Organic chemistry

Howard Davis Haskins
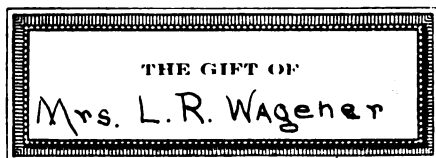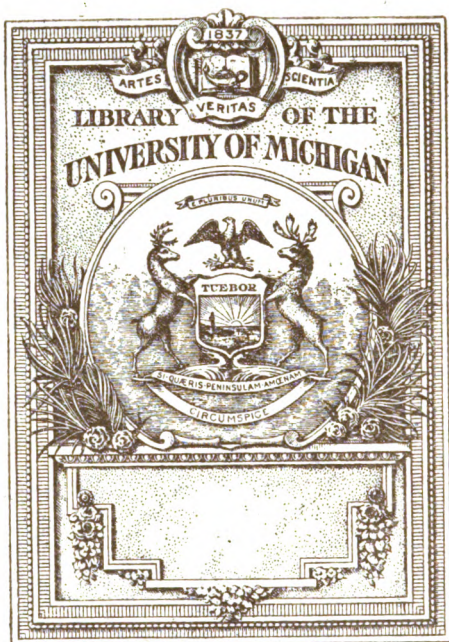
ORGANIC CHEMISTRY

INCLUDING CERTAIN PORTIONS OF

PHYSICAL CHEMISTRY

FOR

MEDICAL, PHARMACEUTICAL, AND BIOLOGICAL STUDENTS

(WITH PRACTICAL EXERCISES)

BY

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PREFACE TO THIRD EDITION

In this edition the subject matter has been rearranged to a considerable extent. Numerous revisions have been made.

The discussion of the physical chemistry topics has been amplified, and, in some cases, partly re-written (e.g., osmotic pressure and colloids).

It will gratify the author greatly to receive for consideration suggestions and criticisms from any who are using this text-book.

HOWARD D. HASKINS.

PORTLAND, OREGON.
Nov. 1, 1916.

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PREFACE TO SECOND EDITION

THE. author has endeavored to revise the entire book, striving to make it more reliable as a reference book, and more complete from the standpoint of the student of medical sciences. It is our belief that an organic chemistry text-book for the use of medical students should give the chemistry of all the organic compounds (of any importance) that enter into the study of physiology, biochemistry, and pharmacology.

H. D. HASKINS.

July 1, 1912.

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PREFACE TO FIRST EDITION

AMONG the most important of the recent advances in medical science are those relating to the chemistry of the various organic substances which enter into the composition of animal tissues and fluids, and to the physico-chemical laws which govern, or at least influence, many physiological processes. The discovery of the chemical constitution of the purin bodies, of many of the urinary constituents, and of sugars and fats, as well as the new theories of solution and catalysis, has revolutionized the teaching of biological and clinical chemistry; and in pharmacology and pharmacy a knowledge of organic and physical chemistry is almost essential. The study of these parts of chemistry is, therefore, daily coming to be of greater importance to the medical student and is already included in the curriculum of the best medical schools.[1]

As taught in the regular college classes in organic chemistry, the subject certainly absorbs too great a proportion of the medical student's time, and much is included in the course which has no bearing on

[1] The recent application by Arrhenius of certain physicochemical laws in explaining the mode of action of antitoxins, etc., is an illustration of the increasing importance of a knowledge of physical chemistry for the medical student.

his future work, and much is omitted which is of
immense importance to him.

It was with the idea of presenting in the simplest
manner the facts of organic and physical chemistry
which have an essential bearing on medical science
that the present book was written.   For the sake of
simplicity, the subject-matter is arranged in a some-
what different manner from that usually followed in
text-books for chemical students.   In the first por-
tion of the book considerable attention is given to a
description of the methods employed for purifying
and testing the purity of substances preparatory
to their further investigation.   It is to this part
of his work that the investigator in bio-chemistry
has to give his closest attention and in which he
often meets with the greatest difficulties.   A chap-
ter giving a fairly full description of the methods of
elementary analysis follows, and then a chapter on
the principles of physical chemistry as applied to
molecular weight determinations and to the theories
of osmosis, solution, etc.   Those facts of physical
chemistry which it is desirable to call attention
to that are not included in this chapter are inserted
where they can most conveniently be studied along
with the organic compounds.   The remainder of
the book includes a description of the various groups
of organic substances, and, where possible, there is
chosen, as the representative of each group, some
body of medical or biological importance.   Numer-
ous practical exercises accompany the text, and these
have been chosen and arranged so as to occupy about
four hours of laboratory work per week for a thirty-

week session. A few more advanced exercises are given for the sake of completeness, and it is left to the teacher whether or not he shall have them performed by the student. The cyclic compounds and the more complicated of the benzene derivatives may also be omitted at the discretion of the teacher.

In the Appendix will be found a schedule showing how the work of the class in our own institution is arranged so that all the members of it may do those experiments involving the use of expensive apparatus. The laboratory work is required of our students. We believe that by conducting an elementary analysis and by doing cryoscopic experiments with Beckmann's apparatus, as also preparing pure organic compounds, the student acquires an idea of accuracy and an insight into the principles of chemical methods which he cannot otherwise obtain, and which, without any doubt, will be of immense value to him in all his future work. Our experience is, also, that students of whom laboratory work is required get a grasp and understanding of the subject of organic chemistry such as others rarely acquire.

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H. D. HASKINS.

J. J. R. MACLEOD.

</div>

April, 1907.

