alcohol is converted into the corresponding olefine, as suggested in § 211. Where more than four carbon atoms are present in the molecule, more than one olefine may be derived from a single experiment. The slightly ambiguous commercial name "amylene" is given to the mixture of isomeric pentenes obtained in the reaction described below.

$$(CH_3)_2C_2H_5COH \rightarrow \underset{\text{(presumed intermediate)}}{(CH_3)_2C_2H_5C.HSO_4} \rightarrow (CH_3)_2C{=}CH.CH_3 + CH_3.C_2H_5.C{=}CH_2$$

In the second part of the experiment the well-known calcium salt of acetylene, commercial calcium carbide, is treated with water, which causes rapid hydrolysis and evolution of the gaseous product. Acetylene, a triply bonded compound, is thus regarded as a weak acid, playing a role unusual for a hydrocarbon. For such a role the triple bond alone is not sufficient; there must be at least one hydrogen atom attached to a carbon atom carrying a triple bond.

$$CaC_2 + 2H_2O \rightarrow C_2H_2 + Ca(OH)_2$$

PART 1

214. Amylene. Attach a Hempel fractionating column to a 500 cc. round-bottomed flask, fit a thermometer (110° range) to the top of the column, and connect the delivery tube to a water-jacketed condenser. Inasmuch as the product of this experiment is a very volatile liquid, it is desirable to avoid pouring it out later when a record of yield is to be made. Accordingly, weigh the clean dry receiver (a 100 cc. conical flask) in advance, and set it in a large beaker of crushed ice and water. A bent adapter, attached to the condenser, facilitates passage of the distillate into the receiver with minimum loss.

With stirring, cautiously add 25 cc. of concentrated sulfuric acid to 40 cc. of water in a small beaker. Cool the solution, place in the 200 cc. flask of the apparatus above described, and add 75 cc. of tertiary amyl alcohol.

Heat the reaction mixture gently over the wire gauze. Regulate the heat so that the temperature of the vapors at the top of the column does not exceed 40°. Stop the distillation when no more distillate can be sent over without exceeding this temperature. Remove the receiver, wipe the outside with a towel, weigh,

and calculate the yield of crude amylene. Dry the preparation over anhydrous calcium chloride, using the original conical flask. Stopper the flask securely for use in Part 3 of this assignment.

Part 2

215. Acetylene. Assemble the acetylene generator as described below, but do not proceed to the actual production of the gas until the amylene has been prepared and there is time (one to two hours) to complete the experiment.

Fit a small dropping funnel to a 100 or 125 cc. distilling flask containing about 10 g. of calcium carbide. See that the stopcock is properly lubricated and in good working order. With care slowly drop water from the funnel upon the carbide, thus generating acetylene gas.

Pass the acetylene through a wide-mouthed safety bottle and thence to a pan of water or a pneumatic trough, where it can be collected by downward displacement. Fill a small test-tube, two narrow-mouthed bottles and a wide-mouthed bottle *in the order named,* and proceed to Part 3(*a*) at once.

Part 3. Comparison of Amylene and Acetylene

216. (*a*) *Action on Ammoniacal Cuprous Chloride.* Dissolve 0.5 g. of cuprous chloride in 5 cc. of ammonium hydroxide and dilute to 20 cc. (Be sure to leave the cuprous chloride bottle well stoppered after use, to prevent oxidation.)

(1) Pass acetylene into 10 cc. of the cuprous chloride solution. Collect the precipitate on a Buechner filter (see § 74) and dry it between filter papers. Explode it by heating small pieces in a flame.

(2) Treat about 2 cc. of amylene with cuprous chloride solution. Record results.

(*b*) *Action on Ammoniacal Silver Nitrate.* Add dilute (N) ammonium hydroxide drop by drop to 1 cc. of N/10 silver nitrate solution until the precipitate which forms just redissolves, then add water to bring the volume to 6 cc.

Add one half of the silver solution to a test-tube of acetylene gas, and the other half to a test-tube containing 1 cc. of amylene. Filter; wash and dry any precipitate forming. Explode by heating small pieces in a flame.

NOTE: Before leaving the laboratory, destroy all the remaining silver precipitates and any ammoniacal silver solution by warming the material with dilute hydrochloric acid.

(*c*) *Combustion.* (Out of doors or in a hood.)

(1) Burn 1 cc. of amylene in an evaporating dish.

(2) Ignite the acetylene in the wide-mouthed bottle. Compare the luminosity of the two flames and record any other differences which you observe.

(*d*) *Reaction with Bromine.*

(1) Shake a mixture of 2 cc. of bromine water with 1 cc. of amylene in a test-tube.

(2) Add 2 cc. of bromine water to one of the narrow-mouthed bottles of acetylene and shake. Compare results.

(*e*) *Reaction with Permanganate.*

(1) To the other narrow-mouthed bottle of acetylene add 1 cc. of a very dilute solution of potassium permanganate. Shake well and record results.

(2) Try a similar experiment with amylene.

OPTIONAL SYNTHESIS

217. Butenes. When sec-butyl alcohol is used as a source of an olefine, a mixture of the cis- and trans-isomers of 2-butene is produced. This is an extremely volatile liquid, boiling range approx. 0° to 3° C. If not converted at once into other substances, the butene mixture must be condensed with ice and salt, or solid carbon dioxide, and sealed. (Note precautions mentioned in § 209.)

QUESTIONS

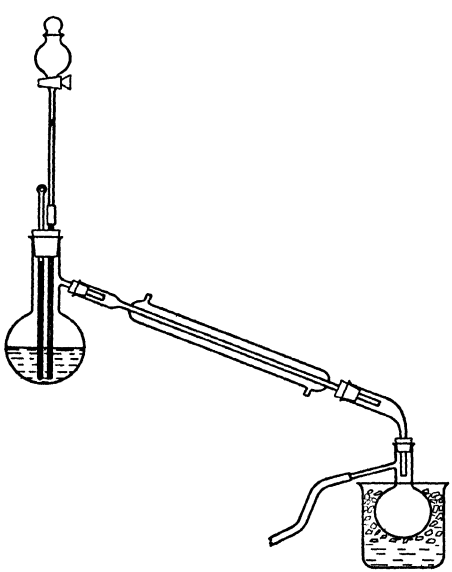
1. From which alcohol may an olefine be most readily prepared—primary, secondary or tertiary?
2. Why do we not purify the amylene chemically as we do ethylene?
3. Give a satisfactory name for each of the isomeric pentenes prepared in this experiment.
4. What isomeric amylene dibromides might be present in the reaction products from amylene and bromine? Which one would likely predominate? Why?
5. Write the equation for the transformation of calcium carbide into acetylene. Does this reaction run to completion? Why?
6. How do you explain the formation of silver acetylide? What is the purpose of the ammonium hydroxide in the experiment?
7. Is the ionization constant of acetylene greater than that of water? How can you tell?

DIETHYL ETHER

$$C_2H_5HSO_4 + C_2H_5OH \rightarrow C_2H_5OC_2H_5 + H_2O$$

218. Ethyl sulfuric acid, prepared in much the same manner as that described in the ethylene experiment (§ 211), is heated with a second equivalent of ethyl alcohol. The temperature is lower than that required for ethylene, and a dialkyl oxide, or ether, is produced.

In a 500 cc. distilling flask place 60 cc. of 95% ethyl alcohol, and slowly add with effective shaking 60 cc. of conc. sulfuric acid. Mount this flask over wire gauze in the manner shown in the accompanying diagram. Attach to it the longest water-cooled condenser available, and place a mixture of ice and salt in the beaker holding the receiver. The receiver should be of about 250 cc. size, preferably with short neck. Attach a high-range (0°–360°) thermometer and dropping funnel as shown, and use a tube of small bore (about 1.5 mm. inside diameter) leading from the delivery tube of the dropping funnel. The restricted bore prevents bubbles from rising in the stem and interfering with the flow of liquid. In the absence of commercial capillary tubing of the bore specified, a substitute may be prepared by drawing down the lower end of a suitable length of heavy-walled 6 or 7 mm. common glass tubing. The rubber tube connected to the receiver hangs over the edge of the desk as a safety precaution (see § 26 (b)).



Heat the reaction mixture to 140° and run into it gradually an additional 125 cc. of ethyl alcohol as fast as the ether collects in the receiver. The temperature should be kept between 140° and 150°. Continue heating for five to ten minutes after the last of the alcohol has been added, but do not allow the temperature to exceed 160°.

With the aid of a common ring, mount a small separatory funnel on a stand, and see that all paper strips are removed from the ground-glass stopper and the stopcock plug. Treat the latter with a small quantity of stopcock lubricant. To this funnel transfer the crude ethereal distillate. Noting the procedures described in § 67, wash the ether first with about 25 cc. of 3N sodium hydroxide, then with about 20 cc. of water, and finally with a volume of saturated calcium chloride solution about equal to that of the remaining ether. Noting methods described in § 91ff., dry the ether over calcium chloride (about 10 g.) for a day or more. Stopper the drying flask securely, since ether is very volatile.

At the next laboratory hour decant the ether from the mass of partially hydrated calcium chloride through a funnel into a small distilling flask. Now mount the distilling flask in a cool water bath, and connect with the water-cooled condenser and receiver in ice, as shown above. Distil the ether with careful attention to fire hazards, collecting the fraction passing over between 33° and 40°. Higher-boiling material contains an excessively large fraction of alcohol. B. pt. of pure ether, 34.5°.

OPTIONAL SYNTHESES

219. *n*-Propyl ether. Analogous preparation, starting with *n*-propyl alcohol.

Unsymmetrical ethers. Ethers in which two different radicals are attached to oxygen are prepared in the laboratory with the aid of an alkyl halide and a sodium alkylate. For example, methyl amyl ethers (Refs. 18, 30), and phenetole, $C_6H_5OC_2H_5$ (Ref. 19).

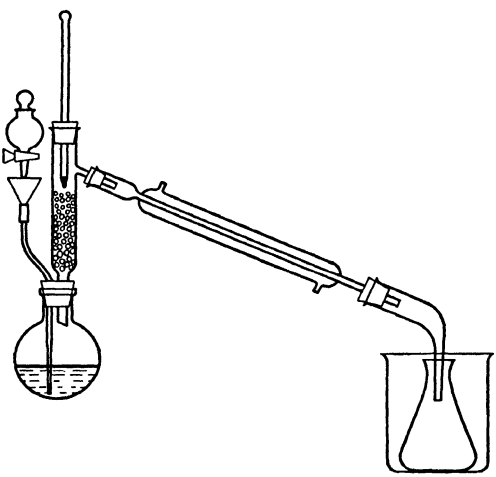
QUESTIONS

1. Which is denser, ether vapor or carbon dioxide?
2. Why is it not satisfactory to use the sulfuric acid process to produce "mixed" or unsymmetrical ethers?
3. Write an equation showing how dimethyl sulfate and an alcohol might be used to prepare an ether.

PROPIONALDEHYDE

Oxidizing and Reducing Agents: $Cr_2O_7^=$ and C_3H_7OH
Reduced and Oxidized Products: Cr^{+++} and C_2H_5CHO

220. The interaction of a primary alcohol, such as *n*-propyl alcohol, with a suitable oxidizing agent such as a chromate, proceeds rapidly provided the acidity of the mixture is high. Accordingly, in this experiment, alcohol, a dichromate and sulfuric acid are mixed. The aldehyde, presumably the first and normal product of oxidation, is then isolated as soon as possible by distillation. In view of the possibility that aldehyde may be oxidized still further, special care is taken in manipulation to reduce that possibility to a minimum.



The whole quantity of alcohol, dichromate and acid should not be mixed in advance, lest a violent reaction take place. It is necessary to make the mixture gradually. On the other hand, any two of the three reagents may be mixed in quantity beforehand without any such violent reaction. It is therefore convenient to mix two, and gradually add the third—or reverse the order of addition. Using the apparatus pictured above, six arrangements are thus possible, as follows:

1. Drop mixture of **alcohol** and **dichromate** into **acid**
2. " " " **alcohol** " **acid** " **dichromate**
3. " " " **dichromate** and **acid** " **alcohol**
4. " **acid** into mixture of **alcohol** and **dichromate**
5. " **dichromate** into mixture of **alcohol** and **acid**
6. " **alcohol** " " " **dichromate** " **acid**

Plan No. 4 is chosen for this experiment. The student should

consider various reasons for selecting or rejecting any or all of the other plans outlined.

Assemble the apparatus as shown above, noting that the funnel is connected as closely as possible by rubber tubing to a piece of 6 mm. glass tubing drawn to a capillary tip about 1 mm. in diameter. The Hempel column should be well filled with beads, and the receiver immersed in a mixture of water and finely crushed ice.

In 200 cc. of water dissolve a quantity of either anhydrous sodium dichromate, or the hydrate ($Na_2Cr_2O_7.2H_2O$), five per cent in excess of the theoretical requirement to convert 0.7 mole of *n*-propyl alcohol into aldehyde. (See § 157 for discussion of method of calculation.) Place this solution in the flask, add to it the 0.7 mole of alcohol and mix thoroughly. Now pour 55 cc. of conc. sulfuric acid into 100 cc. of water in a beaker. Cool the resulting solution and place it in the dropping funnel.

Heat the dichromate-alcohol mixture until it boils, and until the main current of hot vapors reaches the top of the flask; but do not wait until these vapors rise up into the column. Remove the burner, and at once start adding the acid to the mixture in the flask. The acid should drop into the funnel at the rate of about 30 to 40 drops per minute. The resulting oxidation, which proceeds at once, produces so much heat that the volatile product propionaldehyde is at once distilled. The acid should now be introduced just rapidly enough to maintain a steady flow of product without too high a temperature of distillation. The temperature should not exceed 60° at the top of the column while the acid is being added, otherwise an excessive quantity of unchanged alcohol is likely to escape from the reaction zone and contaminate the distillate.

After most of the product has gone over into the receiver the reaction becomes so slow that it is no longer possible to keep up steady production by the use of heat of reaction only. At this juncture apply heat from a burner, but still take care not to exceed the temperature of 60°. Notice that there is a time lag between a change of temperature in the flask and the corresponding effect at the top of the column.

After the acid has all been added, there may still be some aldehyde in the flask. Accordingly continue the distillation, now allowing the temperature to rise slowly to 70°.

Dry the distillate for an hour or more over a suitable neutral drying agent. About 3 to 4 g. of anhydrous magnesium sulfate is suitable. Filter through a very small piece of cotton in a funnel, and distil through the Hempel column into a receiver placed in ice water. The fraction collected below 55° is preserved as the preparation of propionaldehyde (b. pt. when pure 48.8°).

221. Tests. Silver Mirror. A test-tube is thoroughly scrubbed with household washing powder and rinsed with clean water. In this clean, wet test-tube are placed about 10 cc. of dilute (.05 N) silver nitrate, one drop of 6N sodium hydroxide, and enough aqueous ammonia to redissolve the precipitate first formed. If a drop of propionaldehyde is added to this mixture, metallic silver will soon be precipitated. Should the mixture be too warm or too concentrated, the silver will fall as a muddy precipitate all through the solution. If favorable conditions are chosen, a beautiful silver mirror will be deposited on the test-tube. The reaction mixture may require slight warming. After the experiment discard the ammoniacal silver solution at once, as it tends to produce an explosive silver-nitrogen compound. (See also § 252-*b*.)

222. Fehling's Test. Propionaldehyde also gives Fehling's test for aldehydes. A few drops of the aldehyde are heated with a freshly prepared mixture of equal volumes of Fehling's solutions "No. 1" and "No. 2," yielding a bright red precipitate of cuprous oxide. (See also § 252(*c*).)

OPTIONAL SYNTHESES

223. Acetaldehyde. From ethyl alcohol. Since this aldehyde is extremely volatile (b. pt. 21°), it is usually the custom to convert the newly prepared aldehyde vapor directly into the crystalline addition compound with ammonia.

Anhydrous ammonia is desirable for this experiment, which is described in most laboratory manuals.

Benzaldehyde. The simplest aldehyde of the aromatic series; constituent of almond oil. (Refs. 20, 21, 23, 27, 28, 31, 33.)

QUESTIONS

1. Why does not the dichromate oxidize the alcohol without the aid of sulfuric acid?

2. Which of the six plans of admixture of reagents, given in the first part of these directions, do you think to be the worst of the lot? Why?

3. Which do you think would be the best of the plans which were not used; that is, 1, 2, 3, 5 or 6?

4. What reason or reasons might be assigned for the choice of No. 4 instead of the one you selected as your answer to question No. 3 above?

5. Why are such pains taken to have the distillation proceed on prompt and regular schedule?

6. Suppose you wished to prepare *n*-valeraldehyde (pentanoic aldehyde) by an experiment of this type. What new difficulties might arise? (Consider boiling point and solubility relations.)

ACETONE: USE OF THE FRACTIONATING COLUMN

Oxidizing and Reducing Agents: $Cr_2O_7^{=}$ and $CH_3.CHOH.CH_3$
Reduced and Oxidized Products: Cr^{+++} and $CH_3.CO.CH_3$

224. In the presence of strong acid a dichromate will oxidize a secondary alcohol to the corresponding ketone. If care is taken to maintain an excess of alcohol over oxidizing agent during most of the reaction period, oxidation of the ketone itself is largely prevented. In the present case the temperature is kept low until practically all of the alcohol has been consumed, and then only two volatile components remain—ketone and water. A simple distillation yields a mixture of these two free from undesired salts, ready for the principal part of this experiment, viz., the distillation of one particular mixture by two different methods. (See §§ 42 and 56 for theory of these operations.)

To a 700 or 1000 cc. Florence flask containing 25 cc. of water add carefully, with shaking, 50 cc. of conc. sulfuric acid. Cool the flask under the tap; then add 100 cc. of water and one-half mole of isopropyl alcohol. Be careful to note whether anhydrous or aqueous alcohol is furnished. Commercial isopropyl alcohol varies from nearly pure anhydrous material to the constant-boiling aqueous mixture containing approximately 12.5% of water. Make whatever allowance is necessary in your calculations.

Provide an ice bath of size large enough to permit the complete immersion of the body of the flask. This bath should contain at least 500 g. of finely crushed ice, together with enough water to form a thin slush which will readily allow the entrance and removal of the flask from time to time in the later procedures. In a small beaker containing 25 cc. of warm water dissolve that quantity of sodium dichromate (anhydrous or dihydrate) which will be about 5% in excess of the amount required by theory to convert the alcohol into the ketone. For method of calculation see § 157.

A thermometer is now mounted in the flask in a manner so that it is held rigidly, with its bulb in the reaction mixture, but with some arrangement for adding a liquid reagent from time to time.

An old common cork, bored somewhat off center to receive the thermometer, and with one side cut off, will be satisfactory.

Immerse the flask in the ice bath, and add the dichromate solution in from ten to fifteen portions. After each addition shake the vessel momentarily in the open with a gentle rotary motion, and immediately plunge it into the ice bath. If the temperature threatens to rise above 40°, remove the flask from the bath, shake again momentarily and return promptly to the ice bath. As soon as the temperature falls to 25°, add a new portion of dichromate. Do not try to lower the temperature below 25°, lest the oxidation be held up and a large amount of unreacted material accumulate, ready to undergo too vigorous a reaction when the temperature is allowed to rise again. At the end of this operation the color of the mixture should be green, as of chromic salts, possibly with a slight olive or yellowish tint indicating indirectly that no more alcohol is left to react.

When the temperature of the reaction mixture shows no further tendency to rise spontaneously, transfer the material to a 500 cc. distilling flask and add boiling stones. Distil through a water-cooled condenser into a 100 or 125 cc. distilling flask used as receiver. After the temperature of distillation reaches the boiling point of water, continue distilling until about 10 cc. more of liquid comes over at this (constant) temperature. Now discard the dark-colored aqueous residue.

The distillate, obtained as described above, is a mixture of the desired ketone with water. The *entire quantity* of this product is now to be distilled by the simple method (*a*) from an ordinary distilling flask. The product from method (*a*), which is presumably identical with the liquid from which it came, is redistilled by method (*b*), with use of a fractionating column. Since the main purpose of the experiment is to distil identical mixtures by two methods, *no rejection of any part of the boiler contents is permissible in either the* (*a*) *or* (*b*) *procedure.*

Method (*a*). Attach the distilling flask, with its accumulation of crude aqueous acetone and some fresh boiling stones, to the condenser, and provide a bent adapter to convey the new distillate to a 50 or 100 cc. graduated cylinder, which is to be used as receiver. In warm weather it may be well to stand this cylinder in ice water.

Now distil at a steady, uniform rate the entire contents of the

flask, and record in the notebook the *boiling point* and *yield so far collected* at each 2 or 3 cc. interval. In spite of all care, a few drops of less volatile liquid will always be found as a residue in the distilling flask after the apparatus has become cool. Investigate this material, and test your prediction as to its identity. Is it pure water?

Method (*b*). Transfer the distillate in the graduated cylinder to a 200 cc. round-bottomed flask to which is fitted a fractionating column. From this flask and column redistil the aqueous ketone solution slowly (about 2 drops per second) making a record of temperature and yields just as in the previous distillation. There must be no interruption of the distillation while these data are being taken. Watch out particularly for drafts in the laboratory which cause irregular cooling of the column. Any fall in temperature is prima facie evidence that the apparatus is not being manipulated properly.

As the rate of distillation falls, gradually heat the flask more strongly. Soon the temperature will rise suddenly. When it reaches 65°, change receivers. A test-tube or small flask will serve as receiver until the graduated cylinder is again available. Preserve the main distillate as your acetone preparation. Resume the distillation with its accompanying periodic records, and continue until you can get no more liquid to go over into the receiver.

Draw a graph representing the two distillations—with and without the fractionating column. On this graph plot the boiling points as ordinates, and yield in cubic centimeters as abscissas. Either draw this diagram in the notebook, or prepare it on a small piece of cross-section paper and paste it in the notebook.

OPTIONAL SYNTHESES

225. Methyl ethyl ketone. If the isopropyl alcohol of the above experiment is replaced with secondary butyl alcohol (2-butanol), methyl ethyl ketone is produced. The reaction and distillations proceed in similar manner. In this case, however, there is a sharp deviation from Raoult's Law, leading to an interesting example of partial miscibility and a low constant boiling point of the aqueous mixture. (See Marshall, *J. Chem. Soc.*, **89**, 1375 (1906), for particulars.) Incidentally, the slight discoloration often occurring in preparations of this compound is readily eliminated by the addition of 1–2 g. of solid sodium hydroxide to the ketone just before its last distillation.

Diethyl ketone may be prepared in somewhat analogous manner from diethyl carbinol.

Acetone may be prepared by the classical dry-distillation method, employing a salt of acetic acid. (Refs. 20, 21, 23, 30, 31, 33.)

QUESTIONS

1. What is the green substance produced in this reaction?
2. What is the purpose of the sulfuric acid?
3. Why do the distillation curves differ in form?
4. What would be an ideal curve for distillation of this mixture?
5. Suppose an excess of dichromate were added. What new products might then be expected in quantity?
6. What answer would you give to question No. 5 if secondary amyl alcohol (3-pentanol) instead of secondary propyl or butyl had been used?

GLACIAL ACETIC ACID

$$CH_3COONa + H_2SO_4 \rightarrow CH_3COOH + NaHSO_4$$

226. When a strong acid is mixed with the salt of a much weaker acid, the free weak acid is produced. Acetic, propionic, butyric, etc. acids may thus be readily prepared.

In a distilling flask of from 100 to 250 cc. capacity place 40 grams of coarsely powdered anhydrous sodium acetate (see note below). Using a long-stemmed funnel to prevent wetting of the neck of the flask, add cautiously 25 cc. of concentrated sulfuric acid. If the mixture becomes so hot that loss of vapors is threatened, cool the flask in tap water.

Attach a thermometer and water-cooled condenser in the manner customary for distillation, and heat the flask over the wire gauze. The distillate is glacial acetic acid. A very careful worker, using clean apparatus, will obtain a good product directly from this distillation. Often it is necessary to redistil the product. For this purpose a 50 cc. distilling flask is appropriate, or the one first used may be cleaned and dried for the purpose.

(NOTE. Commercial sodium acetate of the so-called "anhydrous" grade always contains more or less water. It may be rendered anhydrous by being heated cautiously in an evaporating dish of ample size, or a clean iron pan. Stir the melted salt until the water vapor has been expelled, but avoid overheating. Allow the mass to cool, and when solid grind in a mortar.)

227. Purity of the Acid. The principal impurity in the acid is water. Inasmuch as water lowers the melting point of acetic acid markedly, a determination of this constant serves as a method of analysis:

Place the whole quantity of acetic acid as prepared above in a clean, dry 8-inch test-tube. (See that the test-tube is well made, with a sound bottom, and is not cracked or in any way likely to break when used in this experiment.) Insert a clean dry thermometer in the acid, and place the outfit in a bath of finely crushed ice and water. If the product contains much water, it will be necessary to add a little salt to the ice.

Stir the acetic acid gently with the thermometer until it freezes. Probably it will be necessary to undercool the liquid many degrees before it will start to crystallize. When crystallization starts, remove the tube from the cooling bath. Continue stirring, and note the temperature when the last few crystals are just about to disappear. This temperature is the so-called "melting point" of the preparation. Consult the table in the Appendix (§ 408) which shows the percentages of acid corresponding to various melting points; also see § 148.

QUESTIONS

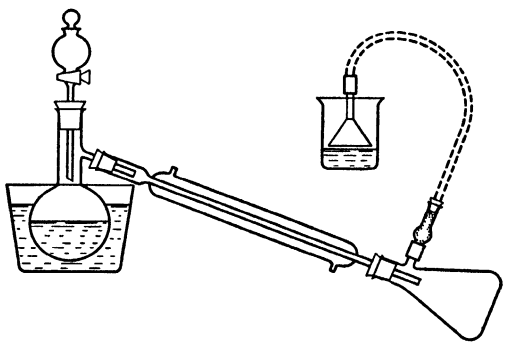
1. What fundamental principle of general chemistry would lead one to expect an acid such as sulfuric to react with the salt of an organic acid? Explain in terms of chemical equilibrium.
2. What change of technic and reagents would you make if you were trying to get oxalic acid from its salt, instead of acetic acid from sodium acetate?
3. At the time when you had part crystals and part liquid during the melting point test, what was the difference in composition between the solid and the liquid?
4. Why do we not record the temperature when melting *starts*, instead of that when it just ends?
5. Why does the melting point of acetic acid fall so rapidly when *water* is added as an impurity?
6. What objection might there be to the substitution of hydrochloric acid for sulfuric acid in this experiment?

ACID DERIVATIVES

ACETYL CHLORIDE

$$PCl_3 + 3CH_3COOH \rightarrow 3CH_3COCl + P(OH)_3$$

228. Either phosphorus trichloride or pentachloride normally converts a carboxylic acid into the corresponding acid chloride. Although much phosphorous acid [$P(OH)_3$, or H_3PO_3] is formed in the case of the trichloride, there may also be produced certain



less hydrated forms of that acid, also mixed anhydrides, as suggested in the experimental directions below. Such by-products are of necessity accompanied by considerable hydrogen chloride, which is absorbed in water so as to prevent a laboratory nuisance.

Arrange apparatus according to the above illustration, including a 500 cc. distilling flask which holds a dropping funnel and is cooled with ordinary faucet water. The condenser is firmly attached to a 500 cc. filter-flask carrying a calcium chloride tube and a funnel which approaches *but does not touch* the solution (1N sodium hydroxide) in the beaker. ***Warning:*** If the solution in the beaker should be permitted to be sucked back into the filter flask, the acetyl chloride will be hydrolyzed so rapidly, and with so much evolution of heat and resulting vapors, that a serious explosion is likely to occur.

Place one mole of glacial acetic acid in the distilling flask, and add, in small portions, 0.4 mole of phosphorus trichloride through

the funnel. Note that phosphorus trichloride is a very offensive substance. Do not pour it out of any vessel except under protection of a hood, or out-of-doors. Be especially careful not to throw either phosphorus or acetyl chloride into a sink in the laboratory.

As soon as the trichloride has all been added to the acetic acid in the flask, gently heat the water bath to 50°. The reaction mixture soon separates into two layers. indicating that the reaction is nearly complete. Continue to hold the temperature at about 50°, if necessary, until the desired separation occurs. Now heat the water to boiling, and distil the crude acetyl chloride until no more liquid passes over. (NOTE. Do not attempt to obtain a larger yield by removing the water bath in order to heat the flask in the open. It is reported that such attempts may lead to the formation of some unknown explosive substance.) Pour out the syrupy residue of phosphorous acid into a bottle provided for the purpose in the laboratory.

Redistil the crude product from the same apparatus, substituting a thermometer for the dropping funnel. Collect the distillate coming over at temperatures below 57°, and preserve it in a glass-stoppered bottle. Neither rubber stoppers nor corks are admissible here. The boiling point of pure acetyl chloride is 52°.

Acetyl chloride made by this method contains a very small amount of some volatile phosphorus compound which causes a white precipitate to appear in the final product after it stands a few days. This volatile compound may be residual phosphorus trichloride, or possibly acetoxy-phosphorus dichloride ($CH_3CO.O.PCl_2$). It is not necessary to remove the white precipitate before practical use of the acetyl chloride preparation.

OPTIONAL SYNTHESES

229. Benzoyl chloride. A valuable laboratory reagent, whose preparation illustrates the use of phosphorus pentachloride instead of trichloride. The experiment also gives a good illustration of fractional distillation of a mixture of two liquids (benzoyl chloride and the by-product phosphorus oxychloride). It should not be attempted without good facilities for ventilation. (Refs. 19, 20, 22, 23, 25, 27, 28, 31, 33.)

***p*-Nitrobenzoyl chloride.** A solid acid chloride. (Refs. 3, 6, 18, 19, 20.)

Conversion of acetyl chloride into an ester. See § 237.

QUESTIONS

1. What products are formed in the possible serious explosion referred to in the description of apparatus given above?
2. Why is "glacial" acetic acid preferred to dilute acid?
3. Why does the product start to boil before its temperature reaches 52°? Why does the boiling temperature rise above 52°?
4. Why do you not dry this preparation with calcium chloride or similar drying agent?
5. Of what practical value is this type of acid derivative?
6. Devise apparatus for the conversion of acetyl chloride into ethyl acetate, knowing that ethyl alcohol and acetyl chloride react with each other vigorously.
7. Can you offer any argument which might reasonably explain why the reaction mixture first exists in one phase, but separates into two phases later on in the experiment? (This question presupposes class discussion on solubility of organic substances.)
8. Why should it be necessary to distil this preparation a second time when it has already been distilled in clean apparatus in the first operation?
9. Suppose you had occasion to prepare both volatile, liquid acid chlorides and involatile, solid acid chlorides. Would these differences have any bearing on your choice of phosphorus pentachloride in some cases instead of trichloride?

ACETIC ANHYDRIDE

$$CH_3COCl + CH_3COONa \rightarrow CH_3CO.O.COCH_3 + NaCl$$

230. Through union of the "acetyl" and "acetate" radicals of the starting materials shown above, an acid anhydride is formed. It is essential not only that the sodium salt be thoroughly dried, but that the acyl halide reagent be allowed adequate time to penetrate the granular solid mass of that salt before final distillation occurs.