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ORGANIC CHEMISTRY

CHAPTER I

THE NATURE AND COMPOSITION OF ORGANIC COMPOUNDS

Definition of Organic Chemistry. The various inorganic chemical compounds are classified by the chemist into groups, a group comprising all the compounds of some particular element. Thus we have the iron group, the sulphur group, and so on. On account, however, of the great number [1] of compounds containing the element carbon, the group of carbon compounds is set apart for consideration as a special branch of chemistry. Organic chemistry is that branch: *it is the chemistry of carbon compounds*. This definition is, however, not strictly accurate, for it is customary to treat of the oxides of carbon and the carbonates in inorganic chemistry.

The name organic owes its origin to the old-time belief that these compounds of carbon could be produced only by the agency of vegetable or animal organisms, by so-called vital activity. That such a notion is untenable was first shown by Wöhler, who, in 1828, obtained urea—the main organic

[1] About 150,000.

constituent of urine—by simply evaporating an
aqueous solution of ammonium iso-cyanate, his
intent being to recrystallize the latter salt (p. 278).
Since that date thousands of organic compounds
have been prepared in the laboratory without
any assistance from vital processes. In fact, a great
proportion of the compounds known to organic
chemists have never been discovered in nature,
but have been created in the chemical laboratory.

Elements and Their Detection. In organic com-
pounds carbon may exist in combination with one,
two, three, four, or even five other elements. The
most important elements present in organic com-
pounds, together with their atomic weights and
valences, are as follows:

Carbon   C, atomic wt. 12, valence IV.
Hydrogen,   H,   " " 1, "   I.
Oxygen,   O,   " " 16, "   II.
Nitrogen,   N,   " " 14, "   III and V.
Phosphorus, P,   " " 31, "   III and V.
Sulphur,   S,   " " 32, "   II, IV and VI.

Some important compounds contain the halogens
(Cl, Br, I). The presence of most of these elements
in organic compounds can be quite readily detected
by simple tests, the principal ones being incorporated
in the experiments that follow. The presence of
oxygen cannot be directly determined; it is detected
by finding the percentage composition of the com-
pound and observing that the sum of the per cents
of all the other elements is less than one hundred.

EXPERIMENTS. Detection of carbon, hydrogen, nitrogen, sulphur, phosphorus and chlorine.

(1) **C** and **H**. Dry a clean test-tube in the gas-flame. Fit it with a cork through which passes a glass tube bent at a right angle. Mix in a mortar a little dry cane sugar and ten times as much dry CuO, pour this mixture into the test-tube, cork, and dip the outside end of the glass tube into baryta solution contained in another test-tube. Heat the sugar mixture over a flame. Drops of water condense on the cool parts, showing the presence of H.[1] Cloudiness in the baryta is due to carbon dioxide, $BaCO_3$ having been formed, and indicates the presence of C. By heating, CuO is reduced; its oxygen combines with the C and the H of the organic substance to produce CO_2 and H_2O.

(2) **N** and **S**. (*a*) Triturate in a mortar some dry albumin with twenty times as much soda-lime,[2] transfer the mixture to a test-tube, and heat over a flame. Test the vapor that appears for ammonia, the presence of which proves the existence of N in the compound examined.

(*b*) Put into a dried test-tube some dry albumin equal in bulk to a bean. Add a small piece of clean metallic sodium. Heat until the mass is red-hot, then *gently* drop the test-tube into a mortar containing 10 c.c. of distilled water. The tube breaks, and NaCN and Na_2S go into solution. Grind

[1] Water of crystallization must be removed before testing for hydrogen.

[2] Soda-lime is made by gradually adding powdered quicklime to a saturated solution of caustic soda with constant stirring.

up the charred mass with the pestle. Filter and divide the filtrate into portions A, B, C, and D. To A add NaOH until strongly alkaline, then a few drops of freshly made $FeSO_4$ solution [1] and a drop of $FeCl_3$ solution. Boil this mixture two minutes, cool, and acidify with HCl. The appearance of a greenish-blue color or a precipitate of Prussian blue indicates N. To B add a few drops of a *fresh* solution of sodium nitroprusside; [2] a reddish-violet color points to the presence of S. To C add lead acetate solution and acidify with acetic acid. A brownish-black discoloration or precipitate is due to S. Neutralize D with HCl; add a few drops of $FeCl_3$ solution; a red color, which is removed by $HgCl_2$, is caused by the presence of sulphocyanide.

If sulphocyanide is not formed in examining an organic compound by this method (it is not formed if a sufficient excess of sodium is used), halogens may be tested for in the filtrate by boiling some of it with one-tenth volume of concentrated HNO_3 (HCN or H_2S driven off, prolonged boiling may be necessary to remove all the HCN) and then testing with $AgNO_3$ (precipitate of AgCl, AgBr, or AgI). In this test iodine and bromine are set free by the nitric acid and can be detected by conducting the vapor into a test-tube containing a little CS_2 (for this test heat the mixture in a short test-tube and close the tube with a stopper having a bent tube as in exp. 1).

If it is desired to detect N, S, or halogens in a liquid it is best to drop the liquid on melted sodium contained in a test-tube that is held vertically by being thrust through a hole in an asbestos pad.

[1] Sodium ferrocyanide is formed by this treatment.

[2] Formula $= Na_2Fe(CN)_5(NO)$.

(3) **Cl.** Put a little pure powdered soda-lime in a dry test-tube, add as much chloroform as it will soak up, and heat strongly. Break the tube and powder the mass in a mortar. Treat with strong HNO_3 until dissolved. Test with $AgNO_3$. A control test with soda-lime alone should give only a slight turbidity.

(4) **P.** Mix some dry nucleoprotein (or dry yeast) with twenty parts of fusion mixture (1 part Na_2CO_3 $+2$ parts KNO_3). Heat in a crucible until the mass is almost white. When cool, dissolve it in a little hot water and pour the resulting solution into an evaporating dish. Add HCl until neutral and filter. To half of the filtrate add NH_4OH until strongly alkaline, then add magnesia mixture.[1] The phosphates, formed by the oxidation of the phosphorus of the compound, cause a white precipitate. To the other half of the filtrate add HNO_3 until strongly acid, then add an equal volume of ammonium molybdate solution[2] and heat in a water bath until a *fine* yellow precipitate appears.

Having thus determined what elements are present in the organic compound that he is investigating, the chemist next proceeds to its more thorough

[1] Magnesia mixture is made as follows: Dissolve 55 gm. of pure $MgCl_2$ crystals and 70 gm. NH_4Cl in 1300 c.c. of water and add 350 c.c. of 8% ammonium hydroxide.

[2] Ammonium molybdate solution is made as follows: Dissolve 75 gm. of powdered ammonium molybdate in 250 c.c. of water with the aid of heat, and add (when cool) 35 c.c. of C.P. NH_4OH. Pour this into a mixture of 300 c.c. of C.P. HNO_3 and 675 c.c. of water while stirring vigorously.

examination. He first estimates the percentage
amounts of the various elements contained in the
substance, and then he determines its molecular
weight. He is able from these data to calculate
the empirical [1] formula. But more than one sub-
stance may have this same formula; therefore he
studies the reactions of the compound when treated
with reagents in order to get a clue as to how its
molecule is built up, that is, how its atoms are
linked together. And, finally, by causing simpler
substances, the structure of the molecules of which
is known, to become united (*synthesis*), he endeavors
to produce a substance having the same molecular
structure as his compound. If his synthetic com-
pound shows properties that are identical with the
substance under examination, the chemist then
considers that he has established with absolute
certainty the chemical construction of the com-
pound.

But all this work will end in failure unless the sub-
stance under examination be absolutely pure, i.e.,
free from admixture of any other substances. It
is necessary for us at this stage, therefore, to explain
the chief methods of purification as well as the
tests by which the purity of the substance is ascer-
tained. This will be done in the chapter that follows.

[1] The empirical formula gives merely the total number of
atoms of each element in one molecule, as $C_6H_{12}O_6$ (see
p. 98).

PURIFICATION AND IDENTIFICATION OF
SUBSTANCES

PURIFICATION OF SUBSTANCES

THE main methods of separating an organic sub-
stance in a pure state are *crystallization, sublimation,
distillation, extraction* and *dialysis.*

Crystallization. The basis of this method is the
fact that different substances are not usually solu-
ble to an equal extent in the same solvent. For
example, acetanilide can be separated from dex-
trose by dissolving the mixture of these two in hot
water; when the resulting solution is cooled, the
acetanilide crystallizes out because of its slight
solubility in cold water, while the dextrose remains
in solution. By repeated crystallization in this
manner perfectly pure acetanilide can be obtained
(see exp. below).

Inasmuch as crystallization as a method for
separation and purification of organic compounds
is invaluable, it will be well to detail specific direc-
tions for carrying it out. (1) Carefully select a
suitable solvent. Put small quantities of the sub-
stance to be purified into several test-tubes; and
add to each a different solvent (those most commonly
used are water, alcohol, ether, chloroform, benzol,

petroleum ether, acetone, and glacial acetic acid). Discard those that dissolve the substance readily. Heat each of the remaining. Choose the solvent which when hot dissolves the substance readily, but deposits crystals on cooling. The solvent should either hold the impurity in solution when cold or exert no solvent action on it whatever.

(2) Completely saturate at boiling temperature a certain quantity of the chosen solvent with the substance.

(3) Filter the hot liquid through a plaited filter, using a funnel with a short stem. (With a long-stemmed funnel crystals may separate out in the stem and block it.) Heating the funnel in hot water before filtration may be resorted to.

(4) Collect the filtrate in a beaker having a capacity twice the volume of the liquid. With too small a beaker creeping of crystals and liquid may occur.

(5) Cool slowly.[1] If crystals are deposited very quickly, redissolve with the aid of heat, and prevent rapid cooling by wrapping the beaker with a towel.

(6) Cover the beaker with a piece of filter-paper to prevent condensation-drops from falling back into the liquid and disturbing the crystallization. A watch-glass or glass plate completes the covering.

(7) Do not disturb the beaker until crystals have formed. If their appearance is greatly delayed they may often be induced to form by scratching the inner

[1] 5, 6, and 7 may be disregarded except when the form of the crystals is to be studied.

wall of the beaker with a glass rod, or by " sowing "
a crystal of the substance into the liquid.

(8) If the substance is not sufficiently insoluble
in the cold solvent, crystallization may be brought
about by slow evaporation in a loosely covered
crystallization dish.

(9) Collect the crystals on a suction-filter (reject
the crystals that have crept above the surface of the
liquid), and wash them with a little of the pure
cold solvent.

(10) Dry the crystals in a desiccator, except when
they contain water of crystallization.