The laboratory supply of anhydrous sodium acetate is tested for water content by the heating of a sample in a small test tube. If the material gives off an appreciable amount of water, the quantity to be used in this experiment should be freed from water by the method described in the directions for acetic acid, § 226.

Mount a 500 cc. distilling flask, fitted with a dropping funnel and a water-cooled condenser as shown in § 228, over wire gauze, and provide a 100 or 125 cc. distilling flask as a receiver. Place

one mole of pulverized anhydrous sodium acetate in the distilling flask, and run in slowly 0.6 mole of acetyl chloride. In spite of the most careful control of the reaction the mixture will probably become hot enough to drive over a little unchanged acetyl chloride into the receiver. Such premature distillate should be returned to the distilling flask through the funnel.

With the aid of a stout stirring rod mix the reacting materials as thoroughly as possible. Now replace the dropping funnel with a thermometer and cork, and distil the acetic anhydride with the aid of a large, quiet blue flame played over the bulb of the flask. Care must be taken not to heat the flask to redness at any point. (In eastern laboratories, where domestic gas contains much free hydrogen, particular pains should be taken not to operate the burner at high efficiency. The air ports should be so nearly closed that the flame shows a slightly yellow tinge without being sooty. With natural gas less trouble is encountered. Some writers recommend a yellow flame with a hot-burning fuel such as coal gas.)

Add about 2 to 3 g. of finely powdered sodium acetate to the crude distillate and redistil. Collect that portion of the distillate near to the boiling-point of pure acetic anhydride, 137°. If a large fraction of the product comes over at temperatures much below 137°, add 2 g. more of sodium acetate and redistil. Most of the product should now come over between 133° and 137° and this part is preserved.

OPTIONAL SYNTHESES

231. Benzoic anhydride. (Refs. 3, 6.)
Succinic anhydride. See § 232; also Refs. 12, 24.
Conversion of acetic anhydride into an ester. See § 237.

QUESTIONS

1. What difficulty would arise if the sodium acetate were not dried thoroughly?
2. Why is the boiling range of your preparation likely to run low?
3. What side reaction might take place if you heated the flask too strongly at a point where only sodium acetate was present—the acetyl chloride having been driven away too soon?
4. Write an equation showing how you would convert acetic anhydride into an ester.

SUCCINIC ANHYDRIDE

232. In a 200 cc. flask equipped as shown in the illustration of § 314, place a mixture of 11.8 g. (0.1 mole) of finely divided succinic acid and 12 cc. of acetyl chloride. Reflux on the water bath until active evolution of gaseous hydrogen chloride ceases; then remove the water bath, heat the reaction mixture over wire gauze to expel additional gas, and allow to cool. Without removing the reflux condenser add 70 cc. of chloroform and heat on the water bath until the product has dissolved. Use a few more cc. of chloroform if complete solution is not attained. Allow the solution to cool slowly to about 40°; finally use an ice bath. Filter, wash the crystals with absolute ether and dry the product. M. pt. 119°–20°.

ESTERS OF ACETIC ACID

$$CH_3COOH + ROH \rightarrow CH_3COOR + H_2O$$

233. When acetic acid is heated with an ordinary primary aliphatic alcohol, in the presence of sulfuric acid, the two organic reagents combine, with the elimination of a molecule of water, to form an ester. The reaction runs to equilibrium, and does so in the simple cases chosen in a very short time, ranging from a few seconds to a very few minutes. This equilibrium is discussed in Chap. XIII, which should be read before this experiment is performed.

In the first illustration, § 234, the ester is formed so rapidly and is so volatile that it may be distilled as fast as the reaction mixture is made. In the second case, however, (§ 235) the ester is not sufficiently volatile to permit its distillation directly during the reaction period.

234. Ethyl Acetate. A 500 cc. short-necked, round-bottomed flask is fitted with a doubly-bored cork carrying a bent glass delivery tube (like that of Fig. 1, § 25) and a dropping funnel whose stem reaches almost to the bottom of the flask. The flask is mounted in an oil-bath, and is fitted to a water-cooled condenser leading to an ordinary flask as receiver. (Be sure not to put paraffin or any other petroleum product in the oil bath; see § 23.)

Mount a 360° thermometer so that its bulb is in the oil. Place 30 cc. of 95% ethyl alcohol in the flask, and then add 30 cc. of concentrated sulfuric acid. Heat the oil bath to 140° and start dropping in through the funnel a solution of 90 cc. of ethyl alcohol in 90 cc. of glacial acetic acid. Regulate the rate of addition so that the ester is distilled at the rate of about 5 drops per second

Keep the temperature of the oil as nearly as possible at the 140° mark, letting the regulation of distillation be governed by the dropping funnel. Continue heating for five minutes after the addition is completed.

The distillate contains acetic acid, alcohol and water as impurities. To remove the acid, treat the liquid in an open vessel with 2 N (or 10%) sodium carbonate solution until the upper layer will no longer redden wet blue litmus paper. Now discard the aqueous layer, and wash the ester remaining with 10 cc. of water. Eliminate this portion of wash water carefully, with the aim of the most complete possible riddance of carbonate before calcium ions are encountered in the next operation.

Shake the residue of neutral ester with a saturated solution of calcium chloride. This operation removes the alcohol and much of the water. Discard the calcium chloride layer, dry the ester layer with a small amount of anhydrous magnesium sulfate, and distil. Boiling point of pure ethyl acetate 77°.

235. Propyl, Butyl or Amyl Acetate. In a 200 cc. round-bottomed flask place 0.5 mole of either propyl, butyl or amyl alcohol. Either a normal or iso alcohol is suitable. To the alcohol add 3 cc. of conc. sulfuric acid, and an amount of glacial acetic acid about 20% in excess of theoretical requirements. Heat the mixture under a water-cooled reflux condenser, over wire gauze, for one-half hour.

Transfer the reaction mixture to a distilling flask, and distil until nearly all the liquid has gone over into the flask used as receiver. Treat the distillate with a concentrated solution of sodium carbonate until the ester layer no longer reddens blue litmus paper. It is best to conduct this neutralization in a large vessel on account of the effervescence due to carbon dioxide.

With the aid of a separatory funnel, separate and discard the aqueous layer, and wash the ester with 25 cc. of water. Wash with 50 cc. of saturated calcium chloride solution, and dry in a conical flask over about 6 to 8 grams of anhydrous magnesium sulfate. At the next laboratory hour remove the drying agent, and distil the ester.

OPTIONAL SYNTHESES

236. Ethyl butyrate, propyl propionate, etc. A great variety of aliphatic esters may be made by the general method of § 235.

Ethyl benzoate. Prepared in a similar manner, but requiring more time. (Refs. 18, 20, 21, 22, 23, 25, 28.)

237. Esters from acid derivatives. Acetyl chloride and acetic anhydride are readily converted into their esters by the mere addition, perhaps with gentle heating, of any ordinary primary or secondary alcohol. Such reactions are sometimes too vigorous safely to permit the complete admixture of the reagents all at once. Accordingly, one reagent is placed in a flask under reflux condenser, and the second slowly added.

After selecting a suitable alcohol, work out the details of the proposed experiment and submit them to the instructor for approval. The following problems should be considered:

1. Apparatus; examine diagrams of §§ 24, 304, and 314, and consider possible combinations which will not permit the escape of offensive vapors into the laboratory.
2. Which of the two reagents should be placed first in the flask?
3. Should the quantity of alcohol equal, exceed or fall below the value chemically equivalent to the amount of acid derivative used? (See Chap. XIV.)
4. Which is the safer procedure, to keep the reagent in the flask cool or hot while the addition of the other is taking place?

Methyl salicylate (oil of wintergreen, Refs. 22, 26) and **methyl anthranilate** (Ref. 29), an ester of delightful fragrance much used industrially, require reduced-pressure distillation. The salicylate is somewhat more difficult of preparation than ethyl benzoate, while the anthranilate requires still more skill.

***n*-Butyl-*n*-butyrate.** *n*-Butyl alcohol is simultaneously oxidized and esterified without use of an organic acid provided in advance. (Ref. 5.)

QUESTIONS

1. Explain how continuous distillation (§ 234) affects chemical equilibrium.
2. Why is the acetic acid used in the preparation of ethyl acetate not all consumed, although an excess of alcohol is present?
3. Why is sodium carbonate used instead of sodium hydroxide to get rid of acid impurities?
4. How can a solution of calcium chloride, already fully hydrated, remove water from the crude ester preparation?
5. Why is a second drying operation performed?
6. Outline a laboratory procedure for determining the equilibrium constant of the reactions involved in the preparation of butyl acetate.

HYDROLYSIS OF ESTERS

THE EQUIVALENT WEIGHT OF AN UNKNOWN ESTER

238. The equivalent weight of an ester is that weight in grams of the substance from which one equivalent of acid is obtainable by hydrolysis; or that quantity which reacts with one equivalent of alkali. In practice such an equivalent weight is estimated by treating a known weight of the ester with a known quantity of caustic alkali used in excess. The amount of alkali remaining is then readily determined by titration of the reaction mixture with a standard acid solution. The amount of alkali used by the ester is thus revealed, and with it the chemical equivalent of the ester.

To 150 cc. of 95% ethyl alcohol add approximately 6 cc. (measured in a small graduate) of 50%, carbonate-free potassium hydroxide solution. If potassium hydroxide of suitable purity is not available, substitute 4 cc. of 18 N (approximately saturated) sodium hydroxide solution. Sodium carbonate happens to be insoluble in very concentrated sodium hydroxide solutions, and the difficulties encountered with carbonates in alcohol are thus obviously escaped. Place the resulting alcoholic alkali solution in a bottle or flask, stopper securely and shake well.

Pass a quantity of the alcoholic hydroxide solution through a clean burette and back into the stock bottle; and shake the solution again to ensure mixing with any water which may have been carried down from a newly washed burette. None of the solution is wasted. Now fill the burette to the mark with the alkali solution.

In a very small flask, or a weighing bottle, place a quantity of the unknown ester sufficient for three trials of the experiment. Three grams of material is a suitable amount in the case of an ordinary single substance, 8 grams if it is a true fat (olive oil, tallow, etc.). If the ester is a liquid, place a medicinal eye-dropper along with the sample in the flask. If the ester is a low-melting semi-solid material, like coconut oil or butter-fat, melt it and treat as an ordinary liquid; but go ahead with the work promptly, before resolidification takes place. The eye-dropper

permits a neat transfer of the analytical sample without loss by spilling between weighings. Note that some esters are volatile, so that great care must be taken not to allow a sample to evaporate after weighing. If you have not had a course in quantitative analysis, and do not thoroughly understand the significance of the word "quantitatively" in the next paragraph, make the proper inquiries!

Weigh flask, ester and dropper to 5 mg., using a balance of adequate sensitivity. Transfer quantitatively a sample of suitable size (0.8 to 1.2 g., or 30 to 40 drops, of a pure single ester, 2 to 3 g., or 60 to 100 drops, of a true fat) to a 200 to 500 cc. round-bottomed flask, and weigh the flask with dropper again. Do not use samples exceeding the values recommended, or the experiment may be a total failure. Now run about 49 to 50 cc., quantitatively measured to 0.05 cc., of the alcoholic alkali solution into the flask, and boil the mixture under a reflux condenser for one-half hour or more. Even with high-boiling esters this minimum time allowance will carry the reaction so near to completion that any possible shortage is well within the experimental error of this analytical method.

While the reflux operation takes place, take a clean dry flask to the storeroom to obtain the standard acid whose normal concentration will be reported to you by the storekeeper. After cleaning the second burette, rinse it with about 5 cc. of the standard acid, allowing the rinsings to drain away as thoroughly as possible. Now fill the burette with a fresh supply of the standard acid. Use this set-up to determine the concentration of the alcoholic alkali by titration, with phenolphthalein (5 to 10 drops) as an indicator. The addition of a little distilled water (20 to 30 cc.) to the alcoholic mixture undergoing titration will prevent precipitation of potassium (or sodium) sulfate, and facilitate the process. Record all titration data to the accuracy of 0.05 cc. in the notebook.

At the end of the half hour of refluxing the reaction mixture of ester and alkali may contain a mass of crystalline salt, nearly insoluble in alcohol. Sodium hydroxide is perhaps more likely to offend in this manner than the potassium reagent. It is barely possible, moreover, that the ester of a dibasic acid with a short molecular carbon chain, for example diethyl oxalate, $C_2H_5OOC.COOC_2H_5$, might be only half hydrolyzed, precipitating a mixed half-ester-half-salt, of formula such

as $C_2H_5OOC.COO^-Na^+$. Should such a compound be left in solid form without further treatment, the analysis would be ruined. To avoid such a situation, proceed as follows: As soon as no further separation of the salt seems to be taking place, add through the reflux condenser just enough distilled water so that the crystals will dissolve at boiling temperature; but do not add more than 50 cc. Now reflux for fifteen minutes, and then allow the reaction mixture to cool.

Remove the reflux condenser and add 50 cc. of distilled water if such has not already been included in the mixture, as suggested above. Add 5 to 10 drops of phenolphthalein, and titrate the solution with the standard sulfuric acid without removal from the reaction flask. (Do not interrupt this experiment after the reaction of ester with alkali has been started. If the mixture be allowed to stand until another day, carbon dioxide from the air is likely to enter and react with the residual alkali, thus ruining the determination.)

Make the necessary calculations to show what quantity of alkali was removed by reaction with the ester. From this value calculate the equivalent weight of the ester. If the value so reported does not agree with the character of the sample analyzed, repeat the determination. There should be enough alcoholic standard solution left for one repetition, if care has been taken.

239. If the sample is a fat instead of a single substance of definite composition, calculate its **saponification number**—that is, the number of milligrams of potassium hydroxide required to react with one gram of the fat. The resulting value may be compared with known values given in the appendix (§ 409). In view of the international custom in reporting milligrams of potassium hydroxide, report values in such terms, even though sodium hydroxide may actually have been used.

After the titration is complete, add 2 to 3 cc. of concentrated sulfuric acid to the reaction mixture. A volatile substance of characteristic odor may be apparent, or some liquid or solid may separate from the solution. Determine as closely as possible what this material is, noting question No. 3 below.

In making the written laboratory report of this determination, arrange data in tabular form, and after entering the calculations suggested above, show comparison with the theoretical value calculated from the formula of the ester.

QUESTIONS

1. What is the chemical composition of the mixture just after the reflux operation, but before titration?
2. What is the chemical composition just after titration?
3. What is the composition after the excess of sulfuric acid is added at the end of the experiment?
4. Why is alcohol employed?
5. Why is an oversize weighed sample of ester undesirable in this experiment?
6. Why do we weigh out a specially large sample when a fat is being tested?
7. Of what use might this method of analysis be to the chemist in a soap factory?
8. Glycol ($C_2H_6O_2$) is said to contain two alcoholic hydroxyl groups per molecule. How might you use the above experiment as part of a method of proving that fact?
9. Which substance would have the higher saponification number, glyceryl tributyrate or glyceryl tristearate? Why?

HYDROLYSIS OF AN ESTER AND THE IDENTIFICATION OF THE ACID CONSTITUENT

240. In this assignment either a known or an "unknown" ester is analyzed, according to notice given by the instructor. Esters chosen for the experiment are restricted to (*a*) those which yield crystalline acids of **low solubility,** and (*b*) those belonging to the lower range of simple monobasic fatty acids, which are **volatile.**

Place 40 cc. of 6 N sodium hydroxide and 10 cc. of the ester in a 200 cc. round-bottomed flask. Attach a water-cooled reflux condenser and heat the mixture to boiling. If the ester has not dissolved to a considerable extent in the aqueous hydroxide, cool the mixture slightly and add 30 cc. of ethyl alcohol. Boil the final mixture gently for one-half to one hour.

Remove a 1 cc. sample, and acidify it with dilute hydrochloric acid. Under the specified conditions of the experiment, either of two results should be obtained: (*a*) an immediate precipitate of a solid acid, usually of the aromatic series, in which case proceed as in § 241; or (*b*) a clear solution, inferring the alternative of a volatile aliphatic acid, in which case proceed as in § 242.

241. Solid Acid. Filter the reaction mixture if necessary to remove solid impurities. Acidify the filtrate with hydrochloric

acid, and continue to add acid until a sample of the filtered solution yields no more crystalline organic product upon further acidification. Not more than 25 cc. of conc. hydrochloric acid are required. Cool the mixture, collect the product on a Buechner filter, and recrystallize from boiling water, noting suggestions of § 73.

After the crystals are dry, determine their melting point as described in §§ 191 ff., and find the equivalent weight by titrating two or more one-gram samples with standard alkali solution of about N/2 concentration. For details of such an experiment, see a similar assignment given by Bray and Latimer (*Course in General Chemistry*, Macmillan). If the experiment dealt with an unknown ester, report information to the instructor and draw whatever conclusions are possible.

242. Volatile Acid—Duclaux Analysis. In this procedure the volatile acid is freed from all accompanying substances save only water, and in the process is finally obtained as a dilute solution whose concentration is of the order of 2%. This dilute solution is then distilled into certain arbitrary fractions. Analysis of these fractions (by titration) gives the Duclaux numbers. Read §§ 52–53 before proceeding with the experiment.

Distil the alkaline reaction mixture until about 35 cc. (mostly alcohol) has been expelled. To the residue in the distilling flask add two drops of phenolphthalein and neutralize with 3 N sulfuric acid; then add 10 cc. more of the acid. During this process the flask should be cooled in tap water. Distil the resulting solution into a new receiver until the volume of the residue in the distilling flask has been reduced to 20 cc. Dilute the distillate to a final volume of 250 cc., and mix thoroughly.

By titration find how many cubic centimeters of a given sodium hydroxide solution are required to neutralize 10.00 cc., quantitatively measured, of the diluted distillate just prepared. For this purpose a sodium hydroxide solution of about 0.1 N concentration is suitable; it need not be standardized, but an adequate supply must be available for the titrations to follow.

Place 100 cc. of the diluted distillate, which is actually a dilute solution of the acid under investigation, in a distilling flask and distil three 10 cc. portions at a constant rate, collecting each portion in a 10 cc. graduated cylinder. Titrate each 10 cc. portion with the sodium hydroxide used above. Calculate the per cent

of the total acid which came over in each of the three portions, and compare with the Duclaux constants given in § 52.

QUESTIONS ON §§ 240–241

1. Why is alcohol used in this experiment?
2. What is the chemical composition of the mixture just before the hydrochloric acid is added?
3. What is the chemical principle governing the action of hydrochloric acid in this experiment?
4. Would sulfuric acid be satisfactory here in place of hydrochloric acid? (Consider both theoretical and practical laboratory conditions.)
5. Suppose you had desired to prepare acetic acid (from ethyl acetate) instead of benzoic acid. In what way would you change the procedure? Why?
6. Suppose methyl oxalate were issued as an "unknown" in this experiment. What practical difficulties might arise?

QUESTIONS ON § 242 (Duclaux Analysis)

1. What logical relation might the differences in molecular structure of the acids have to the respective differences in Duclaux constants?
2. Make a reasonable prediction of the magnitude of the Duclaux constants in the series of acids above caproic, as the carbon chains become successively longer.
3. How do you explain the fact that the second and third Duclaux constants of acetic acid are larger than the first, whereas the second and third of butyric acid are smaller?
4. How might the Duclaux method be used to determine the ratio of acetic and propionic acids in a mixture of the two?
5. Show how the Duclaux constants of propionic acid prove that acid and water necessarily form an azeotropic mixture of minimum boiling point.
6. The azeotropic mixture of *n*-butyric acid and water contains more than 2% of butyric acid. Assuming that the table of Duclaux constants (§ 52) applies to 2% solutions, show how the above statement about *n*-butyric acid could be predicted from the tabular values.
7. How could the Duclaux method be used to find the azeotropic composition of propionic or butyric acid?

FATS AND SOAPS

$$C_3H_5(OOC.R)_3 + 3KOH \rightarrow C_3H_5(OH)_3 + 3R.COOK$$

243. Inasmuch as all ordinary fats, including vegetable oils, are the glyceryl esters of fatty acids, a mixture of the potassium

salts of these acids may readily be prepared by alkaline hydrolysis of a fat. The experiment is identical in principle with that of § 238. The carbon chains in these potassium salts are mostly fairly long (6 to 20 or more carbon atoms), and the salts have special colloidal properties resulting in their usefulness as soaps.

In a 200 cc. round-bottomed flask fitted with a water-cooled reflux condenser heat a mixture of 5 g. of solid potassium hydroxide, 75 cc. of alcohol and 5 g. of an animal or vegetable fat (or oil). Different students may well select different types of fat:

(*a*) Suet, tallow, or lard.

(*b*) Butter-fat (butter which has been melted and freed from water and salt).

(*c*) Vegetable oil—cotton, corn, olive, rape-seed, sesame.

(*d*) Cocoanut oil.

(*e*) Drying oil—linseed, fish, poppy seed.

(*f*) Hard-hydrogenated vegetable oil (see § 23).

When the reaction is complete (in not more than one-half hour), no globules of oil are obtainable when a test sample of a few drops is mixed with water.

Distil the reaction mixture, recovering the alcohol, and dissolve the residue in about 50–75 cc. of distilled water.

244. Reactions of a Soap. (*a*) To a 10 cc. sample of the solution add a few drops of calcium chloride solution and shake. Now add a quantity of trisodium phosphate approximately equal to the calcium chloride and shake again. Changes in foaming characteristics are significant here.

(*b*) To a second portion add dilute sulfuric acid, and note the characteristics of the resulting precipitate both at room temperature and at 80° or above. The choice of a particular type of fat is particularly significant in this test. Notice odor, if present.

(*c*) Acidify the rest of the solution with dilute sulfuric acid, and separate the insoluble organic product. Dissolve this in a few cc. of carbon tetrachloride, and add a few drops of a solution of bromine in carbon tetrachloride. Compare with results from the saponification of some other fat.

245. Note. The filtrate from experiment (*c*) contains glycerol, which may be obtained by exactly neutralizing the mixture with sodium carbonate, evaporating to dryness and extracting with absolute alcohol. Evaporation of the alcoholic extract yields glycerol.

OPTIONAL EXPERIMENT

246. Myristic acid ($C_{13}H_{27}COOH$) exists in the form of its glyceryl ester as the main constituent of nutmeg oil. The ester and the free acid are thus obtainable by a process similar in principle to that of § 243 above, illustrating the comparatively rare case where a single fatty acid is obtained directly from its simple natural glyceride. (Ref. 6.)

QUESTIONS

1. Explain the primitive process of boiling slaughter-house fat residues with water which has passed through wood ashes.
2. What everyday situation corresponds to the above experiment with calcium chloride? With trisodium phosphate?
3. Explain why soap might be expected to be useful in cleaning.
4. Soiled clothes are often contaminated with acidic substances. Why does this fact concern the laundry operator?
5. What advantages or disadvantages would you foresee in the application in the soap industry of fats from the six groups, respectively, as cited in § 243 above?
6. Why should butter require more careful handling in storage than olive oil, to be acceptable as food?
7. Devise a laboratory method of distinguishing genuine butter from an imitation made of lard and hydrogenated cottonseed oil.
8. Why is linseed oil superior to corn oil for use in paints?

ALIPHATIC AMIDES

ACETAMIDE AND UREA

$$CH_3COONH_4 \rightarrow CH_3CONH_2 + H_2O$$

247. Simple heating of the ammonium salt of an organic acid frequently causes the substance to be converted into the corresponding amide. Since these ammonium salts are relatively uncommon in trade, they are expensive. It is thus more economical to prepare an ammonium salt at the outset of the amide experiment.

Cautiously mix 0.4 mole of ammonium carbonate (monohydrate) and 1.5 mole of glacial acetic acid in a 200 cc. round-bottomed flask and heat under a water-cooled reflux condenser for an hour or more. After this period replace the condenser with a small fractionating column carrying a thermometer. Place the condenser in position for distillation, and distil very slowly, so that the temperature at the top of the column does not exceed 105°. It will probably take more than an hour to reach the point where no further distillate can be obtained at temperatures near 100°. (If the distillation be conducted rapidly, a low yield of amide will result.) When it is no longer possible to continue distillation at temperatures specified above, heat the flask more strongly and expel as much as possible of the excess acetic acid. The temperature may now rise to 120° or more.

After the low-boiling components have been eliminated as completely as is possible with a column in the line, stop the distillation and cool the residue in the flask. Transfer this residue to a small distilling flask connected to an air-cooled condenser.

The mixture consists largely of acetamide dissolved in acetic acid. Despite the wide spread between the boiling points of the components (over one hundred degrees) it is not as easy to separate the substances as the temperature difference suggests. Fractionation is necessary. Read § 55 before conducting this part of the experiment.

Slowly distil three fractions into three small flasks; the first from the initial boiling point to 195°; the second 195° to 210°, and the

third 210° to the end-point. Return fraction No. 1 to the boiler, and distil therefrom a new low-boiling fraction. No. 3, and possibly No. 2, may have produced crystalline acetamide upon cooling. If so, isolate such crystalline product by filtration, and return mother liquors to the distilling-flask for further fractionation. Assemble all fractional yields of solid or semi solid product on a Buechner filter, press down to eliminate mother liquor as much as possible, and weigh the remainder as a finished product without further attempt to dry. Recrystallize about 2 g. of the material from chloroform or benzene in a test-tube. Filter, press the crystals between filter papers, and determine the melting point. M. pt. of pure acetamide, 81°.

248. Urea. This compound, occurring widespread naturally, may be prepared either from its natural source, the urine, or by the famous Liebig-Wöhler synthesis from ammonium cyanate. While urea, like acetamide, is a typical amide (in this case of carbonic acid) it is also a base of appreciable strength, due to excess of amine groups in the molecule. It can thus form salts in water solution.

249. Reactions of Urea. Dissolve 1 g. of urea in 15 cc. of water and add 4 cc. of conc. nitric acid. Upon cooling, crystals of urea nitrate separate.

Place 2 cc. of dilute sodium hydroxide in each of two test-tubes. To one add a few crystals of ammonium carbonate, to the other a like quantity of urea. Note the odor of each tube. Now warm each mixture gently, and again compare odors. On a basis of this evidence, how might salts and amides be distinguished?

Dissolve about 0.5 g. of urea in 3 cc. of water, and mix this with an alkaline solution of sodium hypobromite, prepared by mixing 5 cc. of bromine water with 5 cc. of dilute sodium hydroxide solution. How might the resulting reaction, yielding gaseous nitrogen, be used as the basis of a method of quantitative analysis for urea?

Cautiously heat about 0.5 g. of urea in a dry test-tube until the melted mass becomes opaque and solid. This product contains the double urea complex **biuret.** Its presence is indicated by the characteristic color exhibited when the material is treated with 5 cc. of dilute sodium hydroxide and a few drops of cupric sulfate solution.

OPTIONAL SYNTHESES

250. Acetamide. This compound may be made directly from ethyl acetate, as illustrated in Refs. 18, 19, 30.

Benzamide. Illustrating the use of an acid chloride and ammonia. (Refs. 21, 23, 25, 27, 28, 30, 31, 33.)

Urea. (Refs. 17, 21, 23, 24, 25, 28, 30, 31, 32.)

QUESTIONS ON ACETAMIDE

1. What is the chemistry of the first reaction in this experiment?
2. Why is the first distillation conducted so slowly?
3. What is the relation of the speed of distillation to chemical equilibrium in this process?
4. How could you transform the product into acetic acid again? Into methylamine?
5. Why do we use ammonium carbonate instead of the cheaper ammonium hydroxide?
6. Acetamide has recently been advertised commercially as a peculiarly effective "universal" solvent. Why would one expect the substance to have the ability of dissolving a great variety of organic compounds?

CARBOHYDRATES

251. If a carbohydrate reduces certain mild oxidizing agents, there is thus revealed the presence of the aldehyde group, or possibly the ketone-alcohol group ($-CHOH-CO-$). Sometimes a failure to react is due to the fact that the aldehyde or ketone groups are blocked in multiple linkages, where two or more sugar groups are combined. Hydrolysis breaks these linkages, and the aldehyde reactions then appear as a signal marking the occurrence of the hydrolysis.

Many sugars are difficult to crystallize and thus identify. Phenylhydrazine is then added to dilute solutions, producing beautifully crystalline derivatives known as osazones, of characteristic form and melting point.

(NOTE. The third part of this experiment (§ 255) involves an interruption and delay of a day or more early in the procedure. Start this part of the work first, and then proceed with the tests below.)

252. Aldehyde Reactions. (*a*) *Use of Fuchsine-Aldehyde (Schiff's) Reagent.* Prepare in (four) separate test-tubes, respectively, a mixture of each of the following with about 3 cc. of water:

glucose (approximately 0.5 gram),
sucrose (approximately 0.5 gram),
starch (approximately 0.5 gram),
formaldehyde (approximately 3 cc. of a 5% solution).

Add to each of the above mixtures 1 cc. of Schiff's reagent and record results after 30 seconds.

(*b*) *Ammoniacal Silver Nitrate Reagent.* (NOTE. Test-tubes used in this experiment should be carefully washed with abrasive washing powder and water and thoroughly rinsed before use.) Prepare ammoniacal silver nitrate solution by adding 0.1 N ammonium hydroxide solution drop by drop to 1 cc. of 0.1 N silver nitrate solution until the precipitate which first forms just redissolves; then dilute to 6 cc. To one cc. of the reagent just prepared add one drop of N sodium hydroxide solution. If a precipitate forms add one drop of the 0.1 N ammonium hydroxide to dissolve it. Add a few drops of 5% formaldehyde, and allow to stand until a reaction takes place.

Repeat this test, only substituting for the formaldehyde 0.1 g. of glucose dissolved in 3 cc. of water. Repeat a second time using sucrose in place of the glucose. If results are not obtained within one hour, heat each of the test tubes nearly to the boiling point.

(*c*) *Fehling's Solution.* Prepare this reagent by mixing just before use 2.5 cc. of "No. 1" with a like volume of "No. 2." To this mixture, which should be of a deep blue color and without a precipitate, add a solution of about 0.2 g. of glucose in 5 cc. of water, and heat the mixture to the boiling point.

Repeat the experiment, using instead of glucose 0.2 g. portions of sucrose and starch, in separate test-tubes.

Dissolve 0.2 g. of sucrose in 5 cc. of water in a test-tube. Add 2 drops of conc. hydrochloric acid, and heat the mixture in boiling water for five minutes. Now neutralize the acid with dilute sodium hydroxide and apply the Fehling's solution test.

253. Hydrolysis of Starch. Grind about 1 g. of starch with 10 cc. of cold water, pour the milky suspension into 200 cc. of boiling water, and set aside to cool. Part of the material will pass into a pseudo-solution which is colloidal in nature. Pour out about 5 cc. of this solution and test with a very dilute solution of iodine in potassium iodide.

Now add 10 cc. of concentrated hydrochloric acid to the remainder of the starch solution, and heat the mixture to boiling. Every five minutes pour out 5 cc. of the boiling solution, cool the sample, divide into two equal portions, and apply the iodine and Fehling's tests, respectively. Discontinue the periodic tests when no further change in results is noted.