EXPERIMENT. Put 20 c.c. of distilled water into
a beaker and heat to boiling on an asbestos pad.
Completely saturate it with the mixture of dextrose
and acetanilide which is furnished. Filter while
hot, and cool rapidly. When a good crop of crystals
has formed, separate them by filtration. Dissolve
in a little water and recrystallize. Repeat the proc-
ess until the filtrate from the crystals no longer
gives reduction when boiled with Fehling's solution.[1]
At least three crystallizations should be carried
through. Save the pure white crystals. After
they are dried in a desiccator a determination of
the melting-point may be made (see below).

[1] Fehling's reagent consists of an alkaline solution of cupric
hydroxide, the latter being held in solution by means of Rochelle
salt. The reagent should be freshly prepared by mixing equal
volumes of 7% $CuSO_4$ and of an alkali solution containing
25 gm. KOH and 35 gm. Rochelle salt in 100 c.c. The reagent
is of a deep-blue color, and when it is boiled with even a trace
of dextrose a red precipitate forms in it.

To test the purity of the crystals their melting-point is determined. The method of making a melting-point determination will be described in the experiments that follow. Pure crystals melt quite sharply and completely, i.e., they become completely melted within 0.5° to 1°. The crystals may be considered pure when, after repeated crystallization (preferably from different solvents), the melting-point remains constant for several successive determinations. A bath of water may be used for substances having a low melting-point (below 80° [1]).

Sulphuric acid is used for higher temperatures (up to 280°). For still higher temperatures paraffin is used. The thermometer should be one with the scale engraved on the stem. The crystals should be powdered and thoroughly dried in a desiccator.
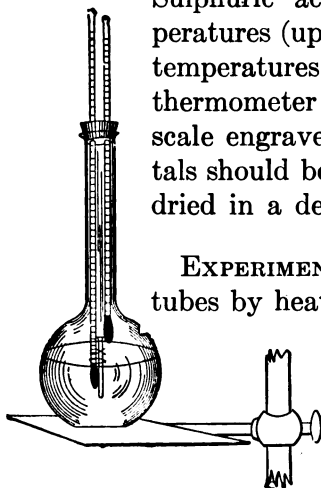
EXPERIMENT. Make melting-point tubes by heating a glass tube of 10 mm. diameter in a flame until a 2-cm. section is red, then drawing it out. A capillary tube about 1 mm. in diameter and 5 or 6 feet long, is thus

FIG. 1.

obtained. Break into lengths of 6–8 cm. and seal one end of each. Put into such a tube some powdered chloral hydrate that has been dried in a desiccator. Gentle scratching with a file

[1] All temperatures given in this book are centigrade.

will cause the particles to travel to the bottom of the tube. Attach the tube to a thermometer by means of a narrow rubber band cut off from rubber tubing, adjusting it so that the main part of the chloral will be opposite the middle of the bulb of the thermometer. Suspend the thermometer in a beaker of water so that the bulb is fully immersed. Heat the water very gradually. Note the temperature at which there is the first indication of melting (beginning transparency or collapsing against the wall of the capillary tube of any portion of the crystalline substance). Note also the temperature of complete fusion. The temperature nearest to the true melting-point is that recorded by the thermometer at the moment when minute droplets are first formed by the melting of the fine particles that are in actual contact with the wall of the capillary tube.

Into another tube put pure dried powdered urea;[1] attach the tube to a thermometer with a fine platinum wire, adjusting it as above. The bath in this case should be pure H_2SO_4 containing 30% of K_2SO_4 (to lessen fuming), contained in a long-necked Jena flask (as, for example, a Kjeldahl incineration-flask). By means of a loosely fitting cork suspend the thermometer in the flask, with its bulb dipping into the bath. In a similar manner suspend another thermometer to take the temperature of the air above the H_2SO_4. Heat gradually. When melting occurs, place the bulb of the second

[1] Where " pure urea " is called for it is best to prepare it by recrystallizing some urea from hot absolute alcohol.

thermometer midway between the meniscus of the mercury in the stem of the first thermometer and the surface of the bath; from this quickly make the reading of the air temperature (this is t in the formula below). Also measure in degrees the height of the mercury column above the surface of the H_2SO_4 ($= L$ in the formula). ·*The correction that must be added* to the observed reading (which is T) on account of the fact that the stem of the thermometer and mercury thread is cooler than the bulb, can be calculated by the formula: $L(T-t)$ (0.000154). The coefficient of expansion of mercury in glass is 0.000154. The corrected [1] melting-point of pure urea is 132.6°.

For the most accurate work in determining melting-points careful attention to a number of things is essential. Tested thermometers of a standard thickness should be used. A set of thermometers of limited range, as 0–50°, 50–100°, 100–150° graduated for 0.2°, would be desirable. The melting-point tube should have about the same thickness of wall as the wall of the bulb of the thermometer.

The crushed crystals should be sifted through a fine-mesh screen, as variation in size of the particles gives variation in melting-point. The tube should be filled for only about 3 mm. of its length, solidly packed. The initial heating may be rapid until a temperature 20° below the melting-point is reached, when the heating should be such as to cause not over 3° rise per minute, and near the melting-point 0.5° per minute. Stirring of the bath is desirable. A double bath by means of which the air about the thermometer is heated as well as the liquid insures greater accuracy. Such an apparatus can be con-

[1] The melting-points marked " corrected " are quoted from *H. Meyer's* Analyse und Konstitution der organischen Verbindungen.

structed by taking a tall Jena beaker (17–20 by 8 cm.) and suspending in it a large test-tube (20×3 cm.). Pour into the test-tube albolene (liquid vaseline) to a depth of 5 cm., and fill the beaker for nine-tenths of its depth with the same liquid. As a stirrer use a piece of gold-plated wire, coiled in a large spiral at the end to fit loosely the inside of the test-tube. Suspend the thermometers in the test-tube as shown in Fig. 1. When the temperature approaches the melting-point, stir steadily. An air temperature of only 3–7° below the oil temperature is secured, hence it is unnecessary to calculate a correction.

A method of purification applicable to certain solid substances is **sublimation.** A substance sublimes when it passes readily from the solid state to a vapor. The method is carried out as follows: A watch-glass or evaporating dish containing the substance is covered with filter-paper which has several pin-hole perforations. A funnel of slightly smaller diameter is inverted over this, the stem being loosely plugged with cotton. The dish is heated gradually until vapor passes into the upper chamber of the apparatus and condenses on the cool walls of the funnel (see exp., p. 359).

Distillation. This method is useful mainly for the purification of liquids. Certain solid substances, however, can be distilled to advantage. When the impurity is a material that will not vaporize at the temperature employed (i.e., at a temperature at which the substance itself readily vaporizes), simple distillation suffices. When, however, a mixture of volatilizable liquids is dealt with, fractional distillation has to be resorted to. This method is described in the following experiment. Certain

mixtures cannot be resolved into their constituents in the pure state by fractional distillation, such as water and alcohol, or methyl·alcohol and benzol.

EXPERIMENT.   Set up a distillation apparatus as shown in the diagram.   Into the distilling flask pour through a funnel about 300 c.c. of 70% alcohol, and drop in some short capillary tubes.   Select a cork that will fit the flask tightly.   Through a hole in the cork insert a thermometer, and hang it so that the bulb is in the stream of vapor, i.e., opposite or below the opening of the side tube. The bulb must not be below the neck nor low enough to be splashed by the boiling liquid.   Heat on a water bath.   Have four clean dry receiving f asks ready and labeled.   In the first flask collect all the distillate coming over while the thermometer registers a temperature between 78° and 83°.   Now dry the outside of the distilling flask with a cloth and change it to an asbestos pad having a hole one inch in diameter. In the second flask collect that distilling between 83° and 88°.   Flask number three is to catch the distillate between 88° and 93°.   The last flask receives all that distills over above 93°.   (Do not distill over all the water.)   Measure the amount of each fraction, and of the residue in the flask.   Drain and dry the condenser tube.
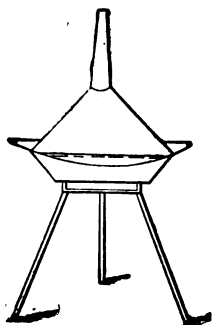
For the second distillation use a smaller distilling

FIG. 2.

flask or a small flask with a bulbed column attached
as shown in the diagram. Pour into it the fluid in
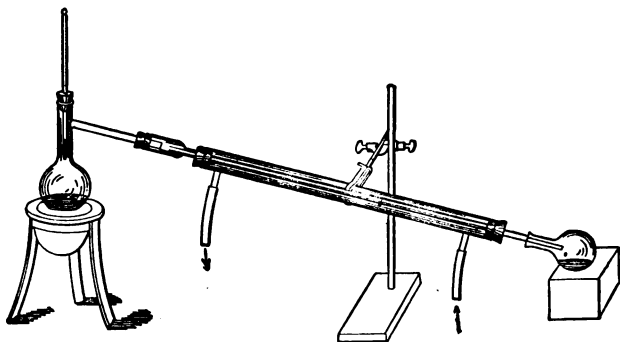
Fig. 3.

flask number one and use the latter as the first
receiving flask for the distillate. When the tem-
perature reaches 80° pour the con-
tents of flask number two into the
distilling flask, and when the tem-
perature again rises to 80° replace
flask number one by flask number
two as the receiver; also change the
distilling flask to the asbestos pad
as before. When the temperature
reaches 83° add the liquid in flask
number three to the distilling
flask, and distill until the tempera-
ture reaches 88°.
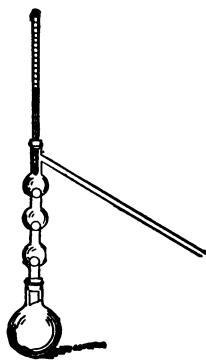
Fig. 4.

Determine the per cent of alcohol in these three
fractions by taking the specific gravity of each with
Westphal's balance (see p. 24), and comparing with
the table (p. 445). By repeated fractionating

practically all of the alcohol is brought into flask number one, and most of the water into flask number four. As, however, it is simply the alcohol that is of value in this case, redistill the first fraction only and secure a distillate coming over at 78–79°. This should contain at least 90% (by volume) of alcohol.

Distillation is sometimes carried out by bubbling steam through the mixture, which is kept at a tem-
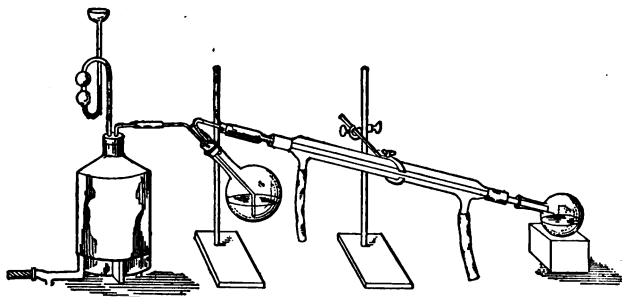
Fɪɢ. 5.

perature of at least 100°. By this means substances that boil even at 200° can be obtained in the distillate, mixed, of course, with a large quantity of water (see Fig. 5). Those substances that do not have a distinct vapor pressure at 100° will not distill with steam.