254. Identification of an Unknown Sugar. Many sugars may be identified by the length of time they require to form osazones with phenylhydrazine. The times for osazone formation are listed below for several sugars. Perform the following experiment with glucose. If the reaction time agrees with that listed for glucose, repeat the experiment with another sugar. This second sugar will be one from the list given below. It may be either a known compound, or an "unknown" issued individually to the student, according to notice given by the instructor.

Place 0.20 g. of glucose in a test-tube with 0.40 g. of phenylhydrazine hydrochloride, 0.60 g. of sodium acetate and 4 cc. of distilled water. (Weigh these materials on a balance accurate to 0.02 g. or less.) Stopper the test tube with cotton and place it in

a beaker of boiling water. Note the time of immersion and the time when precipitation of the osazone first occurs. Shake the tube occasionally to prevent supersaturation.

(Optional.—A more elegant and trustworthy method of handling this problem would include recrystallization of the osazone and the determination of its melting point. The product may also be compared with known osazones with the aid of a low-powered microscope.)

Approximate Times of Osazone Formation

Mannose	0.5 minute
d-Fructose	2 minutes
d-Glucose	4 to 5 minutes
l-Xylose	7 minutes
l-Arabinose	10 minutes
d-Galactose	10 to 18 minutes
(Sucrose)	30 minutes

Note that the product from mannose is the simple hydrazone, and that from sucrose is merely the one obtained from the products of hydrolysis of the disaccharide. Possible confusion of the osazones from arabinose and galactose may be avoided by noting that the first is an oily product as commonly prepared, whereas that from galactose is crystalline in nature.

255. Action of Acetic Anhydride on a Polysaccharide. *Cellulose Acetate.* In a small conical flask place 0.5 g. of absorbent cotton, 20 cc. of glacial acetic acid, 6 cc. of acetic anhydride and 2 drops of concentrated sulfuric acid. With the aid of a glass stirring rod see that the cotton is well distributed through the mass of the solution, and all air bubbles have been eliminated. Stopper the flask and let stand for 12 hours or more. With stirring pour the reaction mixture in a thin stream into a half liter of water. The cellulose ester should separate out in solid form; collect it on a Buechner filter, wash with water and press the mass between filter papers or upon a porous plate until dry.

Dissolve half of the cellulose acetate in 20 cc. of chloroform contained in a small beaker or test-tube. It may require some time for the material to pass into solution. If the solution is turbid, probably water is present, in which case it should be dried with the aid of a small amount of calcium chloride in the usual way. Pour the dry solution upon a watch glass (out of doors) and let it evaporate slowly. When the chloroform has disappeared, add water, which helps to loosen the cellulose acetate film from the glass. Remove the product and test its inflammability.

OPTIONAL EXPERIMENTS

256. Isolation of Individual Sugars from Natural Sources. Lactose from milk, glucose from sucrose, etc., described in several manuals. (For examples, Refs. 20, 23, 25, 29, 30, 31.)

QUESTIONS

1. How do we explain the fact that glucose resists the action of Schiff's reagent?
2. In the light of question No. 1, how do you explain the other aldehyde reactions?
3. Write the equation for the formation of phenyl glucosazone from glucose and phenylhydrazine.
4. Both glucose and fructose give the same osazone. In what way is this fact useful to us in determining the structures of these sugars?
5. In what way are cellulose and starch related to the simple sugars?
6. Explain why sucrose and starch will react with Fehling's solution after hydrolysis but not before.

AROMATIC NITRO COMPOUNDS

NITROBENZENE

$$C_6H_6 + HNO_3 \rightarrow C_6H_5NO_2 + H_2O$$

257. When an aromatic hydrocarbon is mixed with concentrated nitric acid, it may react almost as though it were an acid, releasing hydrogen atoms; while the nitric acid behaves as though it were a basic hydroxide, each molecule releasing a hydroxyl radical to join with the hydrogen from the hydrocarbon. Water of course is produced; and the hydrocarbon residue unites with the nitric acid residue ($-NO_2$) to form a so-called "nitro" compound. The addition of concentrated sulfuric acid promotes this reaction.

During this process oxides of nitrogen, which are virtually the equivalent of nitrous acid, are formed. The addition of about one gram of urea (carbonic acid amide) to the sulfuric-nitric acid mixture, before the reaction with benzene, destroys the nitrous acid. While not necessary, the urea may thus serve as a preventive of slight discoloration of the nitro product which is later isolated.

Add 50 cc. of concentrated sulfuric acid to 50 cc. of concentrated nitric acid in a large flask, and cool the mixture in running water. Place 0.6 mole of benzene, 1 g. of urea and a thermometer (110° range) in a 500 cc. flask, and add slowly in small portions the acid mixture above prepared. From time to time cool the flask in running water so that the temperature of the reacting mixture ranges from 45° to 50°. *Frequent* and *vigorous* agitation is necessary to permit the acids and the benzene to come into contact with each other and react; otherwise they lie in two layers, one of which may become unduly warmer than the other. After all of the acid has been added to the benzene, hold the reaction mixture, with occasional shaking, at the temperature of 60° for 30 to 40 minutes. A hot water bath, and running water should be at hand for use according to the demands of the situation.

Cool the reaction mixture, then separate and discard the acid layer. Wash the nitrobenzene layer first with 100 cc. of water, and then with a mixture of 5 cc. of the laboratory solution of sodium carbonate and 25 cc. of water. If the mixture, after

thorough shaking, is acid to litmus, repeat the sodium carbonate treatment until a neutral or alkaline test is obtained. Finally wash with 100 cc. of water.

The washed product is likely to contain emulsified water. Remove this by heating gently with anhydrous calcium chloride for a few moments, then cooling the mixture, with shaking, to room temperature. Allow the product to stand with the calcium chloride until it is dry, preferably for several hours or days.

Separate the dry nitrobenzene from the calcium chloride, transfer to a small distilling flask and distil through an air-cooled condenser. Collect the distillate coming over between 200° and 209° (uncor.), and reject the high-boiling residue. Do not attempt to distil a higher-boiling fraction, lest there be a violent decomposition of higher nitro compounds present. If any large residue is left, it is likely that the reaction was allowed to take place at too high a temperature, particularly at first when the acids were at maximum concentration.

OPTIONAL SYNTHESES

258. *m*-Dinitrobenzene. Nitrobenzene is heated with fuming nitric acid, or a mixture of solid sodium nitrate and concentrated sulfuric acid, yielding the solid dinitro derivative. (Refs. 18, 19, 20, 21, 23, 27, 28, 30, 31.)

***o*- and *p*-Nitrophenol.** Nitration of the highly reactive phenol with dilute nitric acid is readily accomplished. The experiment also illustrates separation of ortho and para isomers by steam distillation. (Refs. 20, 21, 23, 25, 27, 28, 30, 31, 33.)

***o*- and *p*-Nitrodiphenyl.** This experiment also illustrates the separation of isomers. (Ref. 22.)

Trinitro compounds. *sym*-Trinitrophenol, picric acid. (Refs. 20, 23, 25, 33.) *sym*-Trinitrotoluene, "TNT." See Hauessermann, C., *J. Chem. Soc. Abstracts*, **64**, 14 (1893).

QUESTIONS

1. Why is the acid added gradually to the benzene, instead of benzene to acid?
2. Why should one be more particular to avoid a high temperature at the start of the reaction than toward the close?
3. Is the correction for exposed stem of the thermometer of great significance here? Why?
4. Suppose (*a*) chlorobenzene, (*b*) benzoic acid, were nitrated instead of benzene. What products would you expect?

DINITRO COMPOUNDS

259. 2,4-Dinitrotoluene. The introduction of a second nitro group into the nucleus of a nitro derivative of benzene is more difficult than the introduction of the original nitro group. Accordingly a more active nitrating reagent, such as fuming nitric acid, is commonly employed. ***Caution.***—Be very careful to keep fuming nitric acid off the skin, as it reacts vigorously and causes stains and serious burns.

In a 250 or 300 cc. flask place 18 g. of fuming nitric acid and 30 g. of conc. sulfuric acid. To these is added gradually in small portions 14 g. of *p*-nitrotoluene. After the addition of each portion cool the reaction mixture by immersing the body of the flask in cold water. After all of the *p*-nitrotoluene has been added, place a small funnel in the mouth of the flask, stem down. In this way undue diffusion of vapors from the flask is discouraged; at the same time the small hole in the stem gives adequate opportunity for release of pressure if any.

Heat the flask and contents in a water bath at about 90° or 95° for thirty minutes, and then cool nearly to room temperature. Now pour the reaction mixture in a fine stream into about 800 cc. of ice water containing a few pieces of ice. The solid which separates is crude 2,4-dinitrotoluene. Collect the product upon the Buechner filter, wash well with cold water and recrystallize from hot methyl alcohol. (***Caution.***—Fire hazard in recrystallization with volatile methyl alcohol, boiling pt. 65°.) Pure 2,4-dinitrotoluene melts at 70.7° C.

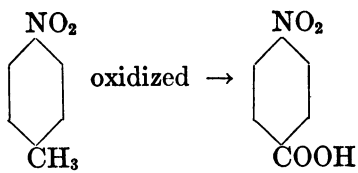
QUESTIONS

1. Why is it better to use *p*-nitrotoluene in this experiment than the cheaper isomer *o*-nitrotoluene?
2. Why not put in both nitro groups at one time, starting with cheap toluene, and using fuming nitric acid?

260. 2,4-Dinitrophenylacetic Acid (Compound used in § 368). In a 200 or 300 cc. flask place 0.5 mole of fuming nitric acid (note § 259), add 50 cc. of conc. sulfuric acid, and insert a thermometer into the mixture. Now add in small portions, with shaking, 0.1 mole of phenylacetic acid, which should not be pulverized. The rate of addition may be as high as possible provided the temperature of the reaction mixture is kept between 60° and 65°, frequent use being made of an ice bath. At the close of the nitration allow

the temperature to mount to 70°, and set the flask aside on the desk for ten minutes. Now pour the reaction mixture (without previous cooling) upon a mixture of about 200 g. of ice and 100 cc. of water in a beaker. Collect the precipitate of crude 2,4-dinitrophenylacetic acid on a Buechner filter, wash it with a little ice water and recrystallize from 650 cc. of water, which has been brought to a boil *before* addition of the organic preparation. (NOTE. This compound should not be heated to temperatures over 80° for any longer than necessary.) It does not have a sharp melting point.

p-NITROBENZOIC ACID



261. Direct oxidation of the methyl group in the molecule of toluene to yield a carboxyl group is difficult in the laboratory. When certain substituent groups are present upon the toluene ring, however, direct oxidation is readily accomplished. In the illustration described below, dichromate ion in the presence of a strong acid is a suitable oxidizing agent for the preparation of *p*-nitrobenzoic acid.

In a 500 cc. round-bottomed flask place 0.1 mole of *p*-nitrotoluene, 48 g. of sodium dichromate (dihydrate), and 60 cc. of water, and attach a water-cooled reflux condenser. Now pour 70 cc. of concentrated sulfuric acid into 35 cc. of water contained in a beaker or flask. Cool the vessel sufficiently so that it may be handled without discomfort, and pour about 30 cc. of the warm, diluted acid through the reflux condenser into the flask. Heat the reaction mixture to boiling, and add about 10 cc. more of acid every minute or two until all is added. Keep the mixture actively boiling during the period of addition, lowering the flame only in case the reaction of oxidation becomes vigorous enough to overtax the capacity of the condenser. In this way a moderated reaction is spread over several minutes; otherwise, without continuous boiling, the oxidation might be concentrated in one period of 30–60 seconds, with attendant flashes of fire inside the flask and boiling over of the contents of the flask. Now reflux the com-

pleted mixture for one half hour. If an appreciable amount of solid *p*-nitrotoluene collects in the condenser, shut off the water supply for a few moments, or until the temperature of the condenser rises above the melting point of *p*-nitrotoluene (51°).

After the reflux period, allow the reaction mixture to become cool. Dilute with 100 cc. of water and filter in the Buechner funnel. Wash the solid product, which is crude *p*-nitrobenzoic acid, upon the filter with 50 to 100 cc. of water, and transfer it to a beaker. Add about 50 cc. of approximately 1N sulfuric acid and 0.5 g. of sodium acid sulfite, and heat the mixture to boiling. This operation extracts possible residues of chromium compounds as soluble chromic sulfate. Now cool the mixture and filter in the Buechner funnel. Wash the solid residue with about 50 cc. of cold water.

Dissolve as much as possible of the solid product in 175 cc. of water to which is added a slight excess of ammonium hydroxide (about 20 to 30 cc. of 6N). Add 1 g. of decolorizing carbon and boil the mixture until the odor of ammonia becomes very faint. Filter, rejecting the solid residue of carbon and unchanged *p*-nitrotoluene. To the hot filtrate slowly add, with stirring, 50 cc. of 6N acetic acid, and allow the solution to stand until cold. Collect the resulting finely crystalline precipitate upon the Buechner filter, and wash it with 50 cc. of cold water. Dry the product for an hour at 100° to 120°. In the absence of a suitable oven, this drying operation may be conducted by spreading the *p*-nitrobenzoic acid crystals over the surface of an evaporating dish resting upon a beaker of boiling water, or even in a dish suspended in an oil bath at properly controlled temperature.

This preparation may be recrystallized from benzene or glacial acetic acid, and will then have a melting point under ordinary laboratory conditions of about 236° (uncor.). A small amount may be sublimed between watch glasses, thus affording a few milligrams of material for melting point test. A slightly higher purity is thus attained.

Potassium permanganate may also be used for this oxidation, as described by Coghill and Sturtevant (Ref. 19).

OPTIONAL SYNTHESES

262. 2,4-Dinitrobenzoic acid. Prepared by a similar method, this compound is valuable as a reagent in qualitative organic analysis. See Buehler and Calfee, *Ind. Eng. Chem. Anal. Edition* **6**, 351 (1934).

***p*-Bromobenzoic acid.** Prepared from *p*-bromotoluene, a product of the Sandmeyer reaction described in § 323. (See Ref. 30.) Similarly, ***o*-chlorobenzoic acid** (Refs. 18, 20) and **terephthalic acid** (Refs. 20, 23, 25, 27, 30).

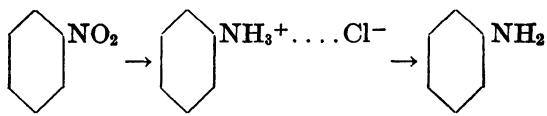
Adipic acid. Cyclohexanol is oxidized with nitric acid. The cycloparaffin ring is broken at the alcohol position, and an open-chain dibasic acid produced (Ref. 5).

QUESTIONS

1. What is the chemical reaction involved in the use of sodium bisulfite with the crude product?
2. If hydrochloric acid is substituted for acetic acid in precipitating the desired preparation, the product comes out as a fine powder instead of the more desirable coarser crystals. Why should this difference in state occur?
3. If the filtrate from the acetic acid reaction is treated with hydrochloric acid, a small additional yield of *p*-nitrobenzoic acid is obtained. Why might this be expected?
4. What conclusion might one draw as to any properties of *p*-nitrobenzoic acid from the fact that this additional yield is actually very small?
5. If the crude nitrobenzoic acid is dissolved in a considerable *excess* of ammonium hydroxide, and the mixture is acidified with acetic acid without prior expulsion of the excess ammonia, little or no precipitate is obtained. Why?

REDUCTION OF A NITRO COMPOUND

ANILINE. *p*-TOLUIDINE



263. When an aromatic nitro compound, such as nitrobenzene or one of the nitrotoluenes, is treated with an active metal such as tin in the presence of hydrochloric acid, the oxygen of the nitro group is replaced with hydrogen. The nitro radical is thus converted into the basic amine group, $-NH_2$. The newly-produced amine immediately unites with excess hydrochloric acid to form the hydrochloride salt; but the addition of alkali, after the main reaction is complete, frees the desired amine, ready for separation and purification.

264. Aniline. To a mixture of 90 g. of granulated ("mossy") tin and 50 g. of nitrobenzene, contained in a 1.5 or 2-liter flask, add slowly in 10 cc. portions 250 cc. of concentrated hydrochloric acid. After the first 20 cc. of acid has been added, attach an air-cooled reflux condenser to the flask and shake the reaction mixture thoroughly during the process. Continue as described in § 266 below.

265. *p*-Toluidine. The procedure is the same as for aniline (above), save that only half quantities of reagents are employed: 45 g. of tin, 25 g. of *p*-nitrotoluene, and 125 cc. of concentrated hydrochloric acid.

266. As the addition of acid continues, the mixture becomes hot and threatens to boil actively. By dipping the flask into a pan of cold water, control the temperature so that there is only a slight ebullition and the mixture is kept just at the boiling point. When the acid has all been added, heat the mixture on a boiling water bath, watching carefully for a few minutes lest the reaction become violent. Great care should be taken that all of the nitro compound is reduced. If any droplets of unreduced material be left on the side walls of the flask, or up in the condenser, they will be carried through the process, and will cause discoloration of the

final product of amine, due to dark-colored addition compounds of amines with nitro derivatives. If only a partial reduction of certain molecules has occurred, azobenzene, azoxybenzene, or the corresponding toluene derivatives may be produced. These are strongly colored yellow or orange substances. The reaction should be allowed to proceed for at least a half hour after all the acid has been added. It may well continue over night or several days if a very light-colored or possibly colorless product is desired.

In case the reaction mixture is allowed to stand for hours and become cool, a large part of the amine, in the form of the hydrochloride, is likely to crystallize with the residual tin chloride as a double salt. No complication is introduced by this occurrence, and the material is treated in the same manner as a fresh solution.

The completely reduced material, still held in the large flask, is placed in apparatus for steam distillation, where the flask rests at an oblique angle as shown in § 29. The whole outfit is assembled and a supply of steam made ready. Do not conduct the next operation unless there is time to complete the steam distillation without interruption.

Prepare a 50% solution of technical granulated or flake sodium hydroxide, using 150 g. of the solid alkali if aniline is being prepared, or 75 g. if *p*-toluidine is to be made. While the alkali solution is still hot (due to evolution of heat of hydration) pour it down the inside wall of the flask gradually and cautiously, in many small portions, with shaking, so that it mixes with the amine hydrochloride reaction product previously prepared. The aromatic amine is immediately freed in the presence of a very hot alkaline solution. In case a fresh, hot amine hydrochloride reaction mixture is employed, so much heat may be liberated that active boiling ensues. Stop this at once by cooling the flask slightly under the tap; otherwise toxic vapors of the aniline or toluidine will escape into the room.

Proceed at once to pass steam through the mixture until the desired product has passed over into the receiver. In the case of *p*-toluidine, which is a solid at room temperature, the preparation may crystallize in the condenser. If this happens, turn off the supply of condenser water, allowing the condenser to get warm and melt the accumulation of toluidine. Subsequent operations with aniline now differ markedly from those with toluidine:

(*a*) Aniline

Saturate the distillate—aniline and water together—with clean, fine granulated or powdered salt, and extract the aniline with a total of 125 cc. of ether, divided into such portions as you think advisable. (See Chap. VI.) Dry the combined ethereal extracts with 6 to 8 g. of coarsely broken pieces of potassium or sodium hydroxide (not powder). After the solution is dry remove the drying agent, taking care to eliminate the few drops of highly concentrated caustic alkali solution which may have been produced.

It is now important to note the difference in technic when diethyl ether has been used, in contrast to that employing di-isopropyl ether. Diethyl ether is dangerously inflammable. Read § 26 carefully before proceeding; then distil the ethereal aniline solution in the appropriate manner until the ether has been removed. The ether so recovered should be placed in a stock bottle or can marked "Recovered Ether," or given to the next student requiring a supply.

After the ether has been expelled, replace the water-cooled condenser with an air-cooled condenser and distil the final product of aniline. If the distillate is of decidedly yellowish-orange color, it may sometimes be improved by redistillation from the same distilling flask in the presence of a pinch of aluminum or zinc dust. Distillation under reduced pressure in the presence of the metallic dust is often effective. In any case, however, the product, even if colorless when freshly prepared, will become dark on standing. Boiling point of aniline 184° (cor.).

(*b*) *p*-Toluidine

If the toluidine, fresh from the steam distillation, is still liquid, cool the receiver with shaking until the preparation crystallizes in leaflets. If the crystals are discolored, they may be returned to the steam apparatus, which in the meantime has been cleaned. About 2 g. of tin and a like quantity of solid sodium hydroxide are added. Upon redistillation in steam the preparation should emerge in snow-white leafy crystals.

The crystals are collected on a Buechner filter, with use of suction (see § 73). After as much water as possible has been removed, the crystals are placed upon a piece of filter paper lying in

an evaporating dish. The dish is loosely covered with paper to exclude dust, and the preparation allowed to dry in an atmosphere free from acid fumes. It is particularly important that oxides of nitrogen, equivalent to nitrous acid, be kept away from an amine preparation.

If the toluidine still has an unsatisfactory color, it may be improved by recrystallization from a considerable quantity of water. Unfortunately the low melting point of the substance is likely to cause trouble to the novice from separation of an "oil"; see § 149.

In view of the fact that toluidine not only has a methyl group in its molecule, but furthermore is solid instead of liquid as with aniline, its solubility in water is low. Wherefore, the ether extraction is omitted.

p-Toluidine reacts readily with acetic anhydride or acetyl chloride to form the toluidide, which may be crystallized neatly from water. See §§ 365–366. Melting point of *p*-toluidine, 44°; of aceto-*p*-toluidide, 151°.

OPTIONAL SYNTHESES

267. *m*-Nitroaniline. Reduction of one of the two nitro groups of a dinitro compound with the aid of a mild reducing agent (sulfide ion). (Refs. 18, 19, 20, 21, 23, 27, 28, 30, 33.)

***p*-Aminodimethylaniline.** A more difficult synthesis, involving reduction of either *p*-nitrosodimethylaniline (§ 342) or methyl orange (§ 331). May be converted into methylene blue. (Refs. 18, 20, 23, 27, 28, 29.)

Ethylaniline. Illustrates the alkylation of aniline upon the nitrogen. (Refs. 24, 30.)

268. Economy of reagents. The preparation of aniline may be conducted with substitution of a mixture of but 10 grams of the expensive tin with 80 grams of mossy zinc, in place of tin alone. The resulting aniline, like that obtained from the directions above, contains a small fraction of *p*-chloroaniline; but the amount of this byproduct is greater than it is when tin alone is employed. Iron may also be used, as described by E. F. Degering, *Jour. Chem. Education*, **13**, 377 (1936).

QUESTIONS

1. Why is it necessary to add sodium hydroxide before steam distillation is carried out?

2. What can you judge of the vapor pressure of aniline, based on your experience in the steam distillation of the substance?

3. Why must nitrous acid vapors be excluded from an amine preparation?

4. Suppose you had used tin and hydrochloric acid in the preparation of an amine which was not volatile in steam, although it was soluble in water. Devise a method of isolating the product.

5. Tin has two valence changes, $Sn \rightarrow Sn^{++} \rightarrow Sn^{++++}$, during the aniline reaction. Why might this be considered favorable in contrast with zinc, which has only one valence change, $Zn \rightarrow Zn^{++}$?

β-PHENYLHYDROXYLAMINE

(Reduction of Nitrobenzene in a Solution of Low Acidity)

$$C_6H_5NO_2 + Zn \xrightarrow{(H_2O)} C_6H_5NHOH + ZnO$$

269. In neutral or nearly neutral aqueous solution, nitrobenzene is reduced by zinc to the aryl hydroxylamine, an unstable compound which should be converted into a derivative at once. In alkaline solution a hydrazobenzene is formed. These variant products are the result of the differing reduction potential of the zinc in solutions of widely different pH value.

In a two-liter flask equipped with a mechanical stirrer and a thermometer, place 12.5 g. of ammonium chloride, 400 cc. of water and 25 g. of nitrobenzene. Stir the mixture vigorously, and add during a fifteen-minute period 40 g. of high grade zinc dust. The addition of zinc dust should be rapid enough so that the temperature rises rapidly to about 55°–60° and remains in this range until the zinc has all been added. When the temperature starts to fall, filter the reaction mixture, and saturate the filtrate with clean common salt. Wash the zinc oxide precipitate with 50 cc. of warm water and treat the washings with salt also, thus getting a small additional yield. β-Phenylhydroxylamine crystallizes in feathery needles, and is collected on filters after the crystallizing mixtures have stood for an hour in the ice bath. Proceed at once to convert the product into whatever secondary preparation is desired.

270. Nitrosobenzene. Dissolve 12 g. of β-phenylhydroxylamine in 300 cc. of ice-cold 6N sulfuric acid contained in a 1.5- or 2-liter flask. Dilute the solution with 500 cc. of ice water, and run in rapidly a solution of 12 g. of sodium dichromate (dihydrate) in 200 cc. of water, with intermittent shaking, and cooling of the flask in an ice bath. Nitrosobenzene is precipitated, collected on

the Buechner funnel, washed with water and distilled in steam. The resulting purified nitrosobenzene, while white or colorless in the solid state, is green when liquid. It may be recrystallized from a very small volume of alcohol. M. pt. 68°.

271. Cupferron. The phenylhydroxylamine may be converted into the valuable analytical reagent ammonium nitrosophenylhydroxylamine ("Cupferron") with the aid of sodium nitrite and hydrochloric acid. (Refs. 4, 23, 28.)

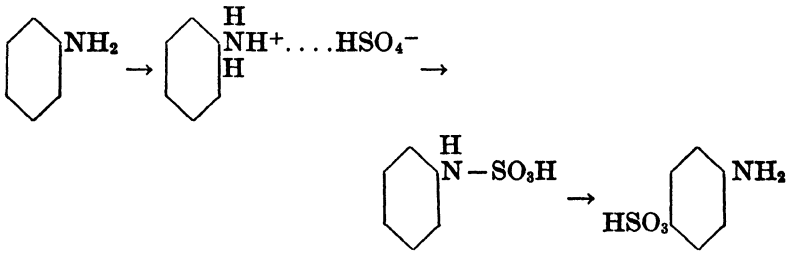
OPTIONAL SYNTHESES

272. Hydrazobenzene. Nitrobenzene is reduced in alkaline solution, using zinc dust. The product may be used in the benzidine rearrangement. (Refs. 18, 20, 21, 23, 25, 27, 28, 32, 33.)

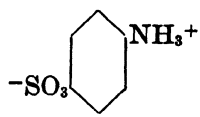
SULFONATION OF AN AROMATIC COMPOUND

273. When an aromatic compound reacts with concentrated sulfuric acid, usually with the aid of heat, an aryl sulfonic acid may be produced. Sometimes the more active fuming sulfuric acid, described in § 405, is necessary to effect substitution of the sulfonic group.

Should the original aromatic compound be an amine, there is first an immediate reaction to form the salt, and then possibly a transformation to the sulfonamide. Strong heating, however, rearranges these intermediate compounds into the sulfonic acid.



Since the resulting product is both basic and acidic, its formula may well be represented as an inner salt:



SULFANILIC ACID

274. When aniline is subjected to the sulfonation reaction the rules of orientation would predict the formation of ortho and para sulfonic acids. At about 180°, however, the ortho-derivative either does not form, or is rearranged and transformed into the para compound. As a result, the single para compound, known to the trade simply as "sulfanilic acid," is obtained.

Place 0.3 mole of freshly-distilled aniline in a 200 cc. flask, using a funnel to avoid wetting of the neck of the flask with the aniline. Remove the funnel, and cautiously add 45 cc. of concentrated sulfuric acid. Heat the mixture in the open flask for 4 to 5 hours in an oil bath, keeping the temperature of the oil between 180° and

190°. The reaction is complete when a sample of one or two drops of the liquid is completely dissolved by 3 to 4 cc. of 2N sodium hydroxide solution.

Pour the cooled reaction mixture, with stirring, into 200 g. of cold water or of crushed ice. Collect the precipitated mass of crude sulfanilic acid upon the Buechner filter, wash with cold water and dissolve in the least possible amount of boiling water. Add 2 to 3 g. of decolorizing carbon to the boiling solution and filter through a fine-grained filter paper upon the Buechner funnel. Upon cooling, the solution deposits crystals which contain one molecule of water of crystallization. Should the temperature of the solution be reduced much below room temperature, however, a dihydrate may also crystallize. The substance does not melt sharply, and no attempt should be made to estimate melting point.

If the product is dark colored (due to carelessness in regulation of the oil-bath temperature), it may often be purified to advantage in alkaline solution, as follows: Dissolve the impure solid in as small an amount as possible of warm 2N sodium hydroxide solution, add decolorizing carbon, boil 3 minutes and filter. To the filtrate then add an amount of concentrated hydrochloric acid slightly more than the quantity chemically equivalent to the sodium hydroxide used. Collect the resulting precipitate on a Buechner filter and recrystallize from the minimum volume of boiling water.

The drying of sulfanilic acid should not be conducted in the open air unless the preparation is taken away from the laboratory, or to a place where there will be no possibility of contact with nitrous vapors. If the moist crystals should be exposed to nitrous vapors (as from nearby work in the nitration of benzene) and then to vapor of aniline or dimethylaniline escaping from a nearby distillation, it is likely that small quantities of a red dye would be produced on the surface of the crystalline product.

p-NITROTOLUENE-*o*-SULFONIC ACID (POTASSIUM SALT)

275. In a 500 cc. flask, suspended in a water bath at room temperature, place 20 g. of *p*-nitrotoluene and 30 cc. of (20%) fuming sulfuric acid, and mix well. After the mixture has stood for 10 minutes, slowly heat the bath to the boiling point. The reaction is complete when 5 drops of the mixture dissolve com-

pletely in about 5 cc. of water. The reaction mixture should not be heated above 100°.

Now pour the mixture into 550 cc. of water. Decolorize the resulting solution with carbon by the standard procedure (§ 88) and neutralize the filtrate by the cautious addition of the requisite quantity of solid potassium carbonate. A change in color from light yellow to brownish marks the neutral point. Heat the resulting mixture until any precipitate dissolves. Upon cooling, the desired potassium salt crystallizes in yellowish brown needles along with a little potassium sulfate. Recrystallize from boiling water. The purified product is light yellow.

OPTIONAL SYNTHESES

276. Benzene sulfonic acid may be prepared by the sulfonation of the hydrocarbon. (Refs. 17, 18, 20, 23, 27, 28, 30, 33.)

***p*-Toluene sulfonic acid.** (Refs. 19, 23, 24, 28, 30.)

***p*-Bromobenzene sulfonic acid** (sodium salt). (Ref. 17.)

DERIVATIVES OF *p*-NITROTOLUENE-*o*-SULFONIC ACID

277. Interesting sequences of preparations may be arranged to follow this sulfonation experiment. The methyl group may be oxidized (see method of § 261), to the carboxyl group, and the nitro group then reduced—or the oxidation step may be omitted. An amine thus prepared is then diazotized and converted into various azo dyes (§ 325) which are acidimetric indicators. Consult Beilstein's *Handbuch* and journals.

QUESTIONS

1. What is the general value of introducing the sulfonic acid radical into an aromatic compound?
2. What is the scientific basis for the test for completeness of reaction given in the sulfonation experiment which you conducted?
3. What effect does the entrance of the sulfonic acid group have upon the strength of aniline as a base?

BROMOBENZENE AND *p*-DIBROMOBENZENE

$C_6H_6 + Br_2 \rightarrow C_6H_5Br$ and $C_6H_4Br_2$ (byproduct, HBr)

278. When an aromatic hydrocarbon is treated with bromine in the presence of a small amount of iron, which virtually means with bromine and ferric bromide, hydrogen is replaced by bromine. In the case of benzene, substantial yields of bromo- and *p*-dibromobenzene are produced, together with minor quantities of ortho and meta derivatives. Apparently the iron is a catalyst.

To a 500 cc. round-bottomed flask, fitted with a doubly-bored cork, attach a dropping funnel and a water-cooled reflux condenser. (If these two pieces should conflict in position, connect the condenser to the flask with an intervening adapter, or use an addition tube, as shown in § 304.) Connect the top of the reflux condenser to an inverted funnel suspended over water in the manner shown in the illustration of § 314. Now place in the flask 0.5 mole of benzene and two or three shingle nails, or 2 to 3 g. of tacks. After special care is taken that the stopcock of the dropping funnel is securely fitted, pour 0.75 mole of chilled bromine, taken from the refrigerator, through a small funnel into the dropping funnel.

Gently heat the benzene nearly to the boiling point, and remove the burner. Start running in the bromine slowly, with constant caution not to allow bromine to leak out at the stopcock. The addition may now be as rapid as possible without excessive ebullition of the reaction mixture.

On account of the great stability of the bromine derivatives of benzene, there need be no fear of interruption of this experiment at any point in the subsequent procedure. If the mixture is allowed to stand for a day or more, the residual bromine will be used up, and thus the next procedures will involve less vapor nuisance.

Wash the crude mixture with several portions of water. Either of two plans of purification may now be followed according to time available. The first (§ 279), involving fractional steam distillation, gives a neater separation of the two desired compounds, but is time-consuming. Otherwise follow § 280. In any case note vapor pressure data in § 410.

279. Fractional Steam Distillation. The crude wet product is steam-distilled from a flask of at least 1½ liters capacity in the manner employed with aniline. As soon as crystals appear in the condenser, change to a second receiver and continue distillation.

The first distillate is mainly bromobenzene with accompanying water. The second is principally *p*-dibromobenzene. Separate the first product, dry over anhydrous calcium chloride, and distil from a small distilling flask, collecting the product coming over between 150° and 160°. Boiling point of pure bromobenzene, 156°. Recrystallize the solid dibromobenzene from ethyl alcohol of 80 to 90% grade. Melting point of *p*-dibromobenzene 89°.

280. Ordinary Fractionation. After thorough washing with water to remove hydrobromic acid, separate the oil and dry over anhydrous calcium chloride, magnesium sulfate or well-dried anhydrous sodium sulfate. Distil the product into four receivers in the manner described in § 55 with the aim of separating the mono- and dibromobenzene fractionally. After repeated distillations nearly all of the final distillate should be found in the first and fourth flasks. The first is of course bromobenzene, the last *p*-dibromobenzene. The fact that the latter is normally a solid may necessitate modification of the ordinary technic of fractional distillation.

OPTIONAL SYNTHESES

281. *p*-Bromoacetanilide. This is prepared by direct bromination. (Refs. 17, 18, 20, 24.)

***m*-Bromobenzoic acid.** A good example of a case where bromination requires an elevated temperature, introducing the technic of conducting a reaction under pressure in a so-called "bomb" of heavy glass tubing. (Refs. 20, 25.)

Iodobenzene. Direct iodination of benzene is practicable only with aid of nitric acid. (Refs. 9, 19.)

QUESTIONS

1. How may a "theoretical yield" be calculated from an experiment such as the preparation of bromo and dibromobenzene?

2. On the basis of the vapor-pressure tables in the Appendix, explain why fractional distillation in steam is more effective here than simple fractionation in the absence of water. Would a change to reduced-pressure technic affect this situation?

See also questions 16–18, page 62.

PHENOL

$$C_6H_5NH_3HSO_4 + NaNO_2 + H_2SO_4 \rightarrow C_6H_5N_2HSO_4 + NaHSO_4 + H_2O$$

$$C_6H_5N_2HSO_4 + H_2O \rightarrow C_6H_5OH + N_2 + H_2SO_4$$

282. The salt of a primary aromatic amine, such as the hydrochloride or sulfate, when mixed at low temperatures with sodium nitrite and a strong inorganic acid, is transformed into the corresponding aryl diazonium salt. When this diazonium salt is heated, nitrogen is evolved and a phenol is produced.

In a 400 cc. beaker place 150 g. of crushed ice and 18 cc. of conc. sulfuric acid; then add with effective stirring 14 g. (0.15 mole) of purified aniline. After the aniline has been added, introduce in small portions, with stirring, 12 g. of sodium nitrite. Now allow the reaction mixture to stand in an ice bath (0 to 3°) for ten minutes; then add 2 g. of urea to remove the excess nitrous acid.

In a 1-liter distilling flask place 300 cc. of water, and add 20 cc. of conc. sulfuric acid. Including this flask, assemble apparatus like that pictured in Fig. 3, § 25, but substitute a dropping funnel for the thermometer shown in that figure. Now heat the sulfuric acid solution to boiling, and pass in the diazonium salt solution through the funnel as fast as is practicable without either causing foam to rise up into the neck of the flask, or overrunning the cooling capacity of the condenser. Keep the mixture actively boiling during the period of addition. Note carefully that the mere evolution of small bubbles of nitrogen gas *is not boiling*. In other words, keep the temperature up in the vicinity of 100° and see that steam is being expelled in quantity into the condenser.

After all of the diazonium salt solution has been added, distil the mixture until 350 to 400 cc. of distillate has been collected. Saturate this distillate with clean common salt, and provide a 200 cc. supply of ether, which is to be used in three portions: first a 100 cc. portion, then two 50 cc. portions. Di-isopropyl ether is preferred on account of both safety and economy, but diethyl ether is satisfactory. See § 68 for discussion of relative merits of ethers.

Warning. Phenol ("carbolic acid") is injurious to the skin, and will cause painful burns. If the substance gets upon the skin, wash at once thoroughly. If irritation develops from exposure to phenol, consult the instructor or a physician.

Following the technic described in § 68, extract the distillate three times, and dry the combined ethereal extracts over anhydrous magnesium sulfate. Now pour about one half of the dried ethereal extract into a 250 cc. distilling flask fitted with a thermometer (high range) and a water-cooled condenser. With the aid of a water bath, distil, and thus recover, as much ether as possible. There will now be room in the distilling flask for the rest of the ethereal extract, which is now added. Distil again until the maximum recovery of ether is accomplished. Now set aside the recovered ether, and expel the residual ether content of the phenol extract with the aid of a flame, in the manner described in § 26. During this procedure the ether is slowly distilled until the temperature shown by the thermometer reaches 170°.

Now replace the water-cooled condenser with one of air-cooled type and distil the residue. The fraction boiling between 176° and 182° is collected as phenol. Boiling point of pure phenol 182°; melting point 41°.

OPTIONAL SYNTHESES

283. β-Naphthol. This analogous derivative of the naphthalene series is usually prepared by the alkaline fusion of a sulfonate instead of the diazo route. (Refs. 20, 21, 23, 24, 25, 27, 28, 33.)

Hydroquinone (*p*-dihydroxybenzene). This valuable photographic developing agent may be prepared by reduction of the corresponding ketone (benzoquinone). (Refs. 20, 23, 25, 27, 28, 31, 33.) The reverse reaction is described in § 299.

Anisole (methyl phenyl ether) may be prepared by methylation of phenol. (Refs. 20, 23, 25, 26, 28, 30, 31.)

Salicylic acid (*o*-hydroxybenzoic acid).—This important industrial product is made by introduction of carbon dioxide into an alkaline phenol mixture. (Refs. 18, 20, 23, 27, 28, 33.)

QUESTIONS

1. Suppose hexylamine were substituted for aniline in this experiment. What difference in behavior of the materials would you expect?

2. What objection would there be to mixing the nitrite and sulfuric acid, and then adding this mixture to the aniline and ice?

3. How could you modify this experiment to prepare bromobenzene instead of phenol?

4. Why does the undissolved phenol in the original reaction distillate remain as a liquid, whereas the melting point of phenol is ten or twenty degrees higher than the temperature of the distillate and receiver?

5. Which do you think could be more easily extracted from aqueous solution, phenol or aniline?

6. Why does benzoic acid dissolve freely in sodium bicarbonate solution, whereas phenol does not? (See § 164.)

7. In the distillation of the original reaction mixture, why does not the volatile component, water (b. pt. 100°), nearly all pass over first, and finally the less volatile component phenol (b. pt. 182°)? (See § 52.)

8. Why is it desirable that the ethereal extract be slowly distilled, instead of rapidly, as the temperature approaches 170°?

BENZOIC ACID AND BENZALDEHYDE FROM TECHNICAL BENZOTRICHLORIDE

$$2C_6H_5CCl_3 + 4Ca(OH)_2 \rightarrow (C_6H_5COO)_2Ca + 3CaCl_2 + 4H_2O$$
$$(C_6H_5COO)_2Ca + 2HCl \rightarrow 2C_6H_5COOH + CaCl_2$$

284. When toluene is chlorinated, as in industrial practice, a substantial part of the hydrocarbon is converted into benzal chloride ($C_6H_5CHCl_2$) and benzotrichloride ($C_6H_5CCl_3$), two liquid substances whose boiling points are close to each other. It becomes difficult to separate the di- and tri-chlorides, so that the common technical preparation of the latter may contain a small fraction of the dichloride. When the technical product is hydrolyzed with the aid of calcium hydroxide, the principal component, benzotrichloride, is converted into calcium benzoate and thence into benzoic acid; while the impurity of dichloride yields benzaldehyde, the small yield of which is merely given a general examination and not preserved.

Go outdoors, or to a hood, and distil about 35 cc. of technical benzotrichloride through an air-cooled condenser, thus eliminating possible tarry impurities. It should be noted that simple, volatile compounds in which a halogen atom is attached to the alpha-carbon atom of an alkylated benzene ring are likely to be offensive to the eyes and nose.

In a 500 cc. ring-necked round-bottomed flask, equipped with a water-cooled reflux condenser, place 24 cc. of the benzotrichloride, 27 g. of calcium hydroxide and 200 cc. of water. Heat the mixture and regulate the flame so that the mixture boils briskly without foaming. At first little or no outside heating will be necessary on account of the evolution of heat in the reaction; but later the flame will have to be increased. After 45 minutes of refluxing, distil the mixture in steam until any possible benzaldehyde has come over with the water. The aldehyde may be recognized by its odor, and by its reaction with bisulfite. If an appreciable quantity has been obtained, isolate it in a separatory funnel and add it to twice its volume of saturated sodium bisulfite solution. The pasty, or semicrystalline material thus produced is the bisulfite addition compound. Purified benzaldehyde is obtainable from this compound (see other laboratory manuals), but in view

of the small amount of available product this part of the experiment is ordinarily omitted.

Filter the mixture remaining in the steam-distillation flask, and wash the residue on the filter with about 25 cc. of hot water, allowing the washings to pass into the filtrate. Now acidify the filtrate with concentrated hydrochloric acid until all benzoate has been converted into free benzoic acid, which is precipitated. Filter on the Buechner funnel, and test the filtrate with additional hydrochloric acid to be sure the reaction is complete. Cool the resulting mixture of solid benzoic acid and calcium chloride solution, and collect and wash the desired product on the Buechner filter. Recrystallize the acid from boiling water. Melting point of pure benzoic acid, 121.7°.

QUESTIONS

1. What difference in behavior would you have expected if the chlorine in the starting material had been on the ring of the molecule instead of the side-chain?

2. How might you use an indicator to tell when a sufficient quantity of hydrochloric acid had been used in the conversion of the benzoate into benzoic acid?

REACTIONS OF BENZALDEHYDE

285. Benzyl Alcohol and Benzoic Acid; the Cannizzaro Reaction. Benzaldehyde, in the presence of concentrated caustic alkali, is transformed by inter-molecular oxidation and reduction into equimolal quantities of the corresponding alcohol and acid. The acid thus produced is of course converted into the alkali salt, from which it is readily recovered.

$$2C_6H_5CHO + NaOH \rightarrow C_6H_5CH_2OH + C_6H_5COONa$$
$$C_6H_5COONa + HCl \rightarrow C_6H_5COOH + NaCl$$

In a 500 cc. flask mix together 40 g. of benzaldehyde, 50 cc. of di-isopropyl ether and 40 cc. of saturated sodium hydroxide solution. Stopper the flask, shake the mixture at intervals during a half hour, and allow to stand for 24 hours or more. Now add just sufficient water to dissolve the sodium benzoate. Separate and preserve the ethereal layer, and extract the aqueous layer with 100 cc. more of the ether, used in three or four portions.

286. Benzoic Acid. Pour the aqueous residue into a beaker containing a mixture of 125 cc. of concentrated hydrochloric acid and about 200 g. of ice. Recrystallize the resulting precipitate from water. Melting point of benzoic acid, 121.7°. Yield about 22 g.

287. Benzyl Alcohol. Wash the combined ethereal extract with about 5 cc. of saturated sodium bisulfite solution, shaking thoroughly. Discard the bisulfite and any crystalline aldehyde-bisulfite compound which may have formed. Now wash the ethereal solution with two 10 cc. portions of N sodium hydroxide and dry it over anhydrous magnesium sulfate. Evaporate the ether, noting particularly § 26. Now distil the residue of crude benzyl alcohol, preserving the fraction boiling between 200° and 206°. Boiling point of pure benzyl alcohol, 205.8°. Yield about 17 g.

288. Benzalacetone; Aldol Condensation. When an aldehyde is mixed with a ketone or aldehyde which has hydrogen attached to its alpha carbon atom, sometimes with mild alkali as a necessary catalyst, one alpha hydrogen atom presumably may migrate to the oxygen atom of the original aldehyde group. The two modified molecules then combine, carbon to carbon, yielding a

substance of the "aldol" type. In the present case the aldol, if existent, is transitory. Presumably it loses water in the following manner, yielding benzalacetone:

$$C_6H_5.CHOH.CH_2.CO.CH_3 \qquad C_6H_5.CH=CH.CO.CH_3 + H_2O$$

In a small flask place 25 g. of benzaldehyde, 50 cc. of acetone and 25 cc. of water. With frequent shaking of the mixture, slowly add (15 to 20 min.) from a dropping funnel 10 cc. of 3 N sodium hydroxide solution, keeping the temperature below 35°. Allow to stand for a day or more. Next day add hydrochloric acid until the mixture is just acid to litmus. Isolate the oily layer, extract the aqueous layer with one 20 cc. portion of chloroform or benzene, and combine the oil and extract. Dry the oil-extract mixture over calcium chloride, transfer to a Claisen flask, evaporate the solvent, and distil under reduced pressure. The fraction distilling at 150° to 160° (30 mm.) is preserved. It should soon crystallize, yielding a slightly yellow product good enough for use in other work. The substance may be redistilled, or recrystallized from a very small volume of light petroleum solvent.

289. Benzoin Condensation. In the presence of an alkali cyanide, which seems to act as a catalyst, benzaldehyde undergoes an inter-molecular reaction. The carbonyl group of one molecule of the aldehyde condenses with the carbonyl group of a second, yielding the keto-alcohol $C_6H_5.CHOH.CO.C_6H_5$, known as **benzoin.** The benzoin, like any typical secondary alcohol, may be oxidized to the ketone, which in this case is of course a double ketone, $C_6H_5CO.CO.C_6H_5$, known as **benzil.**

290. Benzoin. In a 500 cc. round-bottomed flask, equipped with a water-cooled reflux condenser, place a solution of 3 g. of sodium cyanide in 30 cc. of water. Add 30 cc. of acid-free or freshly distilled benzaldehyde and 50 cc. of 95% alcohol. Reflux the mixture from half to three quarters of an hour on the water bath. Upon cooling, crude benzoin crystallizes, and is isolated on the Buechner filter. Wash the product first with a few cc. of alcohol, and then with several portions of water. Benzoin may be recrystallized from alcohol (note fire hazard), but such purification is not necessary in the preparation of benzil.

291. Benzil. In the same apparatus used for the preparation of benzoin place the crude benzoin with three times its weight of

conc. nitric acid (s.g. 1.42). With occasional shaking of the flask, heat the reaction mixture for one to two hours, or until evolution of oxides of nitrogen ceases. This operation should be conducted in a hood, or outdoors, or with protection of a funnel and beaker of alkali as pictured in § 314. (Note carefully the exact position of the funnel; not too deeply immersed.) Now pour the mixture into four or five times its volume of ice water and filter. Wash the yellow precipitate of crude benzil on the Buechner filter. Set aside about one *milligram* (estimated) of this preparation for use as seed crystals, and use the remainder for the subsequent experiment combining recrystallization with test of supersaturation.

292. Supersaturation Phenomena. In a large conical flask (500 to 700 cc.) place the crude benzil and an amount of 95% alcohol at the rate of 6.5 cc. for each gram of benzil used. Dissolve the benzil in the alcohol with the aid of the water bath, being very careful to leave no residual solid in any part of the vessel. Stopper the flask loosely, and set it aside to cool in a place where it will not be disturbed. When the solution has cooled to room temperature, drop in an exceedingly minute particle of solid benzil, taking care not to move or to disturb the flask. Beautiful yellow needles of purified benzil appear, and are eventually isolated and dried. M. pt. of benzil 95°. The velocity of crystallization, form of crystals, etc., may be varied neatly by slight changes in the 6.5 cc. value specified above.

293. Benzilic Acid; a Molecular Rearrangement. When benzil is heated in a solution of potassium hydroxide in dilute alcohol, a phenyl group shifts from one ketone group to the other. A molecule of water is added, and the substance benzilic acid (diphenyl hydroxy acetic acid) is produced in the form of its potassium salt.

$$C_6H_5CO.CO.C_6H_5 \rightarrow (C_6H_5)_2COH.COOK \rightarrow (C_6H_5)_2COH.COOH$$

In a 500 cc. round-bottomed flask, fitted with a reflux condenser, place 20 g. of benzil, 55 cc. of alcohol, 20 g. of solid potassium hydroxide and 40 cc. of water. Reflux on the water bath for fifteen minutes, then pour the mixture into an evaporating dish and allow to stand over night. On a subsequent day filter the mixture and wash the product of potassium benzilate with a little alcohol.

Dissolve the potassium benzilate in the minimum quantity of warm water and filter, using decolorizing carbon if the solution is

turbid and discolored. Acidify the clear filtrate with concentrated hydrochloric acid, isolate the resulting benzilic acid, and recrystallize all or part from water if purification seems desirable.

294. Cinnamic Acid; Perkin Reaction.

$$C_6H_5CHO + CH_3CO.O.COCH_3(+ K_2CO_3 \text{ or } CH_3COOK) \rightarrow C_6H_5CH=CH.COOK,$$

which upon acidification gives cinnamic acid,

$$C_6H_5CH=CH.COOH.$$

In the Perkin synthesis briefly outlined above a two-carbon-atom nucleus (an acetic group) becomes attached to the aldehyde carbon atom of the aromatic reagent, thus producing the three-carbon-atom side chain characteristic of cinnamic acid. The mechanism of this reaction, involving necessary shifts of hydrogen and oxygen atoms, and some disputed theory, is discussed in advanced texts.

In a dry 200 cc. round-bottomed flask place 10 g. of freshly-distilled benzaldehyde, 15 g. of freshly-distilled acetic anhydride (b. pt. 137°), 5 drops of pyridine (as catalyst), and 7.5 g. of thoroughly dried anhydrous potassium carbonate. Attach an air-cooled reflux condenser, on the top of which is mounted a small calcium chloride tube, and mix the reagents thoroughly by shaking.

Cautiously introduce the flask, with attached condenser, into an oil bath heated to 180°. Foaming will now ensue for five minutes or more, due to escaping carbon dioxide. When the foaming has somewhat abated, heat the reaction mixture steadily for one half hour (see note at end of directions) at 180° to 190°. Now cool the flask to 100° or below, and wash the contents out into a beaker with a solution of 45 cc. of 6N sodium hydroxide in 150 cc. of water. Heat the resulting alkaline mixture until all lumps are disintegrated, and cool until the oily matter becomes somewhat solid. Now filter to eliminate the major part of this impurity.

Wash the filtrate with 15–20 cc. of benzene, heat to boiling and decolorize with carbon as described in § 88. To the clarified hot filtrate (80°–90°) add 25 cc. of glacial acetic acid, and wrap the beaker or flask with a towel to encourage slow crystallization. The resulting cinnamic acid may be recrystallized from boiling water. M. pt. 133°.

NOTES. The oily liquid residue above mentioned contains a small amount of cinnamic acid. If heated with boiling water (25 cc.) and decolorizing carbon, a small additional yield is obtained.

Acetic acid is used instead of hydrochloric to give slower crystallization.

Much longer time (three to eight hours) is usually recommended for this synthesis, but with use of sodium acetate instead of potassium carbonate, and without the pyridine. In the potassium carbonate-pyridine method, however, it is doubtful whether much greater yield is obtained by conducting the main reaction more than one half hour. It is suggested that different members of a class test this point, using variations of one half to three hours, and possibly using for the longer time a gradual increase in temperature from some value much below 180° (see directions of Adams and Johnson, Ref. 17).

SUBLIMATION OF SUBSTANCES

295. Hexachloroethane. A 2 g. sample of this compound is placed in an evaporating dish of about 4 inch size. A piece of three-inch filter paper is placed over the substance in the dish, and the whole covered with a watch-glass placed convex side up. The outfit is now placed in a sand bath and heated to a temperature not exceeding 190°, and preferably about 185°, the temperature at which the vapor pressure of hexachloroethane reaches a value near one atmosphere. It should be noted that too much heating of the sand bath will drive the volatile substance entirely out of the apparatus only too easily, so that close attention should be paid to the temperature.

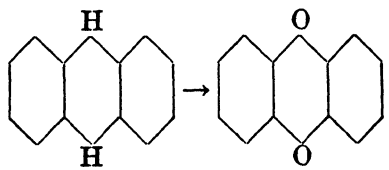
The vapors of the hexachloroethane gradually work their way upward and finally cause an accumulation of sublimate upon the watch-glass. After the transfer from dish to glass seems to be complete, allow the sand bath to cool to about 120° or less. Now remove the dish and lift the watch-glass over to a paper, or dry open dish, and scrape off the crystalline sublimate.

Since the melting point of hexachloroethane is above the true sublimation point, it is necessary to seal a sample in a completely closed tube for a determination of the melting point. If you wish to try this experiment, use only a minute quantity in a micro tube, so that no danger of bursting of apparatus of any size will be possible. For the theory of sublimation, with particular details of the behavior of hexachloroethane, see Chap. X.

296. Anthracene. About 3–4 g. of this hydrocarbon is placed in a 400 cc. beaker which rests upon wire gauze over a stand and burner. The beaker is covered with a piece of stiff card, or asbestos paper, about 15 cm. square, which has a circular opening about 2 to 3 cm. in diameter cut through the middle. A piece of filter paper, slightly oversize, is wedged tightly against the perforated plate of a 3-inch Buechner funnel. The funnel is inverted over the beaker and card, and is connected by rubber hose to the suction service or aspirator. It should be held in position securely with the aid of a clamp.

Apply gentle suction, thus drawing air from the beaker through the paper. Heat the anthracene so that vapors, mixed with air, may pass freely into the funnel which serves as subliming chamber. If the heating be too rapid, vapors pass entirely through the paper, and sublimate gets out into the rubber tube. When little or no more product seems to be accumulating, allow the apparatus to cool, collect the anthracene, and wash out the residue of tarry anthracene with naphtha, benzene, or like solvent mixed with abrasive washing powder.

297. Anthraquinone. The preparation of purified anthracene is suitable for use in a reaction of direct oxidation. Chromic acid attacks the two most central hydrogen atoms, numbered as 9 and 10, replacing them with oxygen. The resulting derivative, anthraquinone, is thus structurally two benzene rings connected by two ketone groups, $C_6H_4-(CO)_2-C_6H_4$.



In a small flask equipped with a reflux condenser place two grams of purified anthracene and 20 cc. of glacial acetic acid. Prepare a solution of 3 g. of chromic anhydride in a mixture of 10 cc. of glacial acetic acid and 10 cc. of water. Heat the anthracene mixture to boiling, and slowly add the chromic solution through the top of the condenser. (If the preparation be attempted on a large scale, a two-necked flask and dropping funnel should be provided.)

Boil the reaction mixture for ten minutes and filter by suction. The solid residue is crude anthraquinone. Wash it with water, dry on a steam bath, or in an oven, or in the open air, and sublime in a manner similar to that employed with anthracene. It is preferable to use a smaller beaker in which to vaporize the anthraquinone.

298. Preparation of Chromic Anhydride. Dissolve 6 g. of sodium dichromate (dihydrate) in 15 cc. of water. To this solution add 25 cc. of concentrated sulfuric acid in a fine stream, with stirring. Cool the mixture to room temperature to permit adequate crystallization. Mount a common conical funnel in a

suction flask, and place in the funnel a piece of glass wool just large enough to block the passage into the stem. Quickly pour out the chromic anhydride mixture upon this funnel, and suck down as much mother liquor as possible. No washing should be attempted.

Without further treatment the crystalline mass of chromic anhydride is used in the oxidation of anthracene. If the work is done carefully the yield will be greater than 3 grams, but the excess will do no harm, and the whole product may be used as described above.

QUESTIONS

1. Why would you expect the middle hydrogen atoms of anthracene to be removed rather than some of the outer ones?
2. Draw a vapor-pressure curve for anthracene based on your observation of its behavior in the laboratory during the process of sublimation.
3. What becomes of the chromic anhydride?
4. Why was glacial acetic acid employed?

STEAM SUBLIMATION

299. Quinone (Benzoquinone). Set up the apparatus for steam distillation as represented in § 29, and place the receiver in an ice bath, required on account of the volatility and offensive character of quinone. In the steam-flask mix 11 g. of hydroquinone, 50 cc. of water, and 9 cc. of conc. sulfuric acid. It is not necessary to dissolve the hydroquinone. When the outfit is all ready, with supplies of steam and ice at hand, introduce into the steam flask 14 g. of powdered manganese dioxide. Mix quickly and thoroughly, complete assemblage of apparatus and pass steam through the reaction mixture. Watch the distillation closely, as the accumulation of solid quinone may tend to clog the condenser. In the latter event allow the water to run out of the condenser, so that the quinone may melt and run into the receiver. When the aqueous distillate coming into the receiver becomes colorless, the operation is complete.

Collect the yellow quinone crystals on the Buechner filter and dry. No recrystallization is necessary. Yield 8–8.5 g. M. pt. of pure quinone 115.7°. Preserve in a dark container, such as a brown bottle.

300. Quinhydrone. Quinone and hydroquinone combine instantly, mole for mole, at ordinary temperatures to form the addition compound quinhydrone ($O=C_6H_4=O\cdots\cdots HOC_6H_4OH$). This substance is a valuable reagent in potentiometric analysis.

Dissolve 0.5 g. of hydroquinone in 30 cc. of lukewarm water (30°–40°) in a small beaker or flask. Into this solution pour with stirring a solution of 0.5 g. of quinone (approximately an equimolal quantity) in 8–10 cc. of ethyl alcohol. Allow to stand in a cool place without further agitation. Shiny, greenish-black crystals of quinhydrone separate. Collect on a filter, wash rapidly with a little cold water, and dry. Do not attempt to recrystallize, as partial decomposition, difficult to detect, may occur.

If one wishes to prepare quinhydrone in quantity with economy of effort, it is best to add to a solution of commercial hydroquinone just half of the amount of a suitable mild oxidizing agent (ferric ion) required to produce quinone. Quinhydrone then crystallizes directly. The method of preparation, including the problem of impurities, is discussed by W. Mansfield Clark, *The Determination of Hydrogen Ions*, Third Edition, page 410, The Williams and Wilkins Company, Baltimore (1928).

CONDENSATIONS WITH ALKYL AND ARYL HALIDES

301. Wurtz Reaction. The reaction of an alkyl halide with metallic sodium normally causes the formation of a paraffin hydrocarbon by the combination of alkyl radicals, with elimination of a sodium halide as a by-product.

$$2RBr + 2Na \rightarrow R-R + 2NaBr$$

302. *n*-Octane. Purified *n*-butyl bromide should be provided for this synthesis. For this purpose a crude technical or student preparation of the bromide (about 100 cc.) should be washed successively with 25 cc. portions of water, concentrated sulfuric acid (two portions), 3N sodium hydroxide, saturated sodium bicarbonate, and water again. The washed butyl bromide is dried over calcium chloride or magnesium sulfate and distilled.

Fit a 200 cc. round-bottomed flask with a water-cooled reflux condenser. In the top of the condenser place a two-holed stopper holding a small dropping funnel and a small glass L-tube connected with a calcium chloride tube. Place in the flask 14 g. of clean sodium metal which has been cut into small cube-like fragments. Now pass through the funnel 50 cc. of pure *n*-butyl bromide at a rate of 20 to 60 drops per minute. Too rapid addition of the bromide might cause dangerously high temperatures. It is necessary to shake the flask vigorously from time to time (with aid of a loose adjustment of a swiveled condenser clamp), and occasionally to cool the mixture in an ice bath. Finally heat the reaction mixture for an hour on the water bath, and distil the crude octane from an oil bath until no more product can be obtained even when the bath temperature is finally elevated to 170°. Note precautions described below in disposal of waste sodium.

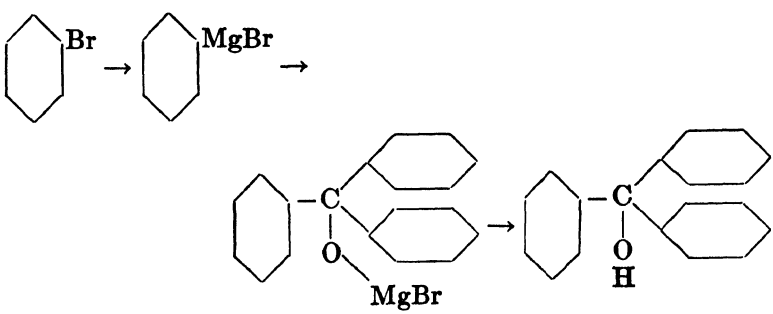
Test the crude octane for organic bromide, using suggestions from the latter part of § 392. (If such bromide is still present, reflux the crude octane with a few pieces of sodium until a negative test is obtained.) When no more halide remains, new pieces of sodium no longer turn blue when introduced into the octane. Now decant the octane from the blue residue, and treat the latter

with the minimum quantity of 95% alcohol needed to react with all of the sodium. After all of the sodium is gone, add 25 cc. of water, and combine the resulting two-phase liquid mixture with the main quantity of octane previously set aside.

Separate the octane layer, and wash with successive 25 cc. portions of conc. sulfuric acid (two portions), water, sodium carbonate solution (about N), and water again. Dry over magnesium sulfate or calcium chloride and distil. B. pt. of pure octane 125.5°.

303. Disposal of Waste Sodium. Any remnants of alkali material containing possible metallic sodium should be treated with 95% alcohol until the metal has disappeared. Never throw sodium wastes into sinks or water, lest there be a dangerous explosion.