Vacuum distillation is employed in certain cases, particularly when it is desirable to lower the boiling-point in order to prevent any decomposition of the substance. Many substances decompose at a temperature below their boiling-points. The

distilling apparatus is closed up air-tight except
for a finely pointed tube which dips below the sur-
face of the heated liquid and, passing through
the stopper, is open to the air; through this tube
fine bubbles of air keep the contents of the flask
in commotion and prevent bumping.   The receiv-
ing flask is connected with a suction-pump.   A
reduction of pressure in the apparatus to 30 mm. of
mercury (atmospheric pressure being about 760 mm.)
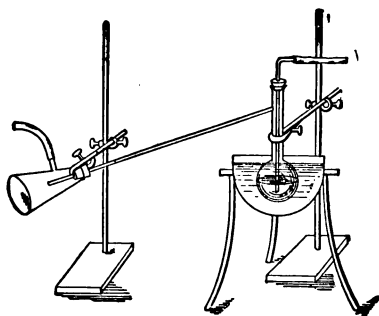
Fig. 6.

will usually lower the boiling-point of a high-boiling
substance by nearly 100°.   An ordinary suction-
pump is usually quite satisfactory for lowering the
pressure (see Fig. 6).

The test of purity of a substance that distills is con-
stancy of boiling-point.   If, after repeated frac-
tional distillation, a material is obtained which has
the same boiling-point each time and which distills
over completely at that temperature, it is most
likely to be a pure substance.

EXPERIMENT.   The boiling-point flask should be either a long-necked distilling flask which has the side tube coming off very high up near the cork, or an ordinary distilling flask into the neck of which is fitted an open tube slightly expanded at the lower end so as to fit the neck, while the latter has been dented with a blast-flame at the proper point to prevent the tube from slipping into the chamber of the flask (see Fig. 7).   In such an apparatus the vapor passes up to the cork, then descends outside the tube, heating the stem of the thermometer for the whole length of the mercury column, the thermometer being lowered sufficiently to permit this.
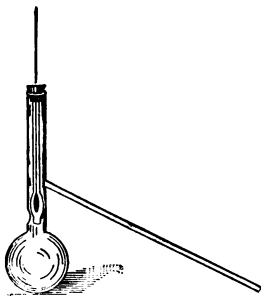
FIG. 7.

The thermometer used should be of the same kind as those specified for melting-point determination (p. 12).

Put 20 c.c. of pure chloroform into the flask; support the flask on wire gauze (it is advisable to interpose between the gauze and the flask an asbestos pad having a hole one inch in diameter). Attach a long tube as an air-condenser and place a receiving flask in position.   Heat with a small flame.   When vapor passes freely into the condenser, note the temperature.   Continue distillation until the temperature has remained constant for at least five minutes.   Take the reading as the boiling-point.   No correction is necessary except

for barometric pressure. This correction can be calculated approximately by adding to the observed boiling-point 0.038° for each mm. below 760 mm. barometric pressure or subtracting 0.038° for each mm. above this.[1] The boiling-point of chloroform at 760 mm. pressure is 61.2° (corrected).[2]

The author has devised a simple apparatus by which the boiling-point can be determined under standard pressure without the calculation of a correction.[3]

The special distilling flask (see Fig. 7) is connected with an air-tight condensing apparatus, a filtering flask (as receiver) being fitted to the end of the condenser. The side tube of this flask is connected with tubing containing air under pressure coming from the blower part of a large Wetzel suction pump. A calcium chloride tube or tower is interposed to prevent moisture getting into the flask. The compressed-air system is connected also with a barometer (or with a second distilling apparatus, as suggested below) of the older type bent in U form at the bottom; and furthermore is connected with a tube that is suspended in a tall cylinder of water. By raising or lowering this tube, the pressure in the distilling apparatus as recorded by the barometer can be brought to any height

[1] If the boiling-point is around 100° the factor of correction is 0.044, if 150° it is 0.05, if 200° it is 0.056, and if 250° it is 0.062. For water, alcohol, organic acids, and other liquids whose molecules become associated (p. 69) the figures are lower; around 50° it is 0.032, 100° it is 0.037, 150° it is 0.042, 200° it is 0.046, and 250° it is 0.051.

[2] The boiling-points marked " corrected " in this book are those given in *Traube's* Physico-chemical Methods.

[3] Smith and Menzies have recognized the desirability of securing the boiling-point at this standard pressure. They recently (1910) described an apparatus for the purpose. Their method, however, makes use of a small boiling-point bulb tied to a thermometer, and submerged in a bath.

which could occur as atmospheric pressure.   It must be remembered that a small correction of the barometer must be made for the temperature, since standard barometric pressure is 760 mm. when the scale and the mercury of the barometer are at 0°.   For example, if the temperature of the room is 15°, the apparent pressure in the apparatus must be 762 mm. (761.9 mm. if the barometer has a brass scale), in order to get the boiling-point under 760 mm. pressure.

The apparatus can be used to demonstrate the amount of change of boiling-point for definite changes of pressure.

After accurately determining the boiling-point of an absolutely pure liquid that is stable and not inclined to absorb moisture (as benzene), the apparatus can be arranged to eliminate the barometer by connecting a second air-tight distilling apparatus in which to boil the liquid that is under examination.   Now regulate the pressure so that the liquid of known boiling-point distills at a temperature corresponding to standard pressure as previously determined (read to 0.1°); then the temperature at which the other liquid distills will be the boiling-point of the latter at 760 mm.