304. Triphenyl Carbinol; Grignard Reaction. By the interaction of metallic magnesium with bromobenzene in the presence of a very weakly basic solvent such as ether, magnesium phenyl bromide, a "Grignard reagent," is formed. This reagent is then mixed with its molar equivalent of an appropriate compound containing the carbonyl group, such as benzophenone. Hydrolysis of the resulting intermediate product then yields triphenyl carbinol.



Ethyl benzoate (one half molar equivalent) may be substituted for the benzophenone, giving the same ultimate product. While slightly more complex in graphic representation, this optional method gives a preparation which may be somewhat easier to purify, and is accordingly employed below.

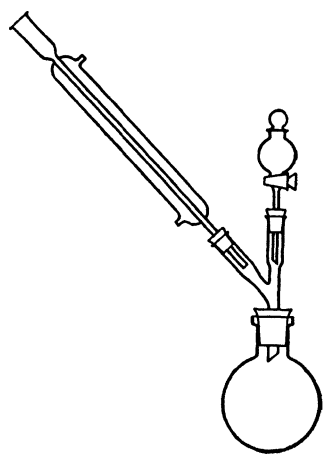
All apparatus as well as materials must be thoroughly dry before a Grignard synthesis is attempted. First prepare a supply of dry diethyl ether as follows: Wash 200 cc. of commercial ether with two 10–15 cc. portions of water and three 25 cc. portions

of saturated calcium chloride solution. Now add about 15 g. of granular anhydrous calcium chloride and set aside for a day or more in a well-stoppered vessel.

At this point either phosphorus pentoxide, or freshly prepared metallic sodium wire, may be used to complete the drying process. Although the sodium method gives very satisfactory results, serious accidents have occurred with careless handling, and the pentoxide method is recommended here. See earlier manuals for details of the sodium method.

After removing the solid calcium chloride from the partially dried ether, weigh rapidly 10–12 g. of phosphorus pentoxide and introduce it at once into the ether. Mix well and distil into a dry receiver protected as in Fig. 1, § 25. Di-isopropyl ether is not suitable for use in this experiment without special purification.

Using clean dry corks, attach a long water-cooled reflux condenser and a small dropping funnel to a 500 cc. round-bottomed flask. If the air is humid, protect the condenser with a calcium chloride tube. If the Y-shaped addition tube shown in the illustration is not available, mount the funnel in the top of the condenser. Place in the flask 0.16 gram-atom (3.9 g.) of freshly-cut magnesium turnings, about 15 cc. of the ether, and a small crystal of iodine, used as catalyst. Also provide an ice bath suitable for cooling the flask when necessary. Now weigh out 0.17 mole of bromobenzene, and add through the dropping funnel about 4 cc. of this halide directly to the reaction mixture in the flask. With a water bath heat the ether to the boiling point. When the reaction is well started, as evidenced by bubbling of the liquid without aid of external heat, and change of color to a grayish black, add 70 cc. more of the dry ether. Now add through the funnel the rest of the bromobenzene at a rate slow enough so that the condenser can readily take care of the expelled ether. Reflux the final completed mixture for one half hour.



Dissolve 0.08 mole of ethyl benzoate in the balance of the ether (about 35 cc.). Pass this solution gradually into the Grignard reagent in a manner similar to the addition of the bromobenzene. Before starting the hydrolysis, be sure that the slightly viscous reaction product is thoroughly mixed. After allowing the mixture to stand for one half hour, pour it into a flask in which have been placed 100 g. of ice, 150 cc. of water, and 10–12 g. of conc. sulfuric acid. Stir so that the Grignard complex will be completely disintegrated, and the resulting triphenyl carbinol dissolved in the ether. Add more (ordinary) ether if necessary to dissolve the product. Separate the ethereal solution and wash with two 25 cc. portions of 2 to 3 normal sulfuric acid.

Set up the standard outfit for steam distillation (§ 29), and place the ethereal solution of crude triphenyl carbinol in the main flask. With the aid of a water bath distil the ether, and then pass steam through the residue to carry out any volatile residues of the raw materials employed. Recrystallize the solid product from ethyl alcohol.

NOTE. In some cases, usually with other halides, the reaction with magnesium is difficult to start, even with the aid of iodine. See Fieser (Ref. 24) for a discussion of other methods.

OPTIONAL SYNTHESES

305. Triphenyl carbinol may also be prepared from benzophenone. Use the above directions, substituting 0.16 mole of benzophenone for the 0.08 mole of ethyl benzoate called for above. Additional ether may also be required to dissolve the benzophenone.

Ethyl dimethyl carbinol is prepared from ethyl bromide or iodide and acetone. (Ref. 26.)

Acids may be prepared by the novel method of introducing solid carbon dioxide ("Dry-Ice") into a Grignard reagent. (Ref. 24.)

Substitution of other halides for the bromobenzene specified above may be made, but should not be made indiscriminately. Many Grignard reagents do not behave in the conventional manner, and side reactions prevail. Illustrations of both practical and impractical modifications of this experiment are given by Kharasch and Weinhouse, *Jour. Organic Chem.*, 1, 209 (1936).

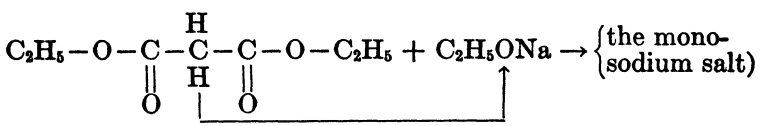
Mechanical stirring is often of advantage in the performance of a Grignard synthesis. If the proper equipment is available, therefore, the complete assembly of three-necked flask, mercury-sealed

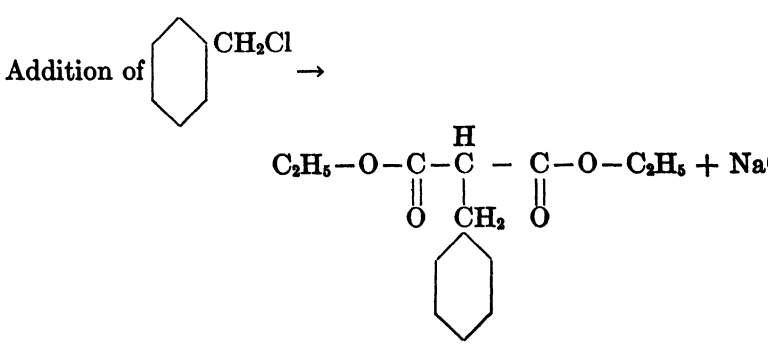
stirrer, dropping funnel and reflux condenser, as described in § 307, is recommended.

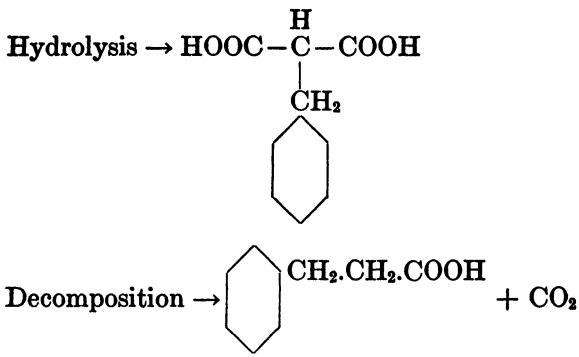
QUESTIONS

1. What undesired reaction would take place if water were admitted early in the experiment?
2. What chemical principle would lead you to expect such a reaction with water?
3. Why is sulfuric acid used in this experiment?
4. Using the Grignard reaction, how would you prepare
   (*a*) Methyl phenyl carbinol?
   (*b*) Benzyl carbinol?
   (*c*) Trimethylacetic acid?

306. Malonic Ester Synthesis. Diethyl malonate is not only an ester, but also is classed as an acid since the hydrogen attached to its central carbon atom is replaceable in such a manner as to yield a salt, e.g., sodium malonic ester. In this salt but one of the hydrogen atoms is replaced. For the conversion of the ester into this mono-sodium salt, sodium ethylate is a suitable reagent. Since ethyl alcohol is a weaker acid than malonic ester, the alcohol is expelled from its salt in the process. If an appropriate halide like benzyl chloride or *n*-butyl bromide is now introduced, the new organic radical—benzyl or butyl—becomes attached to the central carbon atom, with formation of sodium halide as a by-product. By hydrolysis and loss of carbon dioxide the resulting complex substance is cut down to a simple carboxylic acid in which the original radical (benzyl, butyl, etc.) is found attached to the residue $-CH_2.COOH$:

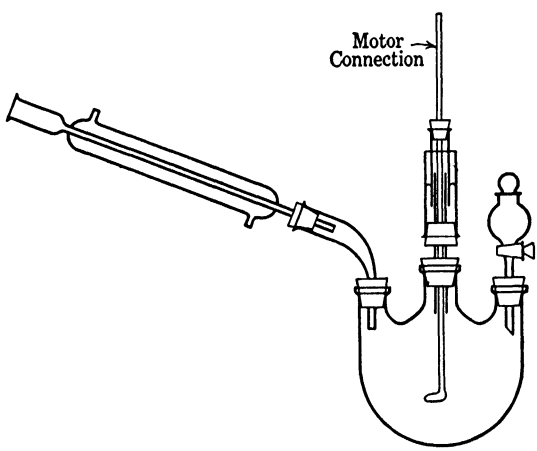






See works of theoretical organic chemistry for discussion of the structure of the sodium salt, which involves some dispute.

307. Hydrocinnamic Acid. Place 250 cc. of absolute alcohol in a 1-liter three-necked flask fitted with a dropping funnel, a mercury-sealed mechanical stirrer and a water-cooled reflux condenser without constricted tip. The alcohol must be of the most nearly anhydrous grade obtainable, preferably not below 99.9% and under no circumstances below 99.8. Any water present



quantitatively eliminates its equivalent of the useful organic reagent. See § 115 for method of preparing extremely dry alcohol. Provide also a cold water bath which may be used to cool the flask as the reaction becomes vigorous.

Gradually introduce through the condenser 11.5 g. of clean metallic sodium which has been cut into 15–20 fragments. After

the sodium has all reacted, add slowly, with continuous use of the stirrer, 78 cc. of diethyl malonate, and then run in very slowly, with stirring, 58 cc. of freshly distilled benzyl chloride. Reflux the completed mixture on the water bath until it is neutral to moist litmus paper. A quantity of sodium chloride is precipitated.

After rearranging the condenser for downward distillation, heat the reaction mixture in a water bath. Still employing the stirrer, distil as much of the remaining ethyl alcohol as possible, and then add 200 cc. of water to the residue. Separate the oily layer (crude benzylmalonic ester), using a little ether if necessary to make the two layers distinct. Remove by distillation any ether thus added.

Reassemble the main apparatus in the original reflux position, and place in it 125 g. of potassium hydroxide and 125 cc. of water. Into the resulting hot alkaline solution run the benzylmalonic ester prepared as described above. Reflux until hydrolysis is practically complete. Separate and discard any traces of non-hydrolyzed oil, using a little ether to facilitate this process. Distil the alcohol and filter the residual aqueous solution of potassium benzylmalonate.

To the aqueous solution of the potassium salt add 300 cc. of concentrated hydrochloric acid, and reflux until no more carbon dioxide is expelled from the decomposing benzyl malonic acid. Now separate the resulting oily acid with the aid of ether. Dry the ethereal solution, distil out ether and fractionate the residue under reduced pressure. The fraction boiling at 194° to 197° at 75 mm. is preserved. It will slowly crystallize at room temperatures. The production of nicely crystalline hydrocinnamic acid in this part of the operation gives a slightly more rigorous test than usual of laboratory skill. The product may also be recrystallized. For this purpose dissolve the crude acid in the minimum quantity of benzene, and slowly add ligroin (light petroleum solvent) to precipitate the hydrocinnamic acid.

When *n*-butyl bromide is used instead of the benzyl chloride, a liquid product (*n*-caproic acid) is obtained. Purification of this product is somewhat simpler than that of hydrocinnamic acid. See Refs. 17, 18.

308. Acetoacetic Ester Synthesis. Acetoacetic ester, like malonic ester, has in its molecule a methylene group attached on either side to a carbonyl group. It may accordingly be put

through a transformation much like that with the malonic derivative, with use of sodium ethylate followed by an alkyl halide.

$CH_3CO.CH_2COOC_2H_5 \rightarrow$ (mono-sodium salt)

Mono-sodium salt + $C_4H_9Br \rightarrow CH_3CO.CH(C_4H_9).COOC_2H_5$.

Hydrolysis and loss of CO_2 cause the formation of a ketone;

$$CH_3CO.CH_2.C_4H_9.$$

Other modifications of the acetoacetic ester synthesis may be found in advanced texts.

309. Methyl *n*-Amyl Ketone. In a 1-liter round-bottomed flask, fitted with a mercury-sealed mechanical stirrer (see § 306), reflux condenser protected with a calcium chloride tube, and a dropping funnel, place 200 cc. of absolute alcohol (99.8% or better; see first paragraph of § 307). Mount the flask in a water bath. Over a period of twenty minutes add 8.5 g. of metallic sodium, cut into small pieces. Next introduce gradually 48 g. of ethyl acetoacetate, with stirring. To this mixture slowly add 55 g. of purified *n*-butyl bromide, and then reflux the mixture on the water bath (for several hours) until it is neutral to litmus. Remove the sodium bromide by decantation or filtration.

Distil the reaction mixture on the water bath to remove as much alcohol as possible, and add to the residue of ethyl butylacetoacetate 500 cc. of a 5% solution of sodium hydroxide. Stir, or shake intermittently for an hour, and allow to stand for from three to twenty hours longer. A small amount of unhydrolyzed by-product may remain; this is separated and discarded.

To the aqueous remainder slowly add sulfuric acid (30 to 50% concn.) until the mixture is acidic, then add about 20% excess. After most of the carbon dioxide has escaped, distil until about half of the liquid has passed over. Make the distillate alkaline with sodium hydroxide, and redistil until 80 to 90% of the distillate has again passed over.

Separate the ketone layer, and redistil the aqueous layer as many times as necessary to get an appreciable additional yield, each time isolating the new portion of ketone. Wash the combined ketone product twice with half its volume of saturated calcium chloride solution, dry over magnesium sulfate (5 g.) and distil. Collect the fraction boiling at 145°–152°.

310. Friedel-Crafts Synthesis. If benzene or a similar aromatic compound is mixed with an alkyl halide in the presence of anhydrous aluminum chloride, one hydrogen atom is removed from the benzene molecule, joining with the halogen atom. The two organic residues unite to form a new hydrocarbon or similar derivative.

$$C_6H_6 + C_6H_5CH_2Cl(+ AlCl_3) \rightarrow C_6H_5.CH_2.C_6H_5 + HCl.$$

311. Diphenylmethane. In a fume hood, or out of doors, place 120 cc. of *dry*, thiophene-free benzene (purified if necessary by agitation with conc. sulfuric acid, washing and drying) and 34 cc. of dry benzyl chloride in a 1-liter flask fitted with a water-cooled reflux condenser and, preferably, having a second neck. Now weigh out 11 g. of anhydrous aluminum chloride into a dry test tube. (If a new unopened bottle of the commercial product is provided, consult the instructor or storekeeper about danger from gas pressure in the sealed bottle.)

Add the aluminum chloride in several portions, waiting after each addition until the initial vigor of the reaction subsides. Reflux the final mixture on a water bath for a half hour, allow to cool and add 100 g. of ice. Separate and preserve the upper, or benzene layer.

Dry the benzene solution thoroughly, and distil it to eliminate the benzene, using a small outfit like that pictured in § 27. After as much benzene as possible has been eliminated, reduce the pressure to 20 or 30 mm. and collect the diphenylmethane. B. pt. of pure diphenylmethane at 760 mm., 262°; at 22 mm., 145°. M. pt. 27°.

OPTIONAL SYNTHESES

312. Benzophenone. Benzoyl chloride is condensed with benzene, yielding a ketone instead of a hydrocarbon. (Refs. 8, 16, 20, 23, 24, 25, 27, 28, 30, 32.)

Acetophenone. (Refs. 17, 18, 20, 21, 22, 23, 28, 31.)

CYANIDE SYNTHESES

313. The cyanide group may be attached to carbon by the reaction of an alkyl halide with sodium cyanide, yielding a nitrile:

$$RCl + NaCN \rightarrow RCN + NaCl$$

If an aldehyde or ketone is substituted for the halide, hydrogen cyanide is then employed, yielding a cyanohydrin:

$$R.CHO + HCN \rightarrow R.CHOH.CN,$$

or

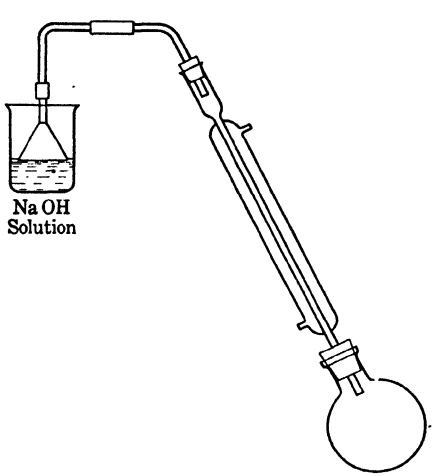
$$RCO.R + HCN \rightarrow RCOH(CN).R$$

In view of the danger in handling free hydrogen cyanide, that reagent is merely formed just when needed from its salt in a mildly acidic reacting mixture.

Either the nitrile or cyanohydrin is now hydrolyzed, yielding the corresponding acid (RCOOH, or RCHOH.COOH, or R.COH.COOH.R).

The preparation of halides suitable for the nitrile synthesis is first described.

$$CH_3.CH_2.COOH + Br_2 \rightarrow CH_3.CHBr.COOH + HBr$$



314. α-Bromopropionic Acid. In a 500 cc. round-bottomed flask, as illustrated in the accompanying figure, place 74 g. (1 mole) of freshly-distilled propionic acid (b. pt. 139°–140° uncor.), 1 g. of red phosphorus and 224 g. (1.4 mole) of bromine which has been dried by shaking with concentrated sulfuric acid in a separatory funnel.

In selecting the rubber stopper which connects the reflux condenser to the flask it is well to choose an old specimen which has slightly hardened, and thus has a surface somewhat more resistant

to the reactive bromine. The funnel which delivers the by-product of hydrogen bromide gas to the sodium hydroxide solution should barely dip beneath the surface of the liquid in the beaker. In the event that the pressure inside the flask should fall, the sodium hydroxide will not be sucked into the condenser.

The reaction mixture is slowly heated on the water bath until hydrogen bromide is freely liberated. Usually the evolution of gas starts at a temperature between 50° and 60°. The heating is then gradually increased until all bromine seems to have reacted with the propionic acid. The time may vary from 4 to 8 hours according to the rate of heating. The mixture is now transferred to a 250 cc. Claisen flask and distilled under reduced pressure with the aid of a water pump. The fraction boiling at 105°–109° at 27 mm. pressure is collected. Yield, 85 to 90% of the theoretical.

OPTIONAL SYNTHESIS

315. Benzyl chloride. If commercial cylinder chlorine is available, benzyl chloride may be prepared by the careful chlorination, under the influence of light, of boiling toluene. (Refs. 19, 20, 21, 23, 25, 31, 33.)

316. Methylmalonic Acid. In a 2-liter round-bottomed flask place 153 grams (1 mole) of α-bromopropionic acid. To this add a 25% solution of sodium carbonate until the solution is alkaline to phenolphthalein. For this purpose dissolve 60 g. of the anhydrous carbonate in 180 cc. of water. If this amount is insufficient, add 6N sodium hydroxide, a few cc. at a time, until the alkaline reaction is obtained. A supply of crushed ice should now be provided, also means for cooling the 2-liter flask under the tap.

Now add a solution of 53 g. (1 mole) of 95% sodium cyanide in 150 cc. of warm water and heat the resulting mixture to 50°–60°. The reaction which now sets in is likely to be so vigorous that the flask will have to be cooled under the tap. If such water-cooling is insufficient to control the reaction, add a few pieces of ice to the reaction mixture. When the temperature no longer tends to rise spontaneously, heat the mixture in a boiling water bath for 45 minutes. An excess (80 g.) of commercial solid sodium hydroxide is now added slowly and the mixture boiled on an oil bath until all ammonia has been expelled. The passage of

a slow current of air through the solution expedites the removal of ammonia.

When only traces of ammonia remain, cool the liquid to 20°. Add cautiously, with continued cooling, an excess (300 cc.) of commercial conc. hydrochloric acid. (***Warning.*** Some *hydrogen cyanide* may be liberated at this stage; accordingly perform this part of the experiment out of doors or in a hood.)

Now add to the mixture 160 g. of hydrated sodium sulfate ($Na_2SO_4.10H_2O$), cool in ice water and filter through a Buechner funnel. After the salts on the funnel have been sucked as dry as possible, transfer the filtrate to a large separatory funnel, leaving the salts on the filter. Replace the empty filter flask in position, and wash the salts with 100 cc. of ether. Use this wash ether as the first of six 100 cc. portions of ether which are now to be used, in turn, for six extractions of the aqueous solution in the separatory funnel. (***Warning.*** Note precautions described in § 68, dealing with danger in shaking aqueous solutions with ether.)

Dry the combined ether extract over anhydrous magnesium or sodium sulfate, and filter. Distil the ethereal filtrate through a well-cooled condenser. As the rate of accumulation of ether slackens toward the close of the distillation, boil the water in the water bath rapidly to insure as complete removal of the ether as possible. Now discontinue the heating, and add to the boiler residue 100 cc. of dry benzene.

To the resulting benzene solution gradually add 250 cc. of petroleum ether, "light ligroin," or other light petroleum solvent whose boiling range lies below 120°, and continue the cooling operation. During this process about 80 to 82 g. of nearly white crystalline methylmalonic acid should separate. Collect this on a Buechner filter, and spread upon a porous clay dish to remove water and propionic acid.

Yield (80 g.), 70% of the theoretical.

QUESTIONS

1. Why is the bromopropionic acid neutralized before addition of the sodium cyanide?

2. Why is the sodium sulfate added before the solution is extracted?

3. Of what use is the benzene in the recrystallization process?

4. What compound would have been produced if the cyanide had been reduced instead of hydrolyzed?

317. Benzyl Cyanide. In a 500 cc. round-bottomed flask, fitted with a water-cooled reflux condenser, place a solution of 30 g. of sodium cyanide (poison!) in 35 cc. of warm water, and add 50 cc. of alcohol. Add through the condenser in several small portions during 10–15 minutes, 63 g. of benzyl chloride. Boil the mixture for three hours, cool, filter to eliminate the product of sodium chloride, and distil the alcohol from the filtrate. Separate the crude benzyl cyanide, dry for a few minutes over magnesium sulfate, and distil under reduced pressure, 40 mm. being sufficiently low. B. pt. of benzyl cyanide at 40 mm. is about 140°; at 760 mm., 232°.

OPTIONAL SYNTHESES

318. Benzyl cyanide. Those wishing to prepare this very useful compound in larger quantities should consult Organic Syntheses (both Ref. 2 and the Collective Volume).

Hydrolysis of benzyl cyanide; phenylacetic acid. The nitrile is hydrolyzed in acid solution, as contrasted with the alkaline hydrolysis of § 316. (Refs. 2, 23, 28, 33.)

***n*-Butyl cyanide and *n*-valeric acid.** *n*-Butyl bromide is converted into the nitrile, which in turn is submitted to alkaline hydrolysis. (Ref. 17.)

Acetonitrile (methyl cyanide). This nitrile is commonly made by removal of hydrogen and oxygen (in the ratio of H_2O) from acetamide. (Refs. 17, 18, 20, 23, 27, 28, 30, 31, 32, 33.)

Benzonitrile. This strictly aromatic nitrile is prepared from a diazo intermediate. See § 323.

319. α-Hydroxy-α-Methylbutyric Acid; Cyanohydrin Reaction. Provide 82.5 g. (1.6 moles) of 95% sodium cyanide (poison!), if necessary crushing the commercial product into pieces not more than 1 cm. in diameter.

In a 3-necked 2-liter flask, equipped with a mechanical stirrer, a dropping funnel, and a long air-cooled condenser, place 200 g. of cracked ice, 25 cc. of water, the 82.5 g. of sodium cyanide, and 108 g. (1.5 moles) of ethylmethylketone. Weigh out 190 g. of sodium metabisulfite, $Na_2S_2O_5$ (equivalent to 2 moles $NaHSO_3$), and dissolve as much as possible of this salt in 240 cc. of hot water (75° to 100°) in a beaker. As the cyanide-ketone mixture is vigorously stirred, introduce from the dropping funnel, during the course of eight or ten minutes, the bisulfite solution. By the time that 150 to 175 cc. of the bisulfite solution has been added the

temperature should have arisen to about 35°. Place a cooling bath of ice and water around the flask, and hold the temperature of the reaction mixture between 30° and 40° for ten minutes after the last of the bisulfite has been added. After the solution is all in, add the balance of the (solid) sodium metabisulfite directly to the reaction mixture. It should be noted that the minute quantity of gaseous hydrogen cyanide which might be volatilized in this operation is carried up through the condenser and allowed to escape at a high level where it will be diffused in the atmosphere instead of appearing where the worker below might breathe it in an unduly high concentration.

The main cyanohydrin reaction should now be complete. Place an ice-salt bath around the reaction flask, and continue the stirring until the temperature of the reaction mixture falls to 0°. At this low temperature the solubility of the cyanohydrin in the salt solution is negligible. Pour the oily cyanohydrin from the mushy salt layer; then add 50 to 100 cc. of water to the latter, and shake thoroughly. Additional oil may rise to the top; if so, pour this off also and place with the first quantity separated. More or less of the aqueous salt solution is likely to flow over with the oil; isolate this in a separatory funnel and discard it, preserving the oil for the hydrolysis reaction next described.

320. Conversion into Acid. The hydrolysis of the cyanohydrin in hydrochloric acid solution requires seven hours if one must carry on the procedure continuously to the end. Time is saved, on the other hand, by preparing the reaction mixture in the cold, and allowing it to stand for twenty-four hours or more. When the work is resumed at the next laboratory period, only four hours of refluxing are required.

Heat the crude cyanohydrin, of which there should be about 160 g., at 90° to 100°, under a reflux condenser, with 200 g. of conc. hydrochloric acid, and for either the four or seven hours according to the more favored plan of those cited above. It is not advisable to heat the solution above 100°, since both hydrogen chloride and the desired organic product would be lost by volatilization. Now cool the solution to room temperature. Without attempting to remove the ammonium chloride, add 100 g. of hydrated sodium sulfate and shake thoroughly. This operation converts most of the acidic hydrogen into the bisulfate ion (HSO_4^-), and thus markedly reduces the acidity. The sodium

sulfate should actually dissolve in order to accomplish its purpose; but it is difficult to determine whether or not the solution is really complete on account of the mass of other salts in suspension. It is well to agitate the solution for about 15 minutes. Now cool the mixture to 10°, and filter with the aid of strong suction, as from an effective filter pump. Reject the residual solid salts. The filtrate, containing the desired α-hydroxy-α-methylbutyric acid, is now to be extracted with ether, and a 500 cc. separatory funnel is convenient for the purpose.

If the intensely acid hydrochloric acid solution had not been weakened by the addition of sulfate, there would have been too large a mutual solubility of the aqueous and ethereal phases for a satisfactory performance of the extraction process. Should the first portion of ether dissolve completely, or almost completely, in the aqueous solution, that fact shows that insufficient sodium sulfate has gotten into the solution. The slightly basic character of ether is responsible for this influence on solubility, so that in the case of the untreated hydrochloric acid solution ether would have played the undesired role of "reaction solvent" (see § 119). Under the specified conditions, however, the desired organic acid is effectively extracted. Four 75 cc. portions of diethyl ether are used.

The combined ethereal extract may have an adjacent watery layer. If so, reject this aqueous material. Dry the combined extract with 50 g. of magnesium or sodium sulfate, and distil the ether as completely as possible. Now heat the flask containing the residual product to 100° until no more ether distillate is obtainable. Introduce a capillary tube (as in reduced-pressure distillation, § 27) and cool the flask to room temperature. When the flask is cool, exhaust it to the limit of the filter pump, and gradually heat the vessel again to 100°.

To the residue add 25 cc. of benzene and 75 cc. of light petroleum distillate (petroleum ether, or "thinner" solvent with boiling range below 120°), and heat almost to the boiling point of the mixed solvent. Shake the mixture to permit maximum extraction by the solvent, and without cooling immediately decant as much of the clear solution as possible into a second flask, cooled with ice and salt.

After the maximum crystallization of the desired solid acid has taken place, decant as much of the benzene-petroleum mother-

liquor as possible back into the first flask. Now add another 25 cc. of benzene and 75 cc. of petroleum, and use this new enlarged volume of solvent for the next extraction. Repeat the heating, extraction and decantation as often as may be necessary to transfer the product and obtain the maximum yield of crystals. Yield about 64% of the theoretical, and the product melts at 72.5° (cor.).

If the product is dark colored or contains foreign matter, dissolve it in the minimum quantity of hot benzene, and filter the solution. Now add a quantity of the light petroleum solvent just sufficient to cause maximum precipitation of crystals at the temperature of an ice-salt bath.

OPTIONAL SYNTHESES

321. Mandelic acid. Benzaldehyde is condensed with hydrogen cyanide, yielding mandelonitrile, $C_6H_5.CHOH.CN$. Hydrolysis yields the corresponding (mandelic) acid, $C_6H_5.CHOH.COOH$. (Refs. 18, 19, 20, 24, 27, 28, 31.)

Amino-nitriles. The introduction of ammonia during the reaction of an aldehyde and hydrogen cyanide causes the formation of an α-aminonitrile instead of an α-hydroxynitrile. Hydrolysis of such a product yields an amino acid. Cf. amino-acetic acid from formaldehyde (§ 359).

DIAZO REACTIONS

322. In each of the following experiments **diazotization** is the introductory operation. Normally a primary aromatic amine is first dissolved in at least three times its molar equivalent of hydrochloric or sulfuric acid. One equivalent of acid forms the amine salt; a second reacts shortly with one mole of sodium nitrite, to produce as needed the desired nitrous acid; and the third (or greater excess) maintains the high acidity required to prevent the newly formed diazonium salt from going astray into by-products.

With aniline as the primary amine, phenyl diazonium chloride is the product of diazotization:

$$C_6H_5NH_2 \rightarrow C_6H_5NH_3^+ \cdots\cdots Cl^- \rightarrow C_6H_5N_2^+ \cdots\cdots Cl^-$$

Equimolal quantities of amine and sodium nitrite are usually required, as an excess of either is likely to introduce trouble. Ordinarily temperatures between 0° and 5° are specified to avoid both excessively slow reaction rates on the one hand, and decomposition on the other. If a beaker is employed as the vessel for diazotization, ice should be placed in the reaction mixture as well as in a surrounding bath, on account of the inefficiency of cooling in a beaker with stirring rod. If the excess water in the reaction mixture is not acceptable, the method of agitation in a long-necked flask in an ice bath (§ 326) is used.

Occasionally the amine is amphoteric, as in the case of § 330, thus introducing the complication of an inner salt and causing considerable change in the technic of diazotization.

One of the simpler products of the diazo method has already been described as an elementary experiment (phenol, § 282). Other illustrations follow.

323. *p*-Bromotoluene; Sandmeyer Reaction. When the solution of an aryl diazonium salt, such as phenyl diazonium sulfate, is heated with a mixture of a cuprous halide and the corresponding halogen acid, the diazonium group is replaced by halogen, with release of nitrogen gas.

$$CH_3C_6H_4.N_2.HSO_4 + Cu_2Br_2 + HBr \rightarrow CH_3C_6H_4Br + N_2 + Cu_2Br_2 + H_2SO_4$$

In a 1-liter flask mix 0.4 mole (42.8 g.) of *p*-toluidine and 350 cc. of water, and then add 45 cc. of concentrated sulfuric acid. Warm the mixture if necessary to get all reagents dissolved, and

provide an ice bath large enough to permit the flask to be effectively cooled by shaking in the ice slush. A handful of salt should be added to the ice.

Cool the toluidine sulfate solution to about 0°, and very slowly add a solution of 30 g. (a slight excess) of sodium nitrite in 50 cc. of water. Keep the temperature of the diazotization reaction between 0° and 5° with the aid of effective shaking in the ice bath, and allow the completed mixture to stand one-half hour, but not over one hour, in the ice bath. In the meantime, prepare a supply of cuprous bromide as follows:

Divide into two equal parts a solution of 0.5 mole (125 g.) of cupric sulfate (hydrate) in about 600 cc. of water. Into one part stir 0.25 gram-atom (16.3 g.) of zinc dust. If the blue color persists—indicating impure zinc and thus an inadequate quantity—add just enough zinc to complete the reaction. Decant the liquid; wash the precipitate of copper with dilute sulfuric acid to remove possible excess zinc and decant the liquid again. Now add to the copper the second portion of cupric sulfate, 1.0 mole of potassium or sodium bromide and 15 cc. of concentrated sulfuric acid. Stir well. The white precipitate is cuprous bromide, Cu_2Br_2.

Mount a two-liter flask in the customary position for steam distillation (see § 29), and introduce a third tube (7 to 9 mm. in diameter), leading almost to the bottom of the flask. Attach a small funnel to the outer end of this tube. Now place the cuprous bromide-acid mixture in the flask and heat to boiling.

Through the funnel tube slowly introduce from a dropping funnel the *p*-tolyl diazonium sulfate solution while steam is passed rapidly through the mixture. Continue the distillation for an hour or more, or until frothing ceases and no further yield of oily product comes over.

Add 20 cc. of 6N sodium hydroxide to the aqueous distillate to extract *p*-cresol from the product, shake well and isolate the crude bromotoluene. Wash the product once with concentrated sulfuric acid, then with sodium hydroxide and finally with water. Should the product solidify, warm the wash liquids slightly before use. A yellow or brown color may often be removed by washing with stannous chloride solution.

Dry the product over magnesium sulfate or calcium chloride, filter and distil through an air-cooled condenser, preserving the

fraction boiling between 178° and 186°. Boiling point of pure *p*-bromotoluene, 184°; melting point, 26°.

OPTIONAL SYNTHESES

324. Chlorotoluenes. Cuprous chloride is substituted for the bromide of the foregoing experiment. (Refs. 3, 17, 18, 20, 21, 24, 33.)

***p*-Tolyl cyanide and *p*-toluic acid.** Cuprous cyanide is substituted for the bromide, yielding a nitrile which is hydrolyzed to give an aromatic acid. (Refs. 18, 20, 26.)

***p*-Iodotoluene.** Iodine is introduced without the necessity of a cuprous salt. (Ref. 20.)

QUESTIONS

1. Suppose heptyl amine, $C_7H_{15}NH_2$, were substituted for the toluidine ($C_7H_7NH_2$) in the above experiment. What trouble might be expected?
2. Explain the value of sodium hydroxide in purifying the steam-distilled bromotoluene.
3. Do you think that this preparation requires a specially good drying agent? Why?
4. How could you distinguish the product, by chemical reaction tests, from α-bromotoluene, its isomer?

325. Azo Dye. If an aryl diazonium chloride is mixed with a suitable aromatic amine, or a phenol, usually in the presence of alkali of some kind, a hydrogen atom is removed from the ring of the amine or phenol, and the diazonium ion couples—that is, directly combines with the amine or phenol to form an azo dye, of type formula $Ar_1.N=N.Ar_2$, where Ar_1 and Ar_2 are any two of a great variety of benzene and naphthalene derivatives. In the example immediately following it is desirable that the reagents be as pure as possible, and that the quantities be weighed accurately. For example:

$$C_6H_5N_2Cl + C_{10}H_7NH_2(+ CH_3COONa) \rightarrow C_6H_5-N=N-C_{10}H_6NH_2 + NaCl + CH_3COOH$$

326. Phenyl-azo-β-naphthylamine. Dissolve just 0.03 mole of light-colored or freshly distilled aniline in a mixture of 15 cc. of 6N hydrochloric acid and 10 cc. of water (equivalent to 0.09 moles of HCl), and place the resulting aniline hydrochloride solution in a 200 or 300 cc. (preferably long-necked) flask. Provide a slushy ice-and-water mixture containing enough salt to depress its temperature about three degrees below 0°.

With the aid of scissors or a sharp knife cut from the smallest available rubber tubing a slender rubber band, and place this band as a marker upon a thermometer at the 0° point. Insert the thermometer, so equipped, into the flask, and cool the aniline reagent by means of the ice bath to about 0°. Now add slowly, a few drops at a time, but with thorough shaking of the flask, a solution of just 0.03 mole of sodium nitrite in 10 cc. of water. Keep the temperature of the reaction mixture between 0° and 5°.

While the resulting phenyl diazonium chloride solution stands in the ice bath, dissolve just 0.03 mole of β-naphthylamine and 0.07 mole of sodium acetate (anhydrous or hydrate) in 100 cc. of alcohol which is heated under a water-cooled reflux condenser in a 500 cc. (preferably conical) flask mounted in a water bath. Now cool the naphthylamine solution to about 30°–35°.

To the naphthylamine solution add all at once, with vigorous shaking of the mixture, the diazonium chloride solution described above. Within a few seconds the azo dye forms and crystallizes suddenly. Now pour about 5 cc. of ice water into the flask from which the diazo solution has just been taken, for use in a later test, and return the flask to the ice bath. Reconnect the flask containing the dye to the reflux condenser, and heat to boiling, thus completely dissolving the dye. Remove the flask again, stopper it lightly and set aside for slow cooling and crystallization. Collect the product on a Buechner filter, suck down the mother-liquor thoroughly and dry the crystals.

Add the 5 cc. of washings left in the diazotization flask to a solution of a few crystals (0.1 g.) of β-naphthol in 15 cc. of dilute sodium hydroxide. An orange-red azo pigment is produced.

Mix 5 cc. of the alcoholic filtrate with 2 cc. of dilute hydrochloric acid, thus producing the red or acidic modification of the dye. To the remaining filtrate add 200 cc. of water, thus obtaining an additional yield of the yellow modification, but of low purity.

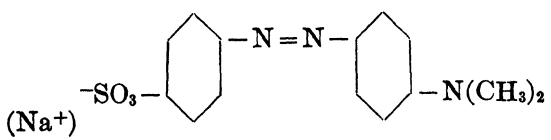
OPTIONAL EXPERIMENTS

327. *p*-Dimethylaminoazobenzene, butter yellow. This azo dye, prepared from phenyl diazonium chloride and dimethylaniline, is used as an indicator to distinguish strong acids in the presence of weak acids. The above directions (§ 326) with but slight modification in volume of solvent will serve for this preparation.

328. Congo red. A double aromatic amine (benzidine) is "tetrazotized" and coupled with a naphthalene derivative, yielding an azo dye of considerable industrial value, as well as of value as an indicator.

329. Para red. An azo pigment, sometimes called American Flag Red. Prepared by rapidly diazotizing *p*-nitroaniline at room temperature, and coupling the diazonium salt with β-naphthol. Used in inexpensive red paints. Cloth may be treated with the diazonium salt solution, wrung out, and dipped into the naphthol solution, producing the color in the fabric.

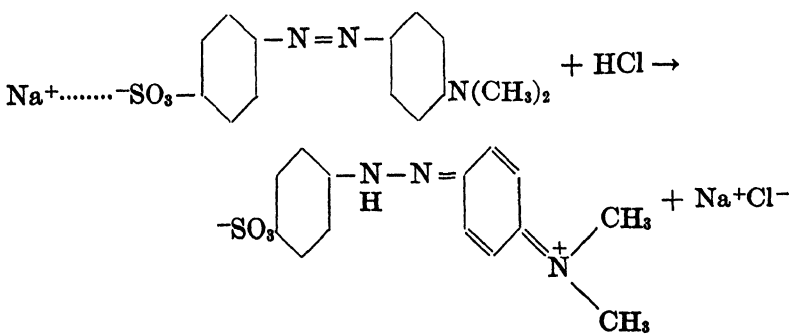
330. Amphoteric Azo Dyes. If a primary aromatic amine has an acid group in its molecule, as in sulfanilic acid, it is amphoteric, being both a base and an acid. Sulfanilic acid (used in the preparation described below) is usually represented as $HSO_3.C_6H_4.NH_2$, but is more likely to react as an inner salt, $^-SO_3.C_6H_4.NH_3^+$, sometimes called a "zwitterion." When such an amine is diazotized, the $-NH_3^+$ group merely becomes $-N_2^+$. It happens that the resulting compound $^-SO_3.C_6H_4.N_2^+$ is but slightly soluble in water. It crystallizes and is separated by filtration. The addition of dimethylaniline, β-naphthol, or similar coupling agent at once yields an azo dye by direct attachment of the $-N_2^+$ group to the new aromatic nucleus:



Methyl Orange

The reaction proceeds to the stage shown above in alkaline solution, thus accounting for the sodium atom which has appeared with the methyl orange nucleus, but not directly bonded thereto. Such a process is described in the short preliminary test of § 332.

Treatment of methyl orange with a strong acid instantly transforms it into a red compound often called helianthin. The presumable explanation of this change is as follows:



Helianthin is thus seen to be another inner salt itself. Actually it may be made by direct coupling in acid solution, and this method, while difficult to explain at the outset, is practically advantageous and is used below. Later the helianthin is neutralized, yielding methyl orange.

331. Methyl Orange; Preparation. Dissolve 0.05 mole of sulfanilic acid (monohydrate or anhydrous) in a solution of 9 cc. of 6N sodium hydroxide in 50 cc. of warm water. When all of the sulfanilic acid is dissolved test the solution to be sure it is alkaline. In this solution dissolve 0.055 mole of sodium nitrite and cool the resulting mixture to about 30° C.

To about 150 g. of crushed ice in a 400 cc. beaker add 6 g. of concentrated sulfuric acid, and stir well. Now add the sodium sulfanilate solution in a fine stream with constant effective stirring. Mark the beaker for identification and set it away in the refrigerator, or in a pan of crushed ice and water, for an hour. If it is allowed to stand much more than two hours there is danger of decomposition of the diazonium salt.

In the meantime prepare a quantity of dimethylaniline acetate just equivalent to the maximum possible yield of diazonium salt which you calculate by theory. This acetate is prepared simply by mixing dimethylaniline with an equimolal quantity of glacial acetic acid.

332. Preliminary Test. At the end of an hour the maximum available yield of the diazonium inner salt should have precipitated in the beaker. A small amount remains in solution. As a preliminary experiment to illustrate the graphic representations already given, decant about 5 cc. of the solution into a test-tube. Make this alkaline with sodium hydroxide and immediately add three or four drops of the dimethylaniline acetate solution just prepared. Methyl orange at once is formed. Shake the test-tube, and acidify the contents with hydrochloric acid. Helianthin is at once observed.

Now collect the precipitate of diazonium salt on a Buechner filter and wash it with a little ice water. Place the compound in a 400 cc. beaker, using about 25 cc. of ice water to aid in a complete transfer.

With vigorous, effective stirring, add the dimethylaniline acetate solution and stir until the resulting pasty mass is uniform in texture and color. The color should be a rich, deep reddish-

purple. This operation requires about ten minutes. Now add 18 cc. of 6N sodium hydroxide, stir well, and add 300 cc. of water. Heat this mixture to boiling, being careful to stir the mixture while heating to prevent bumping. If a clear deep orange-brown solution has not resulted, a little more water should be added.

The hot solution is now divided into two approximately equal portions, each of which is placed in a beaker. One portion is covered with a watch glass and set aside to cool slowly. Out of this separates the methyl orange, which is collected on a filter, washed with a little cold water, and dried in the open air. The other portion is treated as follows: 12 cc. of 6N hydrocloric acid is added very slowly with constant stirring. The beaker is then set aside to cool. When cold, the helianthin is collected, washed, and dried just as the methyl orange above.

OPTIONAL SYNTHESES

333. Orange II. The diazonium salt of sulfanilic acid may be coupled with β-naphthol, yielding a water-soluble dye without the yellow-to-red indicator properties. (Refs. 21, 23, 33.)

Methyl red. Diazotized anthranilic acid (*o*-aminobenzoic acid), another illustration of amphoterism, is coupled with dimethylaniline, yielding the valuable indicator methyl red, which has a beautiful lemon yellow-to-red color change. (Ref. 2.)

Other azo dyes are cited in § 327.

334. Aryl Hydrazines. An aryl diazonium salt may be reduced to the corresponding aryl hydrazine. In this reaction the positively charged diazonium group $-N\equiv N^+$ combines with four hydrogen atoms, the reducing agent furnishing the four necessary electrons, yielding the hydrazine ionic group $-NH-NH_3^+$. The resulting organic compound, in the presence of hydrochloric acid, is phenylhydrazine hydrochloride, $C_6H_5.NH.NH_3^+ \ldots\ldots Cl^-$, a salt. Addition of alkali frees the base phenylhydrazine, $C_6H_5.NH.NH_2$. Either stannous chloride, or sodium sulfite, a less expensive reagent, is a satisfactory reducing agent for the purpose.

335. Phenylhydrazine Hydrochloride. In a 400 cc. beaker place 200 g. of crushed ice and 50 cc. of conc. hydrochloric acid. To this add slowly, with effective stirring, 18.6 g. (0.2 mole) of freshly distilled aniline. Now add in small portions with vigorous stirring 14.5 g. (an excess) of sodium nitrite. After the last portion of sodium nitrite has been added, place the beaker in an ice bath and allow to stand for ten minutes.

While the above solution is standing, prepare a sodium sulfite solution as follows:

In a 1-liter beaker place 20 g. (0.5 mole) of technical flake sodium hydroxide and add 200 cc. of water. When the sodium hydroxide has dissolved, add 45 g. of sodium acid sulfite. (NOTE. The commercial acid sulfite is known as sodium metabisulfite, and has the formula $Na_2S_2O_5$.) Stir until the solid has dissolved, cool the resulting solution to 30° or below and add 4 or 5 drops of phenolphthalein indicator solution. Now add, with stirring, still more sodium acid sulfite, a little at a time, until the pink color of the solution just disappears; then stir in an additional 5 g. (A total of 55 g. should be sufficient in all cases.)

Now cool this solution to about 15° in an ice bath, after which add 100 g. of crushed ice. When the temperature of this solution has fallen to 5°, add the phenyl diazonium chloride solution very rapidly, with stirring. The reaction mixture immediately turns to an orange-yellow color. Now slowly heat this solution on a water bath to 60°–70°. Maintain this temperature for half an hour to an hour, during which time the color changes to a deeper shade of orange-red.

Now make the solution just acid to litmus, using concentrated hydrochloric acid; then heat on the water bath at 80°–85° for three hours. (This heating does not have to be done all at one time.) During this time the color of the solution usually becomes much lighter, though not necessarily. While the mixture is still hot, take it outdoors, or to a hood, and add 200 cc. of concentrated hydrochloric acid, with stirring. Now allow the solution to stand upon the laboratory desk for 10 to 20 minutes, during which time a quantity of coarsely crystalline phenylhydrazine hydrochloride will be precipitated. After the crystallization has been well advanced, place the mixture in an ice bath and cool it to 5° or below. This completes the crystallization; but if the cooling had been conducted rapidly, with ice, at first, an extremely finely divided precipitate might have been obtained. Filtration would be difficult.

Collect the phenylhydrazine hydrochloride upon the Buechner filter, press down well, and suck the residue as dry as possible; then wash with 10 cc. of 3N hydrochloric acid and again suck dry. Spread the crystals upon a piece of 6″ filter paper and dry them. This preparation does not keep well if not well dried. The prod-

uct from this method is usually pale yellow or faintly pink; pure phenylhydrazine is white. It may be purified by special recrystallization (Ref. 18) but this is not necessary for practical use of the compound.

336. Isolation of Phenylhydrazine. Although it is probably better to preserve this reagent in the form of its salt, the free base may nevertheless be readily prepared. To the hydrochloride add an excess of 4 to 6N sodium hydroxide. Extract the resulting phenylhydrazine with ether or benzene, dry over sodium or potassium hydroxide, expel the extracting solvent, and distil under reduced pressure. Boiling points—at 12 mm., 120°; at 18 mm., 137°.

OPTIONAL SYNTHESES

337. Nitro-derivatives. These are valuable as reagents in qualitative organic analysis. For example—*p*-nitrophenylhydrazine (Refs. 20, 23) and 2,4-dinitrophenylhydrazine (Ref. 13).

QUESTIONS

1. What chemical reaction takes place when sodium acid sulfite and sodium hydroxide are mixed?
2. Explain how the sulfite can serve as a reducing agent.
3. Would an excess of nitrous acid be injurious in this reaction?
4. What is the reaction of phenylhydrazine with acetone?
5. Knowing that the free base phenylhydrazine, not the hydrochloride, reacts with the acetone, devise a method of use of our preparation to make the desired derivative of acetone.

338. Aromatic Arsenical Compound. The Bart Reaction. In a reaction resembling the Sandmeyer synthesis (§ 323), an aryl diazonium salt, mixed with arsenite ion in the presence of a trace of a copper compound as catalyst, loses nitrogen and couples with the arsenite group to yield an aryl arsonic acid, of type formula $Ar-AsO_3H_2$.

$$CH_3C_6H_4N_2Cl + Na_2HAsO_3 \rightarrow CH_3C_6H_4AsO_3HNa$$
$$\text{Addition of HCl} \rightarrow CH_3C_6H_4AsO_3H_2$$

339. *p*-Tolyarsonic Acid. To 100 cc. of water add 32 g. of anhydrous sodium carbonate, 18 g. of arsenious oxide, 1 g. of crystalline cupric sulfate and 3 g. of sodium formaldehyde sulfoxylate (also a catalyst). Heat to boiling to dissolve the solids, and cool the solution to 0°.

Following somewhat the technic of § 326, diazotize 0.125 mole of *p*-toluidine, using the minimum permissible quantity of hydrochloric acid (2½ times 0.125 mole). Enough ice is included in the mixture undergoing diazotization to bring the final volume of the *p*-tolyl diazonium chloride solution to 200–225 cc.

To the arsenical mixture previously prepared add 10 cc. of benzene (to reduce frothing) and slowly stir in the diazonium salt solution, keeping the temperature below 5°. Allow the mixture to stand 20 minutes in the ice bath, and then one hour in the open, with frequent and thorough stirring. Now heat to 50°–60°. Gas is evolved and tar coagulates. Cool the mixture, filter and evaporate the filtrate to one-third of its former volume. Add 1 to 3 cc. of conc. hydrochloric acid a few drops at a time, or as long as tar separates. Filter again and add 30 cc. of conc. hydrochloric acid, thus precipitating *p*-tolylarsonic acid. With the aid of decolorizing carbon, recrystallize from boiling water. About 100 cc. will be required.

340. Note. The presence of a soluble aromatic arsenical derivative of this type may be detected by submitting a test-tube sample of a solution of the supposed arsenical to the following test: Heat with a gram of hypophosphorous acid; or saturate with sulfur dioxide and heat with a gram of phosphorous acid. An insoluble "arseno" derivative is promptly formed. Usually this is a characteristic amorphous yellow solid, in the present case arseno-*p*-toluene, $CH_3.C_6H_4.As=As.C_6H_4.CH_3$.

OPTIONAL SYNTHESES

341. *o*-Nitrophenylarsonic acid. Another illustration of the Bart reaction. (Ref. 29.)

Arsanilic acid. Direct arsenation of aniline. (Refs. 3, 16, 23, 28.)

Phenol-*p*-arsonic acid (sodium salt). Direct arsenation of phenol. (Refs. 4, 29.)

Arsphenamine (Salvarsan). This famous arsenical drug, which is an arseno derivative, calls for considerable skill in preparation. (Ref. 29.)

342. Nitroso Derivatives. The substitution of a dialkylaniline for aniline in a procedure arranged as though for diazotization yields instead of a diazonium salt a para-nitroso derivative, in which the nitrous acid is found to have reacted with the para hydrogen instead of the amine group. Being in acidic solution, the product appears in the form of a yellow hydrochloride.

Upon addition of alkali the free base, a brilliant green compound, is obtained.

$$C_6H_5N(CH_3)_2 + NaNO_2 + 2HCl \rightarrow NO.C_6H_4.N(CH_3)_2.HCl + NaCl + H_2O$$

$$NO.C_6H_4.N(CH_3)_2.HCl + NaOH \rightarrow NO.C_6H_4.N(CH_3)_2$$

343. *p*-Nitrosodimethylaniline. In a 500 cc. flask, cooled in an ice bath, mix 80 cc. of water, 45 cc. of conc. hydrochloric acid, about 20 g. of ice, and 20 g. of freshly distilled dimethylaniline. Now add very slowly from a dropping funnel a solution of 12 g. of sodium nitrite in 20 cc. of water, while shaking the flask and keeping the mixture thoroughly cooled in the ice bath. Allow the flask to stand for one hour in the cooling bath, and then collect the precipitate of *p*-nitrosodimethylaniline hydrochloride upon the Buechner filter. Place the product in a large evaporating dish, add 50 cc. of conc. hydrochloric acid, crush all lumps finely and transfer the semi-solid mass to the Buechner filter. Suck down and reject the discolored hydrochloric acid, and divide the resulting yellow crystalline mass into two equal parts.

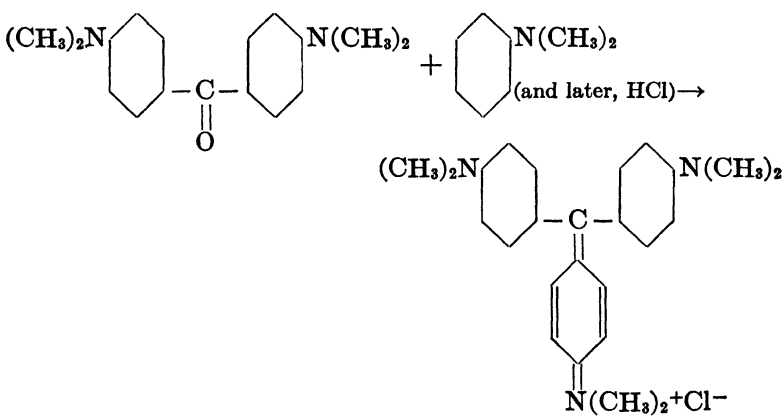
Recrystallize one of the two portions from the minimum quantity (perhaps 150 cc.) of 2N hydrochloric acid, which is not heated over 80° during the process. Cool the solution, wash the crystalline product with 3N hydrochloric acid, and dry in the open air.

After crushing the second portion to a granular powder, free from lumps, place the material in a large separatory funnel with about 125 cc. of benzene. Now add, in 10 cc. portions, 1N sodium carbonate solution, shaking well after each addition. If this reaction is allowed to proceed too vigorously, as in the presence of too much alkali, the dimethylamino group will be removed by hydrolysis, causing an undue amount of the dark red by-product *p*-nitrosophenol to appear.

When the yellow salt is completely converted into the benzene-soluble base, separate the benzene layer, dry it with anhydrous magnesium sulfate, filter and evaporate to a volume of about 25 cc. Transfer the residual solution to a 250 cc. beaker and add 100 cc. of light petroleum solvent (boiling range below 120°). Heat to the boiling point on the steam bath, if necessary adding more solvent to effect complete solution. Cool, collect the crystalline product and dry. M. pt. of *p*-nitrosodimethylaniline, 85°.

TRIPHENYLMETHANE AND PHTHALEIN DYES AND INDICATORS

344. If three amine or hydroxyl radicals are present on the three rings, respectively, of the molecule of triphenylmethane, the resulting derivative is easily transformed into a dye of brilliant color. Crystal violet, with three dimethylamine groups thus located, is described below. Only the last step of the ordinary process of manufacture is given here. The compound thus produced is the mono-chloride salt of a tri-acidic base. That is, but one of three amine radicals in the molecule has been converted into a salt group. In its preparation, therefore, special attention is paid to the degree of acidity of the final solution. If—through carelessness in leaving a residue of alkali, or failure to put in enough hydrochloric acid—the solution contains insufficient acid, one obtains an uncrystallizable amorphous base containing no salt group at all. If too much hydrochloric acid be added, more than one amine group will be converted into the salt form. This results in a green or yellow substance, also uncrystallizable and furthermore unstable.



Select a flask of from 1500 to 2000 cc. capacity which has the necessary accessories for steam distillation later in the process. In this flask place 15 g. of freshly distilled dimethylaniline, 6 g. of Michler's ketone (tetramethyldiaminobenzophenone), and 6 g. of phosphorus oxychloride. Heat the flask in the open for five hours on the water bath.

Add about 250 cc. of water and enough sodium hydroxide to render the solution alkaline. Calculate this quantity on the basis of the hydrolysis products coming from the phosphorus oxychloride. Pass steam through the mixture until all unchanged dimethylaniline has passed over into the receiver. Cool the flask, collect the reddish precipitate of the "color base" upon a Buechner filter, and wash with water. Transfer the precipitate to a clean flask or beaker, and boil it with 250 cc. of water to which just 2 cc. of concentrated (12-normal C.P.) hydrochloric acid has been added. Filter the hot solution, set the filtrate aside to crystallize, and treat the residue with successive portions of the same water-hydrochloric acid mixture until practically all of the color base has been dissolved.

Saturate the combined filtrates with clean common salt, being careful not to add an excess beyond solubility limits. Allow the mixture to stand a day or more. Collect the resulting crystalline preparation on a filter and dry in the open air.

OPTIONAL SYNTHESES

345. Malachite green. A dye of structure very similar to that of crystal violet, synthesized from benzaldehyde and dimethylaniline. (Refs. 18, 20, 21, 25, 27, 28, 30, 31, 33.)

Fuchsine (magenta). Although even simpler in structure than the foregoing dyes, fuchsine is more difficult of preparation. (Refs. 21, 23, 33.)

QUESTIONS

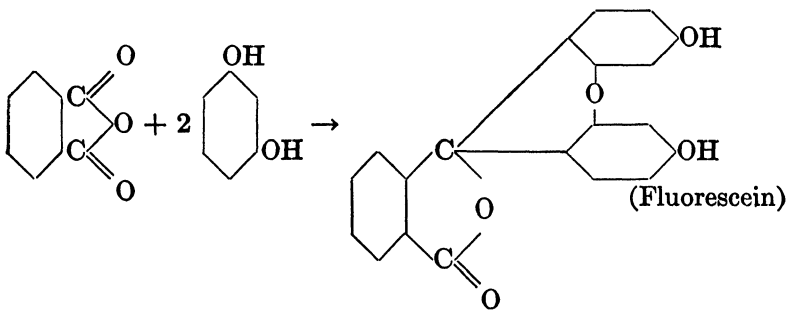
1. In what way is the structure of crystal violet supposed to differ from that of the color base?
2. What happens when the dye is treated with an excess of hydrochloric acid?
3. How may crystal violet serve as an indicator?
4. Why does it have a special usefulness distinct from that of common indicators like litmus, methyl orange, etc.?

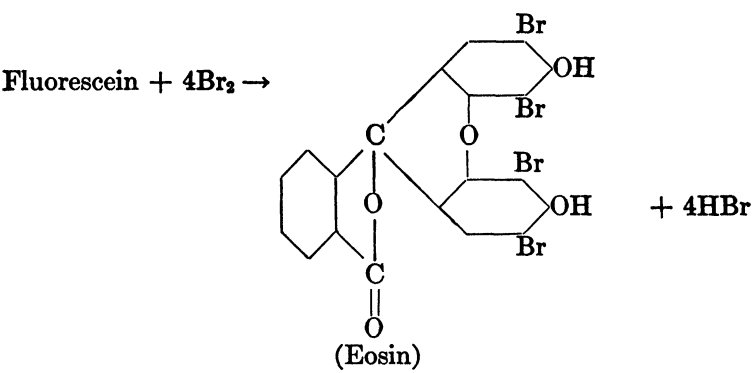
346. Phthaleins. When phthalic anhydride is heated with a phenol, a para hydrogen atom from each of two molecules of the latter combines with one of the outer oxygen atoms of the anhydride to form water. The organic residues unite to form a new large molecule, the resulting substance being called a "phthalein."

When resorcinol (*m*-dihydroxybenzene) is used as the phenol, resorcinol phthalein is produced. On account of its fluorescent behavior, the latter has been named fluorescein. In this com-

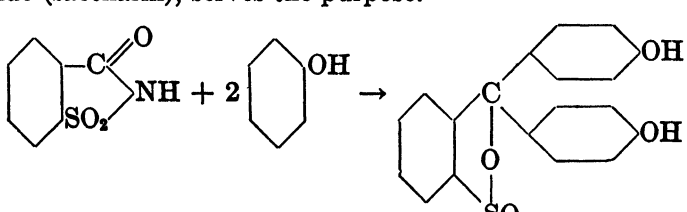
pound two of the phenolic hydroxyl groups react spontaneously to yield an ether group.

The four hydrogen atoms, ortho to hydroxyl groups, are readily replaced by bromine, yielding tetrabromofluorescein, or eosin, a brilliant red dye used in biological laboratories.





If one of the carboxylic groups in the original phthalic anhydride is replaced with the sulfonic group, a closely analogous derivative may be made. Such a product is known as a sulfonphthalein. Although the mixed carboxylic-sulfonic anhydride, supposedly needed for this synthesis, is not commercially available, it happens that a closely allied substance, benzoic-sulfonic imide (saccharin), serves the purpose.



Saccharin

Phenol Red

347. Fluorescein. In a conical flask of 500 to 1000 cc. capacity place 0.1 mole of phthalic anhydride and 0.2 mole of resorcinol. Suspend the flask in an oil bath and heat the oil to a temperature of about 180°. While the oil is being heated, weigh out rapidly 8 to 10 g. of anhydrous zinc chloride and immediately grind it into a coarse powder in a small mortar. (NOTE. The zinc chloride must not be exposed to the air longer than is absolutely necessary. If the laboratory supply is obviously wet or hydrated, dry a 10 g. portion by fusing in a porcelain dish.)

As soon as the zinc chloride is ready, stir the powder into the phthalic acid-resorcinol mixture, which by this time has probably melted. Keep the oil at the temperature of 180°, and stir the mixture every few minutes. The reaction is complete when the solution becomes so viscous that further stirring is not practicable. The dark red mass consists principally of a mixture of fluorescein with zinc chloride and basic zinc salts resulting from partial hydrolysis of the original zinc salt at high temperatures.