If the liquid has a high boiling-point, shield the flask with a metal or asbestos cylinder that rests on the asbestos pad.

Extraction.   Not infrequently the most feasible method of separating an organic compound from a mixture is by extraction.   It may be extracted from an aqueous mixture by shaking the latter with an organic solvent that is immiscible with water.   If the substance that is to be extracted has a greater solubility in the organic solvent than in water, it will be extracted rapidly.   In many cases the solubility of the substance in the water may be greatly diminished by saturating the solution with a salt (as NaCl or CaCl$_2$), then, of course it will be more readily extracted.   The principle involved in extraction is that a substance soluble

in two liquids distributes itself between the two in the ratio of its solubilities in the two solvents. For instance, if a compound in aqueous solution is twice as soluble in ether as in water, then after shaking the solution with an equal volume of ether for a proper length of time, the ether will contain two-thirds of the substance and one-third will remain in aqueous solution. It follows that several successive extractions with small portions of solvent is very much more efficient than a single extraction with a large volume of the solvent. If the solubilities are in the ratio of one to two (as above), extracting once by shaking thoroughly with three volumes of ether will result in one-seventh of the original amount remaining in aqueous solution; but only one-twenty-seventh will remain if the shaking is carried out three times with equal volumes of ether.

If the solvent is one that takes up more than a trace of water, a drying agent should be used to remove the water. The substance extracted is recovered by distillation or evaporation of the solvent. If necessary, it may be purified further by crystallization, distillation, or by treatment with a different solvent.

EXPERIMENT. Measure into a separating funnel 20 c.c. of saturated salicylic acid solution and 20 c.c. of ether, stopper tightly, and shake vigorously for ten minutes. Draw off the bottom layer, and carefully pour the ether out through the mouth of the funnel into a dry flask. Return the aqueous

solution to the funnel, add 20 c.c. of ether, and continue as above. Also extract with a third portion of ether. Test about 1 c.c. of the aqueous solution with a drop of dilute $FeCl_3$, and compare the faint color reaction with the intense color given by saturated salicylic acid. Treat the combined ether extract with a small amount of dried Na_2SO_4. After it has stood for some time, pour the ether into a dry flask, and distill off most of the ether, using a hot water bath or a steam bath (have no flames near by). Now transfer the balance of the ether solution to an evaporating dish, and let the ether evaporate. Note that an appreciable quantity of crystalline residue is obtained.

Dialysis is occasionally employed for purification purposes, especially in biochemistry. It depends on the well-known fact that crystalloids can diffuse through animal membranes or parchment paper, whereas colloids cannot. Thus, to separate sodium chloride from egg protein a solution containing these is placed in a dialyzer suspended in pure running water: the sodium chloride diffuses out, leaving the egg protein in the dialyzer.

IDENTIFICATION OF SUBSTANCES

When the substance has been purified by the above methods, identification may be attempted. For this purpose its *physical properties* are studied; its color, odor, and taste are carefully noted, and determinations are made of its melting-point, boiling-point, crystalline form—including measure-

ment of the angles of the crystals,—density or specific gravity, action on polarized light, spectroscopic appearance, refractive power, and solubilities. The data thus obtained are compared with those of known substances.

Aside from the first five properties mentioned, the most universally useful one for purposes of identification is specific gravity. The method of determining this will be considered next. Descriptions of the
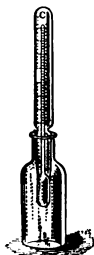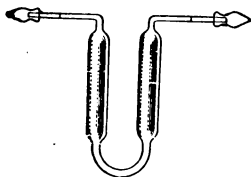
FIG. 8.   FIG. 9.

methods of ascertaining other properties will be found in the larger laboratory manuals.[1]

The specific gravity of liquids may be found by several different methods: 1. The weight of equal volumes of the liquid and of water may be successively determined in a special stoppered bottle called a *picnometer*. The temperature of both fluids at the moment of weighing must be reported.

[1] *Gatterman.* The Practical Methods of Organic Chemistry. Translated by Schober.

Mulliken. Identification of Pure Organic Compounds.

Lassar-Cohn. Laboratory Manual of Organic Chemistry; also, Arbeitsmethoden für organisch-chemische Laboratorien.

The temperature of the water taken as the standard for comparison may be 0°, 4°, or 15°. The most convenient form of picnometer is one which holds exactly 10, 25, or 50 gm. of pure boiled water at 15° (see Fig. 8). Further details are explained in the experiment below.

2. *Westphal's balance* is a very useful instrument for finding specific gravity (see Fig. 9). Riders of different sizes are used on this balance, each one representing a different decimal place in the specific gravity. This instrument gives the specific gravity of the liquid at the temperature of observation compared with pure water at 15°.

3. The *hydrometer* is another empirically graduated instrument for determining specific gravity, water at 15° being the standard. It is a glass float having a long stem; this sinks in the liquid, so that the surface of the latter is on a level with a certain mark on the stem, and the figures that are read off at that mark indicate the specific gravity (see Fig. 10).

The urinometer is a hydrometer for use with urine.

The specific gravity of a solid can be found by weighing it in the air, then reweighing it while immersed in water. This method has very little application in organic chemistry. The specific gravity of crystals or small solids can be determined by placing an accurately weighed quantity of them in a picnometer filled with some liquid in which they are insoluble (see exp. below).