Allow the oil to cool to 100°, and add to the reaction mixture 200 cc. of water and 10 cc. of conc. hydrochloric acid. Now raise the temperature of the oil until active boiling of water ensues. Stir the mixture from time to time after the temperature of the oil passes 110°. Careful attention is required at this time to prevent boiling over of the dilute acid. Continue the boiling until the reaction mixture has been disintegrated and all zinc salts dissolved. The insoluble residue, which should be crushed into small pieces, is fluorescein. It is collected on a Buechner filter, washed well with water and dried in the open air or on a steam bath. The yield is almost quantitative.

348. Eosin. Take a flask containing 15 g. of fluorescein and 60 cc. of alcohol outdoors or to a hood, and add, drop by drop, 11 cc. of bromine from a dropping funnel. See that the stopcock of the funnel is well lubricated in advance, and be careful not to pull out the plug, lest bromine reach the fingers. Should bromine get upon the skin, at once wash with water and follow the suggestions outlined on the inside back cover of this volume.

During the quarter-hour normally required for addition of the bromine, note that the soluble dibromofluorescein first forms. Later the tetrabromide (eosin) is formed. Being only slightly soluble in alcohol, this substance crystallizes out. After the reaction mixture has stood two hours or more, the product is collected

on a filter, washed with alcohol, and dried in the open air. Eosin prepared in this way contains one molecule of alcohol, loosely combined, and removable by heating to about 110°.

NOTE. Eosin may be prepared from fluorescein without the use of alcohol. Glacial acetic acid is used as solvent. (See Ref. 17.)

349. Sodium Eosin. Grind together in a mortar 10 g. of eosin and 2 g. of anhydrous sodium carbonate, and place the mixture in a 200 cc. flask or beaker. Add 10 cc. of alcohol and 10 cc. of water, and warm on the water bath until evolution of carbon dioxide ceases. Add 40 cc. of alcohol, heat to boiling and filter through a fluted filter into a beaker. Sodium eosin slowly crystallizes from the filtrate. It may be necessary to aid the process of crystallization by scratching the walls of the beaker with a glass rod.

Other salts of eosin may be prepared in crystalline form. See various manuals of organic chemistry for the preparation of potassium and ammonium eosin; or devise methods of preparing other salts.

350. Red Ink. If the faint green fluorescence of eosin is not considered objectionable, an acceptable red writing ink may be made according to the following recipe:

Gum arabic (gum acacia)	2 g.
Water	50 cc.
Thymol	0.2 g.
Sodium eosin	2.5 g.
Aqueous NaOH (N/10)	50 cc.

Soak the gum arabic in the water overnight; or pulverize it, stir rapidly into the water and mix thoroughly. As soon as the gum is completely dispersed in the water, add the mixture to a second solution, which is prepared in advance by dissolving the thymol, and next the sodium eosin, in the sodium hydroxide solution. Finally filter the completed mixture through a fluted filter, as described in § 76.

The gum aids in permitting the ink to flow in a desirable manner from the pen, while the thymol serves as a preservative and disinfectant. The amount of sodium eosin may of course be varied to suit personal preference.

OPTIONAL SYNTHESES

351. Phenolphthalein requires longer time for preparation than fluorescein. (Refs. 20, 21, 23, 31, 32, 33.)

Thymolphthalein. Use of thymol instead of phenol gives a beautiful blue phthalein, useful as a special indicator for pH ranges in the vicinity of 10 (see Jakimowicz, P., *Berichte*, **28**, 1876 (1895)).

Erythrosine. The iodination of fluorescein, instead of bromination, yields erythrosine, one of the approved food dyes (see Gomberg, M., *Jour. Ind. Eng. Chem.*, **14**, 1115 (1922)).

Mercurochrome. The mercuration of dibromofluorescein yields the well-known brilliantly colored disinfectant (see White, E. C., *Jour. Am. Chem. Soc.*, **42**, 2355 (1920)).

QUESTIONS

1. In what way does fluorescein differ from phenolphthalein?
2. What change occurs in the structure of a phthalein when it is treated with an alkali?
3. Explain the principle underlying the use of phenolphthalein as an indicator.
4. What is the purpose of the zinc chloride?

352. Sulfonphthaleins. When benzoic-*o*-sulfonic imide ("insoluble saccharin") is substituted for simple phthalic anhydride, a series of phthaleins of striking character is developed. Several of the well-known Clark-Lubs indicators are of this class, including the simplest of the series, which is phenol-sulfonphthalein, or "Phenol Red."

353. Phenol Red. In a small flask mix 10 g. of insoluble saccharin (the free imide containing no sodium), 25 g. of phenol and 12 cc. of conc. sulfuric acid. Heat the mixture in an electric oven at 120° for forty-eight hours. Dissolve the resulting red, viscous reaction product in 200 cc. of water to which is added enough sodium carbonate to neutralize the acids present. Steam-distil the solution until excess phenol is expelled, filter and acidify with hydrochloric acid.

The precipitated Phenol Red may be purified by redissolving in dilute sodium carbonate and reprecipitating with acid. For further details, see Freas and Provine, *Jour. Am. Chem. Soc.*, **50**, 2014 (1928).

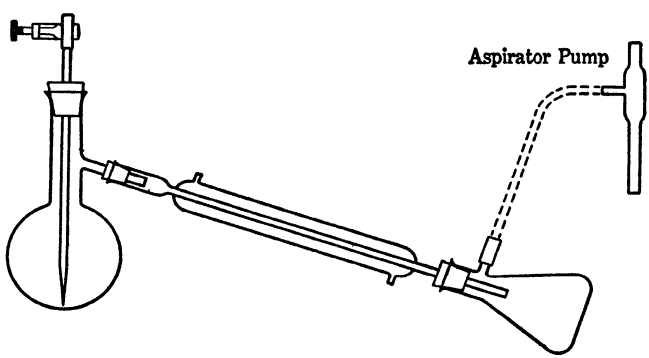
AMINO ACIDS

GLYCINE AND HIPPURIC ACID

$$CH_2Cl.COOH + 2NH_3 \rightarrow CH_2NH_2.COOH + NH_4Cl$$

354. Synthesis of an Aliphatic Amine. Ammonia normally reacts with an alkyl halide, forming first a primary amine, $R-NH_2$. To minimize the tendency of this type of reaction to go still further and produce a secondary or tertiary amine, a large excess of ammonia is used, so as to exhaust the halide as rapidly as possible. With use of a halogenated acid instead of a simple alkyl halide, an amino acid results.

355. Aminoacetic Acid—Glycine. Place a solution of 20 g. of chloroacetic acid in 40 cc. of water in a one-liter round-bottomed flask, and add that quantity of concentrated ammonium hydroxide (12 to 15N) which contains an amount of ammonia thirty



times the molal equivalent of the acid. Mix the two reagents thoroughly and allow the mixture to stand for not less than 24 hours in a room at ordinary temperature. Now remove the excess of water and ammonia by the special modification of reduced-pressure distillation shown in the accompanying figure.

First remove the major part of the ammonia by opening the water faucet slightly, thus allowing a lively stream of air-bubbles to rise in the flask and sweep through the apparatus. When the excess ammonia is gone, add boiling stones to the reaction mixture,

and distil over wire gauze. The flow of water through the filter-pump should be regulated so that a rapid distillation is maintained when the flask is heated with a rather small flame. The flame should not strike the surface of the flask above the level of the liquid, lest the adhering glycine solution inside suffer charring.

When the volume of the solution has been reduced to about 375 cc. transfer the remainder to a 600 cc. beaker, and heat the latter carefully until the volume of liquid has been reduced to about 60 cc. Now cool the solution slightly, and add about 375 cc. of methyl alcohol (95 to 100% grade). Mix thoroughly, and place in a refrigerator for six hours or more to complete the crystallization of glycine.

After crystallization is complete, decant the supernatant liquid through a Buechner filter. Add about 100 cc. more of methyl alcohol to the crystal mass, stir thoroughly, and transfer the whole mixture to the Buechner funnel. Remove the mother liquor as completely as possible by suction, and moisten the crystal mass with about 20 cc. more of methyl alcohol to remove ammonium chloride. Finally apply suction until the preparation is as free as possible from liquid, and dry the crystalline product in air, in a vacuum desiccator or in an oven at 60°. Preserve all alcoholic filtrates in a bottle specially provided for the purpose, or recover the pure solvent by distillation with fire precautions (see § 26(*b*)). Yield, 70%. The product may be purified by dissolving it in water and precipitating by addition of ethyl alcohol. The compound does not have a sharp melting point; it chars at about 235°.

REACTIONS OF AN AMINO ACID

356. Amphoterism—Two Methods of Salt Formation. (*a*) Dissolve 1 g. of glycine in 25 cc. of hot water, and drop in particles of cupric carbonate until the resulting reaction ceases. Heat to boiling, decant the clear blue liquid, and cool. Beautiful blue crystals of the sparingly soluble cupric salt separate, illustrating a reaction with the carboxyl group.

(*b*) Dissolve 1 g. of glycine in the smallest possible quantity (a few drops only) of boiling C.P. conc. hydrochloric acid. Upon cooling, crystals of the amino-acid hydrochloride separate, illustrating a reaction with the amine.

357. Effect of Formaldehyde. Dissolve 0.5 g. of glycine in 5 cc. of water in a test-tube. Add a drop of methyl red indicator solution. If the glycine is pure, a yellow color will be obtained, since glycine is nearly neutral in reaction. If a reddish or orange tint is observed, acidic impurities are present, causing a change in pH value to some point below 6. In such a case touch the solution cautiously with a stirring rod which is wet with very dilute ammonia or sodium hydroxide, thus obtaining a yellow color. Now treat a 3–5 cc. sample of conc. formaldehyde solution (15–35%) with methyl red, and neutralize it in the same way if necessary. Mix the two yellow solutions. The formaldehyde reacts with the amine group. Explain the change in color.

358. Reaction with Nitrous Acid. To a solution of about 0.5 g. of sodium nitrite in 5 cc. of cold water add a few drops of acetic acid. A few fine bubbles appear, indicating slight decomposition of the nitrous acid formed. Now drop in a few crystals of glycine. What is the gas formed? In what way could this experiment be made quantitative? What difficulties might arise?

OPTIONAL SYNTHESES

359. Glycine may be prepared by the aldehyde ammonium cyanide method. (Ref. 4.)

Alanine (α-Amino-propionic acid) may be prepared from α-bromo-propionic acid (§ 314) by a reaction similar to that of § 355. See also Refs. 23, 25, 28, 29.

Cystine from hair. This experiment illustrates the hydrolysis of protein to give an optically active natural amino acid, in this case one containing sulfur. (Refs. 5, 20, 23, 25.)

Tyrosine. (Refs. 20, 25, 28.)

Glutamic acid. (Refs. 5, 20.)

360. The Schotten-Baumann Reaction. When a primary amine is mixed with an acid chloride in the presence of aqueous alkali, the reaction to produce an amide is more rapid than that of ordinary hydrolysis.

$$RCOCl + NH_2.CH_2COOH + NaOH \rightarrow RCO.NH.CH_2COOH + NaCl + H_2O$$

361. Hippuric Acid (Benzoyl-Aminoacetic Acid). Dissolve three grams of glycine in its equivalent of 1N sodium hydroxide solution in a 200 or 300 cc. flask. Place a piece of litmus paper in the flask and add in small portions a quantity of benzoyl

chloride about 15% in excess of that required by theory to react with the glycine. After adding each portion, stopper the flask and shake well until all of the chloride has reacted. The mixture must be kept slightly alkaline, with the aid of additional sodium hydroxide if necessary. (NOTE. Benzoyl chloride is very offensive; work in a hood or outdoors.) Cool the reaction mixture under the tap if it gets warm. Finally eliminate paper or other solid material by filtration, and then place in the solution a piece of Congo Red indicator paper.

On a second piece of Congo Red paper place one drop of 6N hydrochloric acid, and then allow a few drops of water to run upon the acid spot and spread downward on the paper. Notice the appearance of a deep-purple shade, to be used for comparison.

Using an eye-dropper, and stirring the reaction mixture effectively, add just enough dilute (6N) hydrochloric acid to turn the Congo Red paper from deep red to purple, as above described. Cool the flask and allow the mixture to stand for ten minutes or more.

Collect the resulting crystalline precipitate of hippuric acid (benzoyl-glycine) upon the Buechner filter and dry in a vacuum desiccator. When the crystals are thoroughly dry, place in about 25 cc. of carbon tetrachloride and boil very gently in a beaker under a watch glass for about 5 minutes. Filter the mixture while hot, and repeat the treatment, which is virtually an extraction of benzoic acid from the preparation. Finally wash the crystals with diethyl ether and dry again in the desiccator. Yield, 85% of the theoretical. Melting point of hippuric acid, 187°.

362. Synthesis in the Human Body. If benzoic acid or a suitable one of its salts is introduced into the human digestive system, the benzoyl radical of the substance soon combines with an equivalent quantity of glycine, yielding the amide, hippuric acid, which is then eliminated in the urine, from which it may be recovered by crystallization. Sodium benzoate of chemically pure or U.S.P. grade, commonly used as a food preservative, is selected as more palatable than the free acid.

Just before retiring at night drink a solution of 5 g. of pure sodium benzoate in a half glassful of water. Next morning preserve the urine and proceed with the laboratory experiment on that same day. For each 100 cc. of urine add 25 g. of clean solid ammonium sulfate and 1.5 cc. of conc. sulfuric acid, stirring until

the salt is completely dissolved. Cool the mixture in a refrigerator for several hours, or until a maximum crystallization of hippuric acid has been attained.

Filter, and recrystallize the solid product from about 50 cc. of hot water with the aid of decolorizing carbon (see § 88, and boil the mixture ten minutes or more). Cool the final filtered solution for an hour in an ice bath, and collect the purified hippuric acid upon a filter.

363. Benzene-Sulfonamides; Hinsberg's Tests. When primary, secondary and tertiary amines, respectively, are treated by the Schotten-Baumann procedure, using benzene-sulfonyl chloride ($C_6H_5SO_2Cl$) as the acid chloride, striking differences in behavior occur, permitting identification of the type of amine. Aniline, methylaniline and dimethylaniline are successively tested as follows:

Eight to 10 drops of the amine, 10 cc. of 3N sodium hydroxide, and about 1 cc. of benzene sulfonyl chloride are mixed together and gently warmed until the odor of the chloride has disappeared. If the amine was of primary type, a sulfonamide, soluble in dilute sodium hydroxide, is formed. If secondary, an insoluble sulfonamide is formed. If tertiary, no reaction occurs, and the free amine, soluble in ether, remains.

$$C_6H_5SO_2Cl + RNH_2 + NaOH \rightarrow C_6H_5SO_2NHR + NaCl + H_2O$$

$$C_6H_5SO_2Cl + (R)_2NH + NaOH \rightarrow C_6H_5SO_2N(R)_2 + NaCl + H_2O$$

ACETYLATED AROMATIC COMPOUNDS

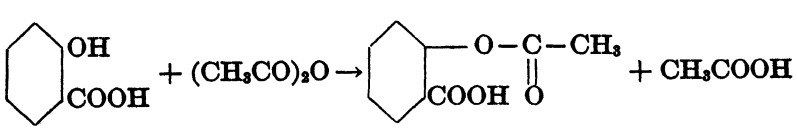
ANTIPYRETIC DRUGS

364. Acetanilide. Heat a mixture of 0.2 mole of aniline and 0.4 mole of acetic acid in a 200 cc. round-bottomed flask fitted with a long air-cooled reflux condenser. Boil the mixture over wire gauze for five to six hours at such a rate that the water, but no appreciable amount of acetic acid, escapes from the condenser. Pour the hot reaction mixture into 300 cc. of cold water and stir. Collect the crude product on a filter, and recrystallize after noting the discussion given in § 149.

365. Acetanilide. Optional Method. This compound may be prepared expeditely, and in beautiful crystalline form, by the Lumière and Barbier method. Dissolve 0.15 mole of aniline, which need not be purified, in slightly more than the theoretical quantity of dilute hydrochloric acid, and dilute the solution to 400 cc. Clarify this solution, if necessary, with the aid of decolorizing carbon. Next dissolve 0.18 mole of acetic anhydride in the clarified solution, and follow this immediately with 0.17 mole of crystalline sodium acetate. Acetanilide at once crystallizes. The mixture is cooled in an ice bath, and the product collected on a filter. See Fieser (Ref. 23) for further details.

366. Phenacetin (Acetyl-*p*-phenetidine). This widely used antipyretic drug is readily made by the Lumière and Barbier method. Corresponding molar quantities of reagents should be chosen. Acetic anhydride and *p*-phenetidine (*p*-ethoxyaniline) are used. Similarly, beautifully crystalline acetyl derivatives of the toluidines and other amines are readily prepared in the same manner.

367. Aspirin (Acetylsalicylic Acid). This ester is somewhat more favored in therapeutic practice, being much safer than acetanilide.



In a small flask heat a mixture of 10 g. of salicylic acid, 20 g. of acetic anhydride, and 10 drops of conc. sulfuric acid to 50° for 10–15 minutes, using a water bath. Now cool the reaction mixture in an ice bath, with stirring, until it thickens to a crystalline, semisolid mass. Add 150 cc. of water, stir until a thin sludge remains, and filter. The solid product is crude acetylsalicylic acid, or aspirin. Dry the product in the open air, and dissolve in the minimum volume of gently boiling ether, heated under reflux condenser over the steam bath. To the resulting solution add an equal volume of light ligroin (petroleum solvent) or petroleum ether, and allow to stand on ice for several hours. Collect the resulting purified crystals on the Buechner filter and dry in the open air. The melting point of pure acetylsalicylic acid is not definite, on account of slight decomposition. Figures around 128°–133° are likely to be obtained.

DECARBOXYLATION OF AN ACID

368. 2,4-Dinitrophenylacetic acid, whose preparation is described in § 260, spontaneously decomposes in a simple manner at temperatures of 100° to 170°, yielding a new compound whose identity is readily proven in a subsequent experiment. Incidentally, this reaction is so nicely controllable that it may be used in a study of rate of reaction. The time required for the reaction ranges from a very few minutes at temperatures over 150° to two hours or more at 100°, the velocity depending not only on temperature but the acidity of the solution. It is suggested that students working in laboratories of both organic and physical chemistry combine the organic preparative experiment with an acidimetric or gasometric determination of reaction order and rate. Consult instructors.

369. Decomposition Experiment. To a 50 cc. distilling flask fit a high range thermometer whose mercury bulb is placed at the bottom of the flask. Attach a short glass delivery tube to the side stem, and insert this tube in a test-tube or beaker containing dilute barium hydroxide solution.

Introduce 2.0 g. of 2,4-dinitrophenylacetic acid into the flask, and add 15 cc. of glycerol, which is to serve as solvent. Heat the mixture to 130°–150°; ordinarily more or less water, normally present in commercial glycerol, escapes in the form of steam. Simultaneously the decomposition reaction sets in. The temperature is slowly elevated to 170°. By this time nearly all of the gaseous product of decomposition should have escaped. When the reaction is over, pour the hot mixture into a beaker containing about 200 cc. of water. Stir the mixture for a minute or two, then cool to 15° or below. Collect the semi-crystalline precipitate on a Buechner filter, wash it with water and recrystallize from about 15 cc. of methyl alcohol. If the preparation does not readily crystallize, agitate the solution, or try seeding it with a crystal of some other preparation of the same compound, such as that called for in the next section of this experiment.

NOTE. If the decarboxylation is to be conducted more slowly, as at 100° or 125°, glycerol is not the best choice of solvent. Partial esterification of glycerol, which of course is an alcohol, may take place.

370. Identification by Melting-Point Method. After determining from theory what this product should be, obtain a few milligrams of a preparation of the substance made in a different manner. Determine successively the melting points of—

(*a*) Your preparation.

(*b*) The second preparation used for comparison.

(*c*) A mixture of about equal quantities of the two dry crystalline substances. (See § 142.)

PROBLEMS

1. What is the importance as evidence of the three results obtained from experiments *a*, *b*, *c*, above?

2. Devise two different laboratory experiments in which the rate of decomposition of 2,4-dinitrophenylacetic acid could be measured. Specify apparatus and outline the procedures.

3. Knowing that a compound such as 2,4-dinitrophenylacetic acid should have a (theoretical) melting point somewhere in the region of 180° to 190°, predict the behavior of the substance in a conventional micro melting-point experiment. In what way do you think you might have better success in determining this supposed true melting point?

4. How might you convert "TNT" into 1,3,5-trinitrobenzene, using a reaction like that of § 369?

5. What part of the standard malonic ester synthesis reminds you of this experiment?

METHYLAMINE HYDROCHLORIDE

HOFMANN REARRANGEMENT

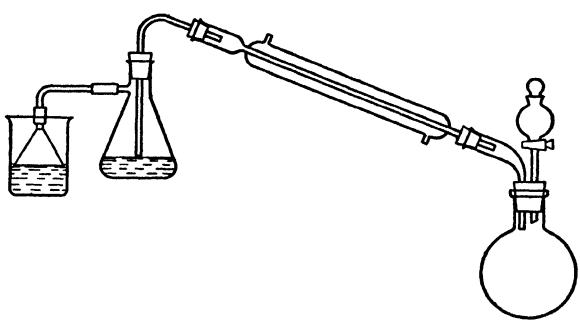
$$CH_3CONH_2 + Br_2 \rightarrow CH_3CO.NHBr$$

$$CH_3CONHBr + NaOH \text{ (presumably} \rightarrow) CH_3N{=}C{=}O$$

$$CH_3N{=}C{=}O \text{ hydrolyzed} \rightarrow CH_3NH_2 + Na_2CO_3$$

371. The foregoing succession of reactions takes place all at once in a single reaction mixture, yielding gaseous methylamine directly, but with ammonia as a byproduct. After the two gases are absorbed as hydrochlorides, the desired methylamine hydrochloride is isolated by fractional crystallization.

To a mixture of 30 g. of acetamide and 100 cc. of water in a 500 or 1000 cc. flask, cooled in an ice bath, carefully add 26 cc. of bromine. Now add to the mixture sufficient 6N sodium hydroxide solution to change its color to pale yellow. Preserve this mixture in the ice bath until required in the procedure below.



Using the apparatus shown in the accompanying diagram, place 60 g. of solid sodium hydroxide and 20 cc. of water in the main or lower flask, and heat the water in the bath almost to the boiling point. Now add slowly through the dropping funnel the yellow solution already prepared. Methylamine is at once expelled, and should all be caught in the hydrochloric acid (200 cc. of 6N) in the upper flask. Be careful not to run the reaction too rapidly, lest an excessive amount of methylamine gas escape.

When no more of the gas is evolved, as shown by cessation of formation of smoky white vapors, reduce the volume of the methylamine hydrochloride solution by boiling to about 100 cc., and continue the evaporation in an evaporating dish placed on a steam bath. When only a damp, crystalline mass remains, heat this very carefully to dryness on an "air bath"; that is, suspend the dish some distance above a quiet Bunsen flame.

Crush or powder the crystalline mass, and extract the methylamine hydrochloride with 100 cc. of ethyl alcohol. Absolute alcohol is best, but 95% alcohol will do. The extraction is performed by heating crystals and alcohol together in a flask on the water bath, filtering the extract, and cooling the filtrate. The alcoholic mother-liquor is returned to the crystal mass and the extraction, filtration, etc., repeated until a crystalline product is no longer obtained upon cooling. The residue insoluble in alcohol is mostly ammonium chloride.

NOTE. This experiment may be conducted in a more conventional set-up, with generating flask delivering its product to a condenser for downward distillation, but with the slight disadvantage of undesired water passing over with the methylamine. See other manuals.

OPTIONAL SYNTHESIS

Anthranilic acid. Preparation of an aromatic amino acid by use of the Hofmann rearrangement. (Refs. 19, 20, 23, 31, 33.)

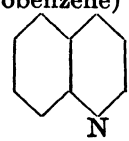
QUESTIONS

1. Referring to rules of solubility, why would you expect methylamine hydrochloride to be amenable to extraction from its mixture with ammonium chloride by the method described above?
2. Why is this method of preparation of methylamine superior to that employing the simpler reaction of methyl chloride and ammonia?
3. What is the special value of the Hofmann rearrangement in organic research?
4. Write a structural formula for methylamine hydrochloride.

QUINOLINE—THE SKRAUP SYNTHESIS

372. Under the influence of proper auxiliary reagents, the three-carbon chain in the molecule of glycerol may be simultaneously attached at one end to the nitrogen atom of aniline, and at the other end to a carbon atom ortho to the amine group. A new ring, of "heterocyclic" character, is thus produced, finally yielding the tertiary amine known as quinoline.

$C_6H_5NH_2 + C_3H_5(OH)_3$ (+ oxygen from nitrobenzene) →



$+ 4H_2O$

In a two-liter round-bottomed flask, equipped with a water-cooled reflux condenser, place successively, in the order named, 10 g. of ferrous sulfate (heptahydrate), 108 g. of anhydrous glycerol, 27 g. of redistilled aniline and 21 g. of redistilled nitrobenzene. (Anhydrous glycerol may be prepared by heating commercial glycerol to 180°.) Mix the reagents thoroughly and add slowly, with shaking, 50 cc. of conc. sulfuric acid. The resulting aniline sulfate should nearly all remain in solution.

With the reflux condenser in place, cautiously heat the flask over wire gauze until the mixture boils. (Careless heating may cause a violent ebullition.) For some time the heat of reaction is sufficient to maintain the boiling temperature and later a burner is employed. Boil the mixture for three to four hours; then cool the mixture below 100°, add 50 cc. of water and pass a current of steam through the material until the excess nitrobenzene has been expelled.

To the residue in the steam-flask add a cool solution of 85 g. of sodium hydroxide in 250 cc. of water. Again pass steam, this time collecting a mixture of water, quinoline and aniline in a second two-liter flask used as a receiver. Add 20 cc. of conc. sulfuric acid to the mixed distillate. Cool this solution to 0° and add a concentrated solution of sodium nitrite until a drop of the reaction mixture colors potassium iodide-starch mixture a deep blue or purple instantly. As this diazotization process approaches

completion, the reaction becomes slow. It is not considered to be complete until the aniline mixture, after a five minute interval with stirring, gives—instantly—a positive test for excess nitrous acid. From six to eight grams of sodium nitrite will be required.

With the aid of a water bath heat the diazotized solution for an hour, and then add a solution of 40 g. of sodium hydroxide in 150 cc. of water, cooling the flask under the tap. Steam-distil the mixture, and saturate the distillate with common salt. Extract with ether, dry the extract over potassium hydroxide, filter, expel the ether, and distil the residue of quinoline through an air-cooled condenser, preferably with the aid of an oil bath. Boiling range, about 235°–238°. Although colorless when pure, quinoline from this process has a pale yellow tint. Reduced-pressure distillation of the final product is desirable but not necessary.

SUPPLEMENTARY EXPERIMENTS

SYNTHETIC SEQUENCES

373. Students desiring the opportunity of carrying through a succession of preparations, each of which in turn becomes the starting material for the next, should note the following suggestions, none of which offers very difficult problems of technic. Taken as a whole, however, a given sequence serves as an important test of one's ability to see a relatively long problem through to a successful finish without excuses of spilling or evaporation by the way.

In searching the literature for directions for a sequence, it is advisable in general first to look up the final product proposed in that sequence. The desired method is then readily traced backward. Consult the laboratory instructor or assistant before starting any of these sequences. Outline the process in the notebook, and see that the method is approved:

1. Butyl alcohol, butyl bromide, butyl cyanide, valeric acid, butyl valerate.
2. *n*-Butyl alcohol, *n*-butyl bromide, *n*-butyl magnesium bromide, *n*-hexyl alcohol.
3. iso-Propyl alcohol, acetone, pinacol, pinacolone.
4. Chloroacetic acid, diethyl malonate, diethyl *n*-butylmalonate, *n*-caproic acid, α-bromo-*n*-caproic acid, norleucine.
5. sec-Butyl alcohol, ethylmethylketone, nitrosoethylmethylketone, dimethylglyoxime (reagent for nickel).
6. Nitrobenzene, *m*-dinitrobenzene, *m*-nitroaniline, *m*-nitroiodobenzene.
7. Nitrobenzene, hydrazobenzene, benzidine, Congo Red.
8. *o*-Nitrotoluene, *o*-nitrobenzoic acid, *o*-aminobenzoic acid, Methyl Red (indicator).
9. *p*-Nitrotoluene, 2,4-dinitrotoluene, TNT, 2,4,6-trinitrobenzoic acid, 1,3,5-trinitrobenzene.
10. Benzyl chloride, benzyl cyanide, *p*-nitrobenzyl cyanide, *p*-nitrophenylacetic acid, *p*-aminophenylacetic acid, *p*-bromophenylacetic acid.

11. Aniline, acetanilide, *p*-nitroacetanilide, *p*-nitroaniline, Para Red (pigment).
12. Aniline, acetanilide, *p*-bromoacetanilide, *p*-bromoaniline, *p*-bromochlorobenzene.
13. *p*-Toluidine, aceto-*p*-toluidide, 3-nitro-4-acetoaminotoluene, 3-nitro-4-aminotoluene, *m*-nitrotoluene.
14. Chlorobenzene, 2,4-dinitrochlorobenzene, 2,4-dinitrophenol, 2,4-diaminophenol hydrochloride (photographic developer "Amidol").
15. Bromobenzene, sodium *p*-bromobenzene sulfonate, *p*-bromobenzenesulfonyl chloride (a reagent for identification of amines).
16. Acetanilide, *p*-nitroacetanilide, *p*-nitroaniline, *p*-nitrophenylhydrazine (qualitative reagent for carbonyl group).
17. Benzene, iodobenzene (direct iodination), *p*-nitroiodobenzene, *p*-iodoaniline, *p*-iodo-acetanilide.
18. Aniline, thiocarbanilide, phenyl mustard oil, triphenylguanidine.
19. Phenol, sodium *p*-hydroxyphenyl arsonate, 3-nitro-4-hydroxyphenylarsonic acid, arsphenamine (salvarsan).
20. Phenol, phenetole, *p*-nitrophenetole, *p*-phenetidine, acetyl-*p*-phenetidine ("Phenacetin," drug).

374. Special Syntheses. Certain organic preparations are of special interest, either for their practical applications or for unusual features of technic, as follows:

3-Aminophthalhydrazide ("Luminol") emits light when gently oxidized, illustrating beautifully the phenomenon of chemiluminescence. See Huntress, Stanley and Parker, *Jour. Chem. Education*, 11, 142 (1934).

***n*-Butyl-*p*-aminobenzoate** ("Butesin"), a valuable local anaesthetic employed in salves for treatment of burns.

Camphor may be synthesized in an interesting sequence of preparations from turpentine. The sequence is well described but calls for careful workmanship. See Fisher, Ref. 26.

Diphenyl may be prepared by a pyrogenetic reaction of benzene at furnace temperatures. (Refs. 23, 25, 31.)

Iodoform, used in medical practice, may be prepared by electrolysis of potassium iodide solution in the presence of ethyl alcohol or acetone.

Phenylnitromethane is a compound which exists in two tautomeric forms, which can actually be prepared in the laboratory. See Ref. 27.

Tetraphenylpinacol illustrates a photochemical synthesis. See Ref. 31.

Triphenylmethyl is the classical illustration of a compound of trivalent carbon. (Refs. 18, 20, 28, 31.)

Naphthidine, similar in fundamental structure to benzidine, is used as an oxidation-reduction indicator. See Cohen and Oesper, *Ind. Eng. Chem. Anal. Edition,* 8, 306 (1936).

PREPARATIONS FROM THE ORIGINAL LITERATURE

375. In this assignment there is chosen an organic compound whose synthesis is not described in any laboratory manual. Furthermore, not even the original journal papers may describe exactly the procedures to be followed. Analogous preparations are then traced.

In selecting a suitable compound, it is of course commendable on the student's part to make an original and novel suggestion. Aside from this idea, however, it is highly desirable to select a compound from the field of research in which the laboratory instructor is a specialist. In such manner much more valuable assistance is likely to be available than would be in the other case.

After selecting a suitable compound, approved by the instructor, make as complete a search of the appropriate literature as your library will permit, noting the suggestions of Chap. XVII. Be sure to trace possible references through *Chemical Abstracts* down to date. Record in the notebook all methods of possible usefulness, with volume and page references.

If a course in qualitative organic analysis is given in your institution, the preparation of compounds for use either as "unknowns" or reagents for identification adds a practical touch to the assignment. Consult the instructor in such course, and note suggestions given by Kamm, *Qualitative Organic Analysis,* Second Edition, John Wiley and Sons (1932); also in the list entitled "Special Reagents" published by the Eastman Kodak Company in their regular catalog of organic chemicals.

376. The following brief list is given merely to illustrate possibilities. Many more are given by Wieland on pp. 406–407 of *Gattermann-Wieland* (Ref. 28). In the leading German univer-

sity laboratories, including that of Wieland at Munich, each student makes several of such "preparations from the literature."

Neopentane
n-Heptyl alcohol
Ethyl amyl ether
n-Butylamine
2,3-Butylene chlorohydrin
Ethoxyacetaldehyde
sym-Dipropylglycol
Crotonic acid
Aminosuccinic acid
Diethyl methylmalonate
p-Dinitrobenzene
o-Chloroiodobenzene
p-Azotoluene
m-Dimethoxybenzene
Di-*p*-tolylketone
iso-Amylaniline
Hexyl resorcinol
(para)-Methyl red
Thymolphthalein
Benzarsonic acid

INTRODUCTION TO METHODS OF RESEARCH

403. In this assignment, covering several laboratory periods, an investigation is made of some phase of an organic synthesis. Often the problem involves the challenge of a specific part of certain published laboratory directions. In other cases new procedures are developed. Frequently a simple volumetric estimation of a reaction constituent serves as the center of the investigation. Incidentally, many details in the synthetic directions given in this volume were revised as a result of such experimentation by students.

After solving the problem, or at least collecting and interpreting as much useful evidence as a reasonable time allowance permits, the experimenter is required to submit a written report prepared in the likeness of an article designed for publication in a scholarly chemical journal. The report, preferably in typewritten form, is then filed in the library or other place where students in subsequent classes may later consult it. It may well be entered in a public card index of directions for organic preparations.

The Choice of a Problem

Do not tackle too big a problem. Excessive ambition at the outset is perhaps the most common error in this type of work. A small task well performed is very much better than a large project superficially investigated. The following suggestions illustrate some of the possibilities:

1. How much time is actually required in the reflux esterification procedure during the synthesis of butyl acetate, methyl benzoate, etc.? (Use of acidimetry to determine rate of reaction.)

2. How much time is required for certain procedures requiring hydrolysis or ammonolysis of certain organic halides, such as alkyl bromides, benzyl and benzal chlorides, etc.? (Use of the Volhard method of estimation of free halide ion.)

3. What is the effect of variations in temperature in an organic reaction? (For example, the diazotization of a simple derivative of aniline at various temperatures, involving estimation of free nitrous acid.)

4. Economy of reagents: for example, the substitution of a mixture of solid sodium nitrate and concentrated sulfuric acid for the relatively expensive fuming nitric acid used in nitrations.

5. Adaptation of one of the large-scale procedures of "Organic Syntheses" to a small-scale laboratory experiment, with simplification of apparatus.

6. Development of satisfactory directions for preparation of a homologue of some well-known preparation described in laboratory manuals. For example, derivatives of *n*-propyl, isopropyl and *n*-amyl alcohols, which have become cheaply available only in recent years.

7. Preparation of an uncommon azo-dye indicator and determination of the pH range in which its aqueous solution changes color.

8. Preparation of a new organic compound not described in the literature. A new ester or amide of an uncommon acid might be selected. The compound is thoroughly purified, analyzed, and its physical constants determined as accurately as possible.

9. Problems of physico-organic type.—For example: How many extractions are really needed for a satisfactory yield in the phenol experiment, using di-isopropyl ether, toluene, etc., as extractant? (Iodometric estimation of phenol.) Or, the preparation of a boiling-point-composition graph for some two-component system, in which the concentration of one component is readily estimated by acidimetry, density determination, etc.

Preparation of the Written Report

404. The editorial style used in *Industrial and Engineering Chemistry* is perhaps the most convenient to use as a model, particularly for a typewritten paper. In this plan all literature used in the investigation is cited at the end of the article in a list arranged in order, alphabetical by author. See a recent number of this journal for method of citation, customs of abbreviation, etc. The *Journal of the Chemical Society of London*, in recent numbers, has used a more simple method of literature citation which may prove convenient, although not popular in America.

Before writing the article, prepare a written outline of the material to be presented. The following general outline may be suggestive:

Statement of the problem—what needs to be done and why.
History of previous work in the field, with text and journal citations.
General exposition of your experimental procedure.
Data—measurements, tables, arithmetical calculations.
General conclusion.
(If the problem is one of synthetic method, the final section may well consist of the exact practical directions recommended as most satisfactory.)

If you see further significant problems growing out of your project, outline these as a supplement to your paper. Of course such an outline would not ordinarily form a part of a published paper, for reasons of self-protection if nothing else. Its presence here, however, in a paper to be filed for future use in the same laboratory, is appropriate.

APPENDIX

NUMERICAL DATA

405. Common Inorganic Reagents.

Acid, acetic, "glacial"; density 1.05. This is industrially pure acetic acid, containing less than 1% of water.

Acid, hydrochloric, concentrated; density 1.18. An approx. 38% solution of hydrogen chloride in water; concentration about 12N; colorless. The common commercial grade, usually of yellowish tint, is likely to be of slightly lower concentration and density.

Acid, nitric, concentrated; density 1.42. This is the constant-boiling mixture of 68 parts by weight of HNO_3 and 32 parts of water. Approximately 16N.

Acid, nitric, (yellow) fuming; density about 1.5. This is a product which at the time of manufacture was mainly anhydrous nitric acid. By the time it reaches the purchaser it has probably decomposed slightly, and may consist of about 96% HNO_3, the balance being water and oxides of nitrogen. Approx. 24N.

Acid, nitric, (red) fuming; density about 1.54. This is HNO_3 plus a greater excess of oxides of nitrogen.

Acid, sulfuric, concentrated; density about 1.84. Industrially pure H_2SO_4, containing about 6% of water. Approximately 36N.

Acid, sulfuric, fuming; mixtures of H_2SO_4 with varying percentages of SO_3. Should be labeled with a percentage number; e.g., "20% fuming" acid is a mixture of 80 parts by weight of H_2SO_4 with 20 parts of SO_3. Often called "oleum."

Ammonium hydroxide, concentrated; density 0.90. A 28% aqueous solution of ammonia, NH_3. Approx. 15N.

406. Organic Reagents. For data on numerous organic reagents, as well as inorganic reagents not mentioned above, a chemical handbook is very desirable: for example:

Handbook of Chemistry and Physics, by Hodgman (Chemical Rubber Company).
Olsen's Chemical Annual (Van Nostrand Co.).
Handbook of Chemistry by Lange (Handbook Publishers, Inc.).

407. Boiling Points of Water and Naphthalene at Various Barometric Pressures.

Pressure, mm. Mercury	Boiling Pt. Water	Pressure	B. Pt. of Water	B. Pt. of Naphthalene
610	94.0° C.	720	98.5°	215.7°
620	94.4	725	98.7	216.0
630	94.8	730	98.9	216.3
640	95.3	735	99.1	216.6
650	95.7	740	99.3	216.9
660	96.1	745	99.4	217.2
670	96.5	750	99.6	217.5
680	96.9	755	99.8	217.8
690	97.3	760	100.0	218.1
700	97.7	765	100.2	218.4
710	98.1	770	100.4	218.7

More extended vapor pressure tables for water, and data useful in calculating other vapor pressures for naphthalene, may be found in *Int. Critical Tables*, 3, 212, 226. See also § 410.

Similar incomplete tables for other substances may be found in the *Critical Tables*, handbooks and journal literature. If the boiling point at some unreported pressure is desired, it may often be obtained approximately by extrapolation or interpolation. For this purpose the logarithms of known pressures are plotted against the reciprocals of the corresponding absolute temperatures, yielding a straight line.

408. Melting Points of Mixtures of Acetic Acid with Water.

Percentage of Acid—Degrees C.					
100%	16.67°	92.6%	6.25°	70%	−18.1°
99	14.80	89.2	2.7	60	−26.6
98	13.25	87	− 0.2	47	−19.3
96.2	10.5	75.4	−12.8	10	− 3.4

409. Saponification Values of Common Fats.

Beef tallow	196–200	Linseed oil	188–195
Beeswax	88–96	Mutton tallow	195–196
Butter fat	210–230	Olive oil	185–196
Castor oil	175–183	Peanut oil	186–194
Coconut oil	253–262	Rape seed oil	168–179
Corn oil	187–193	Sesame oil	188–193
Cottonseed oil	194–196	Sperm oil	120–137
Lard	193–203	Wool fat	82–130

410. Table of Vapor Pressures in Mm. of Mercury.

Temp. Deg. C.	Water	Ethyl Ether	*n*-Pentane	*n*-Heptane	*n*-Octane	Bromo-Benzene	*p*-Di-bromo-Benzene	α-Bromo-naphthalene
0°	5	185	183	11	3			
10	9	292	282	21	6			
20	17	442	420	36	10			
30	32	647	611	58	18	6		
40	55	921	873	92	31	10		
..								
50	92	1277	1193	141	49	17		
60	149	1729	1605	209	78	28		
70	233	2296	2119	302	118	44	4	
80	355	2994	2735	427	175	66	7	
90	525	3841	3498	589	253	98	12	
91	546		3580	607	263	102	12	
92	567		3665	625	273	106	13	
93	588		3750	644	283	110	13	
94	611		3838	664	293	114	14	
95	634		3929	684	303	118	15	
96	657		4021	705	313	122	15	
97	682		4114	726	324	127	16	
98	707		4211	748	334	131	17	
99	733		4310	771	344	136	17	
100	760		4410	795	354	141	18	
110	1075			1047	482	199	28	4
120	1489			1367	646	275	42	6
130	2026				859	373	63	9
140	2711				1114	496	89	13
150	3570				1425	649	129	19
160	4636					846	178	27
170	5940					1077	234	39
180	7520					1351	316	55
190	9413					1684	407	75
200	11659						525	102
210	14305						660	134
220	17395							179
230	20978							233
240	25100							300
250	29818							382
260	35188							482
270	41261							604
280	48104							743

SELECTION OF EXPERIMENTS

The following list of experiments is an example of a program for a one-semester course, six hours of laboratory work per week, for students who have had full normal preparation in college inorganic chemistry.

Calibration of Thermometer
Absolute Alcohol
Ethyl Iodide or *n*-Butyl Bromide
Ethylene and Ethylene Dibromide, or Amylene and Acetylene
Diethyl Ether
Acetone (Propionaldehyde for superior students)
Acetyl Chloride, or Acetic Anhydride
Fats and Soaps, Esters of Acetic Acid, or Equivalent Weight of Ester
Acetamide, or Acetanilide
Carbohydrates
Melting Point of Unknown Substance, Longer Experiment
Nitrobenzene, or 2,4-Dinitrotoluene
Aniline, or *p*-Toluidine
Phenol (for those not preparing aniline), or Phenylhydrazine Hydrochloride
Benzyl Alcohol and Benzoic Acid
Sublimation of Hexachloroethane c Anthracene
Phenyl-azo-β-Naphthylamine, or Methyl Orange

The following experiments are suitable for students of limited train ing and skill. A high percentage of success in making preparation may be expected from this list, and without great expenditure of time

Distillation of Petroleum
Recrystallization of a Crude Product
Melting Point of an Unknown Substance (Shorter Experiment)
tert-Butyl Chloride
Amylene
Acetone and Fractional Distillation
Glacial Acetic Acid
Fats and Soaps, and Esters of Acetic Acid
Hydrolysis of Ethyl Benzoate (as in § 240)
Carbohydrates
Nitrobenzene, and 2,4-Dinitrotoluene
Phenol
Benzyl Alcohol and Benzoic Acid
Sublimation of Anthracene
Phenyl-azo-β-Naphthylamine, and Methyl Orange
Fluorescein
Acetanilide (by Lumière and Barbier method)
Qualitative Tests for Elements

A second semester course will usually present many options. Most of the following general suggestions should, however, find place on the program.

A distillation under reduced pressure
Synthesis requiring use of metallic sodium
A Grignard synthesis
A preparation from benzaldehyde
A cyanide reaction; e.g., benzyl cyanide
At least one diazo synthesis
Preparation of an amino acid
A synthetic sequence
An example from qualitative organic analysis
A short research problem, with term paper

LABORATORY SUPPLIES

(*a*) Side-Shelf Reagents and Accessories

Acetic acid, conc. (glacial) and 6N
Hydrochloric acid, conc. and 6N
Nitric acid, conc.
Sulfuric acid, conc.
Ammonia, aqueous, conc. and dilute
Sodium carbonate, dilute (2N)
Sodium hydroxide, 6N

Indicator Solutions: phenolphthalein, methyl orange, methyl violet, Congo Red

Calcium chloride, anhydrous, granular
Carbon, decolorizing (Norite or equivalent)
Cotton and glass wools
Potassium permanganate, cryst.
Salt, common, dairy
Sodium acid sulfite
Sodium dichromate, dihydrate or anhydrous
Stopcock lubricant
Zinc dust

First-Aid Accessories:
Sodium bicarbonate, saturated solution
Boric acid, saturated solution
Sodium thiosulfate, 10% solution
Eye cup
(Also standard first-aid kit)

Solutions Used Occasionally:
Bromine, solution in carbon tetrachloride
Bromine water, saturated
Calcium chloride, saturated
Cleaning solvent, petroleum
Fehling's solutions, Nos. 1 and 2
Schiff's reagent
Silver nitrate, 0.05N

(*b*) Special Materials for the Experiments (Numbered by Section)

The following list indicates the quantities to be provided for the performance of each experiment by one student, and is primarily for use of the laboratory buyer. ***Caution.*** *Students are warned that the quantities specified below are rounded-off values, often somewhat in excess, and are unsuitable for experimental calculations.* Units of measurement are those generally used by American dealers in sales to educational institutions. A generous excess allowance should be provided, especially if the materials are not charged to students by individual items. Side-shelf reagents used in minor quantities are not listed. Materials for which no quantities are specified are used only in very small amounts for test purposes.

176. Cleaning Solution
Sodium dichromate.....0.01 lb.
Sulfuric acid, conc.....0.4 lb.

177. Magnesium Sulfate
"Bath" Epsom Salt.....0.1 lb.

182. Petroleum
Kerosene.....0.02 gal.

183. Recrystallization
Sulfanilic acid, tech., gray.....10 g.

184. Melting Point
Benzoic acid, C.P. ..... 5 mg.
Liquid for bath ..... 150 cc.

196. Molecular Weight
Camphor ..... 3 g.

197. Absolute Alcohol
Quicklime, tech. ..... 0.15 lb.
Alcohol, ethyl 95% ..... 0.04 gal.
Paraffin test oil ..... 0.003 gal.
Cupric sulfate, anhyd.
Potassium permanganate.

206. Ethyl Iodide
Alcohol, ethyl 95% ..... 0.01 gal.
Phosphorus, red ..... 0.006 lb.
Iodine ..... 0 06 lb.
Calcium chloride ..... 0 005 lb.

208. *n*-Butyl Bromide
Potassium bromide ..... 0.18 lb.
n-Butyl alcohol ..... 0.013 gal.
Sulfuric acid, conc. ..... 0.4 lb.
Calcium chloride ..... 0.007 lb.

210. tert-Butyl Chloride
tert-Butyl alcohol ..... 45 g.
Hydrochloric acid, conc. C. P. ..... 0.4 lb.
Calcium chloride ..... 0.02 lb.

211. Ethylene Dibromide
Sulfuric acid, conc. ..... 0.7 lb.
Alcohol, ethyl 95% ..... 0.02 gal.
Sodium hydroxide ..... 0.07 lb.
Calcium chloride ..... 0.01 lb.
Bromine ..... 0.13 lb.
Broken clay plate ..... 0.02 lb.

213. Amylene and Acetylene
Sulfuric acid, conc. ..... 0.1 lb.
tert-Amyl alcohol ..... 0.02 gal.
Calcium carbide ..... 0.03 lb.
Cuprous chloride, silver nitrate, bromine water, potass. permanganate.

218. Diethyl Ether
Alcohol, ethyl 95% ..... 0.05 gal.
Sulfuric acid, conc. ..... 0.25 lb.
Calcium chloride ..... 0.025 lb.

220. Propionaldehyde
Sodium dichromate ..... 0.2 lb.
Sulfuric acid, conc. ..... 0.25 lb.
n-Propyl alcohol ..... 50 g.
Magnesium sulfate ..... 0.01 lb.
Silver nitrate and Fehling's solutions.

224. Acetone
Sulfuric acid, conc. ..... 0.2 lb.
Isopropyl alcohol, anhydrous ..... 0.01 gal.
Sodium dichromate ..... 0.12 lb.

225. Acetic Acid
Sodium acetate, anhyd. ..... 0.1 lb.
Sulfuric acid, conc. ..... 0.1 lb.

228. Acetyl Chloride
Acetic acid, glacial ..... 0.15 lb.
Phosphorus trichloride ..... 0.12 lb.

230. Acetic Anhydride
Sodium acetate, anhyd. ..... 0.25 lb.
Acetyl chloride ..... 0.11 lb.

232. Succinic Anhydride
Succinic acid ..... 12 g.
Acetyl chloride ..... 14 g.
Chloroform ..... 0.3 lb.

234. Ethyl Acetate
Alcohol, ethyl 95% ..... 0.035 gal.
Sulfuric acid, conc. ..... 0.12 lb.
Acetic acid, glacial ..... 0.25 lb.
Magnesium sulfate ..... 0.02 lb.

235. Acetate Esters
Supply of propyl, butyl and amyl alcohols.
Acetic acid, glacial ..... 0.1 lb.
Calcium chloride ..... 0.05 lb.
Magnesium sulfate ..... 0.02 lb.

238. Equivalent of Ester
Alcohol, ethyl 95% ..... 0.04 gal.
Potassium hydroxide ..... 0.01 lb.
Standard sulfuric acid (0.5 N) ..... 100 cc.

240. Hydrolysis
Alcohol, ethyl 95%.....0.01 gal.
Ester sample.....15 g.
Sodium hydroxide.....0.03 lb.

243. Fats and Soaps
Fat or oil (see exp.).....0.02 lb.
Potassium hydroxide.....0.02 lb.
Alcohol, ethyl 95%.....0.02 gal.
Trisodium phosphate, dil. soln.

247. Acetamide
Ammonium carbonate.....0.15 lb.
Acetic acid, glacial.....0.25 lb.
Urea.....5 g.
Bromine water.

251. Carbohydrates
Acetic anhydride.....7 g.
Acetic acid, glacial.....0.05 lb.
Phenylhydrazine
hydrochloride.....0.4 g.
Chloroform.....0.06 lb.
Glucose, sucrose, starch, cotton, sodium acetate, solutions of formaldehyde, silver nitrate; Fehling's solutions.

257. Nitrobenzene
Sulfuric acid, conc.....0.2 lb.
Nitric acid, conc.....0.15 lb.
Benzene.....0.015 gal.
Urea.....1 g.
Calcium chloride.....0.02 lb.

259. 2,4-Dinitrotoluene
Sulfuric acid, conc.....0.07 lb.
Nitric acid, fuming.....0.04 lb.
p-Nitrotoluene.....14 g.
Methyl alcohol.....0.02 gal.

260. 2,4-Dinitrophenylacetic Acid
Sulfuric acid, conc.....0.2 lb.
Nitric acid, fuming.....0.07 lb.
Phenylacetic acid.....15 g.

261. *p*-Nitrobenzoic Acid
p-Nitrotoluene.....15 g.
Sodium dichromate.....0.12 lb.
Sulfuric acid, conc.....0.3 lb.
Sodium acid sulfite.....0.001 lb.
Acetic acid.....0.05 lb.

263. Aniline
Tin, metal, mossy.....0.2 lb.
Nitrobenzene.....50 g.
Hydrochloric acid, conc....0.7 lb.
Sodium hydroxide.....0.35 lb.
Salt, common.....0.05 lb.
Ether, diethyl.....0.3 lb.
or di-isopropyl.....0.05 gal.

265. *p*-Toluidine
Tin, metal, mossy.....0.1 lb.
p-Nitrotoluene.....25 g.
Hydrochloric acid, conc....0.4 lb.
Sodium hydroxide.....0.2 lb.

266. β-Phenylhydroxylamine
Nitrobenzene.....25 g.
Ammonium chloride.....0.03 lb.
Zinc dust.....0.1 lb.
Salt, common.....0.1 lb.

270. Nitrosobenzene
Sulfuric acid, conc.....0.2 lb.
Sodium dichromate.....0.03 lb.
Alcohol, ethyl 95%.....0.01 gal.

274. Sulfanilic Acid
Aniline.....0.06 lb.
Sulfuric acid, conc.....0.2 lb.

275. Sulfonic Acid (Nitro-)
p-Nitrotoluene.....20 g.
Sulfuric acid, conc.,
fuming 20%.....0.12 g.
Potassium carbonate.....0.25 lb.

278. Bromobenzene
Benzene.....0.015 gal.
Bromine.....0.3 lb.
Magnesium sulfate.....0.02 lb.
Shingle nails.

282. Phenol
Aniline.....0.03 lb.
Sulfuric acid, conc.....0.16 lb.
Urea.....2 g.
Sodium nitrite.....0.03 lb.
Ether, diethyl.....0.3 lb.
or di-isopropyl.....0.05 gal.
Magnesium sulfate.....0.02 lb.

284. Benzoic Acid
Benzotrichloride.....35 g.
Calcium hydroxide.....0.06 lb.
Sodium acid sulfite.....0.02 lb.
Hydrochloric acid, conc....0.1 lb.

285. Benzyl Alcohol and Benzoic Acid
Benzaldehyde.....40 g.
Di-isopropyl ether.....0.04 gal.
Sodium hydroxide.....0.06 lb.
Hydrochloric acid, conc....0.4 lb.
Sodium acid sulfite.....0.01 lb.
Magnesium sulfate.....0.02 lb.

286. Benzalacetone
Benzaldehyde.....25 g.
Acetone.....0.015 gal.
Chloroform.....0.06 lb.

290. Benzoin and Benzil
Benzaldehyde.....40 g.
Alcohol, ethyl 95%.....0.02 gal.
Nitric acid, conc.....0.2 lb.
Sodium cyanide.....0.01 lb.

293. Benzilic Acid
Benzil.....20 g.
Alcohol, ethyl 95%.....0.015 gal.
Potassium hydroxide.....0.05 lb.

294. Cinnamic Acid
Benzaldehyde.....15 g.
Acetic anhydride.....20 g.
Pyridine.....0.2 g.
Potassium carbonate.....0.02 lb.
Sodium hydroxide.....0.03 lb.
Acetic acid, glacial.....0.06 lb.
Benzene.

295–6. Sublimation
Hexachloroethane, crude...2 g.
Anthracene, crude.....4 g.

297. Anthraquinone
Anthracene.....2 g.
Sodium dichromate.....0.015 lb.
Acetic acid, glacial.....0.1 lb.

299. Quinone and Quinhydrone
Hydroquinone.....0.03 lb.
Sulfuric acid, conc.....0.04 lb.
Manganese dioxide, powd. .0.03 lb.

302. *n*-Octane
n-Butyl bromide.....130 g.
Sulfuric acid, conc.....0.4 lb.
Sodium, metallic .....0.04 lb.
Magnesium sulfate.....0.01 lb.

304. Triphenyl Carbinol
Diethyl ether.....0.5 lb.
Calcium chloride.....0.2 lb.
Phosphorus pentoxide.....0.03 lb.
Magnesium turnings.....0.01 lb.
Iodine, a crystal.
Bromobenzene.....30 g.
Alcohol, ethyl 95%.....0.02 gal.

307. Hydrocinnamic Acid
Alcohol, absolute ethyl 99.8%.....0.07 gal.
Sodium, metallic.....0.03 lb.
Diethyl malonate.....85 g.
Benzyl chloride.....65 g.
Ether.....0.1 lb.
Potassium hydroxide.....0.3 lb.
Hydrochloric acid, conc....0.8 lb.

309. Methyl Amyl Ketone
Alcohol, absolute ethyl 99.8%.....0.06 gal.
Sodium, metallic.....0.02 lb.
Ethyl acetoacetate.....48 g.
n-Butyl bromide.....55 g.
Sodium hydroxide.....0.1 lb.
Calcium chloride.....0.1 lb.
Magnesium sulfate.....0.02 lb.

311. Diphenylmethane
Benzene, pure.....0.04 gal.
Benzyl chloride.....40 g.
Aluminum chloride, anhyd. 0.025 lb.

314. α-Bromopropionic Acid
Propionic acid.....75 g.
Phosphorus, red.....0.003 lb.
Bromine.....0.5 lb.

316. Methylmalonic Acid

α-Bromopropionic acid ..155 g.
Sodium carbonate.....0.15 lb.
Sodium cyanide.....0.12 lb.
Sodium hydroxide.....0.2 lb.
Sodium sulfate, hydr.....0.4 lb.
Hydrochloric acid, conc....0.8 lb.
Diethyl ether.....1 lb.
Petroleum ether.....0.07 gal.
Benzene.....0.03 gal.
Magnesium sulfate.....0.1 lb.

317. Benzyl Cyanide

Sodium cyanide.....0.07 lb.
Alcohol, ethyl 95%.....0.015 gal.
Benzyl chloride.....65 g.
Magnesium sulfate.....0.02 lb.

319. α-Hydroxy α-Methylbutyric Acid

Sodium cyanide.....0.2 lb.
Methyl ethyl ketone....110 g.
Sodium acid sulfite.....0.5 lb.
Hydrochloric acid, conc....0.5 lb.
Sodium sulfate, anhyd.....0.25 lb.
Magnesium sulfate.....0.12 lb.
Benzene.....0.02 gal.
Petroleum ether.....0.05 gal.

320. p-Bromotoluene

p-Toluidine.....45 g.
Sulfuric acid, conc.....0.3 lb.
Sodium nitrite.....0.07 lb.
Cupric sulfate.....0.3 lb.
Zinc dust.....0.04 lb.
Potassium bromide.....0.3 lb.
Magnesium sulfate.....0.02 lb.

326. Phenyl-azo-β-Naphthylamine

Aniline, pure.....3 g.
Sodium nitrite, C.P.....0.01 lb.
β-Naphthylamine, pure....5 g.
Sodium acetate.....0.02 lb.
Alcohol, ethyl 95%.....0.03 gal.
β-Naphthol.....0.1 g.

331. Methyl Orange

Sulfanilic acid, white.....10 g.
Sodium nitrite.....0.01 lb.
Dimethylaniline.....7 g.

335. Phenylhydrazine Hydrochloride

Hydrochloric acid, conc....0.8 lb.
Aniline.....0.05 lb.
Sodium nitrite.....0.04 lb.
Sodium hydroxide.....0.05 lb.
Sodium acid sulfite.....0.15 lb.

339. p-Tolylarsonic Acid

Sodium carbonate, anhyd. .0.1 lb.
Arsenious oxide.....0.04 lb.
Cupric sulfate.....0.003 lb.
Sodium formaldehyde-sulfoxylate.....0.01 lb.
p-Toluidine.....15 g.
Sodium nitrite.....0.025 lb.
Hydrochloric acid, conc....0.15 lb.

343. p-Nitrosodimethylaniline

Hydrochloric acid, conc....0.5 lb.
Dimethylaniline.....25 g.
Sodium nitrite.....0.03 lb.
Benzene.....0.04 gal.
Magnesium sulfate.....0.02 lb.
Petroleum ether.....0.03 gal.

344. Crystal Violet

Dimethylaniline.....20 g.
Phosphorus oxychloride....0.02 lb.
Michler's ketone.....6 g.

347. Fluorescein-Eosin

Phthalic anhydride.....15 g.
Resorcinol.....22 g.
Zinc chloride, anhyd.....0.02 lb.
Alcohol, ethyl 95%.....0.02 gal.
Bromine.....0.08 lb.

353. Phenol Red

Insoluble saccharin.....10 g.
Phenol.....0.06 lb.
Sulfuric acid, conc.....0.05 lb.
Sodium carbonate.....0.1 lb.

355. Glycine

Chloroacetic acid.....20 g.
Ammonia, aqueous, conc...1 lb.
Methyl alcohol.....0.1 gal.
Cupric carbonate, sodium nitrite, solutions of formaldehyde, methyl red, acetic acid.

361. Hippuric Acid
Glycine.....3 g.
Benzoyl chloride.....7 g.
(Sodium benzoate- for optional method).....5 g.
Congo Red paper.

365. Acetanilide
Aniline.....0.04 lb.
Acetic acid.....0.06 lb.
or—
Acetic anhydride.....20 g.
and—
Sodium acetate.....0.05 lb.

367. Aspirin
Salicylic acid.....10 g.
Acetic anhydride.....20 g.
Diethyl ether.....0.05 lb.
Petroleum ether.....0.01 gal.

368. Decarboxylation
2,4-Dinitrophenylacetic acid.....2 g.
Glycerol.....0.05 lb.
Methyl alcohol.....0.005 gal.

371. Methylamine Hydrochloride
Acetamide.....30 g.
Bromine.....0.2 lb.
Sodium hydroxide.....0.2 lb.
Hydrochloric acid, conc....0.4 lb.
Alcohol, absolute ethyl....0.03 gal.

372. Quinoline
Ferrous sulfate, cryst.....0.03 lb.
Glycerol.....0.25 lb.
Aniline.....0.07 lb.
Nitrobenzene.....25 g.
Sulfuric acid, conc.....0.2 lb.
Sodium hydroxide.....0.3 lb.
Sodium nitrite.....0.02 lb.

377. Qualitative Tests
Cupric oxide, powd.
Copper wire.
Sodium, metallic.
Ferrous sulfate, solution.
Ferric chloride, solution.
Acetic acid, solution.
Lead acetate, solution.
Silver nitrate, solution.

381. Qualitative Analysis
Anhydrous aluminum chloride.
Chloroform.
Sodium nitrite.
β-Naphthol.
Benzene-sulfonyl chloride.
Sodium, metallic.

400. Unknown Alcohol
3,5-Dinitrobenzoic acid....0.3 g.
Phosphorus pentachloride..0.001 lb.
Alcohol, unknown.....1 g.

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