Fig. 10.

EXPERIMENTS. (a) *Specific gravity of petroleum ether*. Weigh accurately an empty dry picnometer which will hold just 25 gm. of pure water at 15°; deduct from the weight 0.027 gm. for the weight of the contained air. Remove the stopper and fill with petroleum ether (boiling at 60–70°). Wrap a strip of folded filter-paper about the neck to catch the overflow, insert the stopper so that no air is left in the bottle, wipe off gently, and reweigh. When weighed, note the temperature as indicated by the thermometer in the stopper, and observe whether air has been drawn into the bottle by cooling and consequent contraction of the fluid. The difference between the two weights gives the weight of the petroleum ether, and this divided by the weight of an equal amount of water (25 gm.) gives the specific gravity as compared with water at 15°. In recording specific gravity report the temperature of observation; for example, petroleum ether $S\frac{18°}{15°} = 0.67$ means that the specific gravity of petroleum ether at 18° is 0.67 when compared with water at 15°. Also determine the specific gravity of the ether with the Westphal balance.

(b) *Specific gravity of urea*. Weigh a little test-tube which contains pure dry urea crystals. Remove the stopper of the picnometer and pour the urea into the petroleum ether. Tap the picnometer to cause the air adhering to the crystals to be dislodged. Now fill the neck with more petroleum ether, insert the stopper as before, and reweigh. The petroleum ether must be at the same temper-

ature as before. Reweigh the urea tube; by deduct-
ing this weight from the previous one find the weight
of the urea in the picnometer. To find how much
petroleum ether has been displaced by the urea
(the latter being insoluble in the former) add to
the weight of the bottle filled with petroleum
ether (exp. *a*) the weight of the urea, then deduct
from this sum the weight of the bottle containing
urea immersed in petroleum ether; the difference
is the weight of the petroleum ether displaced.
Divide this by the specific gravity of petroleum
ether; the result indicates the displacement in
cubic centimeters, or rather the weight (in grams)
of an equal quantity of water, so that the weight
of the urea used divided by this figure gives the
specific gravity. The specific gravity of urea is
about 1.33.

If the substance under investigation is known to
chemists it can generally be identified by comparing
the data gathered as to its properties with tabulated
lists [1] of boiling-points, melting-points, specific
gravities, etc. Generally an accurate determina-
tion of the boiling- or melting-point and of the
specific gravity will definitely locate the substance.
When dealing with a liquid it is advisable, if there
exists any doubt about the nature of the substance,
to determine the specific gravity at several different

[1] Such tables may be found in Physikalisch-chemische
Tabellen by *Landoldt and Börnstein*, Chemiker-Kalendar by
Biedermann (yearly editions), Melting- and Boiling-Point Tables
by *Carnelly*.

temperatures. When relying on melting-point for identification, it is of value to bear in mind that two different substances may have nearly the same melting-point, but a mixture of them melts at a far different temperature. Therefore, mix some of the known substance with that which is supposed to be identical with it and determine melting-point; if this is the same as for the unknown substance, then identification has been completed.

If the substance is still unknown or cannot be positively identified, an accurate analysis is made to determine the percentage by weight of each element present in it.

CHAPTER III

ELEMENTARY ANALYSIS

The estimation of the carbon and hydrogen present in a compound is made by combustion in the presence of cupric oxide, the end-products of combustion being carbon dioxide and water. The method is in principle exactly the same as that for the detection of carbon and hydrogen.

The combustion is carried out in a glass tube of difficultly fusible glass having an inside diameter of about 1.5 cm. This tube should be 10 cm. longer than the furnace in which it is to be heated; 85 cm. is a good length. A tube of this length is charged for combustion as follows: a short roll or spiral of copper gauze is inserted and pushed in 5 cm. from the end; moderately coarse cupric oxide (of wire form) is poured into the other end until it occupies 35–40 cm. of the tube next to the spiral; then another short copper spiral is pushed down to the coarse oxide to hold the latter in place. The next 20 cm. of the tube is occupied by the substance to be analyzed mixed [1] intimately with fine cupric oxide

[1] The substance may be placed in a little platinum or porcelain boat instead of being mixed with CuO. If a liquid is to be analyzed it is sealed in a little glass bulb having a long capillary tube and the tip of the tube is broken off when the bulb is placed in the boat.

28

(wire form) in the manner described in the experiment below. A short copper spiral (which has a wire loop attached) is inserted and finally some coarse cupric oxide may be added. Each end of the tube is closed with a rubber stopper. Through the stopper at the end nearest the fine oxide mixture passes a glass tube, which is connected with the apparatus for purifying the incoming air or oxygen. The absorption apparatus which collects the products of combustion is connected directly with a glass tube passing through the stopper at the other end.

When a tube is in service for the first time, to insure complete removal of any organic matter that might be clinging to the glass or the copper oxide, the fine oxide is used unmixed with any other substance, and the whole tube is heated for several hours while a stream of dry air is passing through. In this case an ordinary calcium chloride tube takes the place of the absorption apparatus. If moisture has collected in the tube toward the end, it must be removed by warming the tube at that point. A stream of air can be used for the combustion process. Pure oxygen, however, is very much better for substances that do not oxidize readily, because of the rapidity and completeness of combustion in its presence. With oxygen, completion of the process is indicated when the outgoing stream from the absorption apparatus causes an ember on the end of a splinter of wood to glow brightly.

It may add to the understanding of the process to trace the air or oxygen stream through the whole

Fig. 11.

Air

30
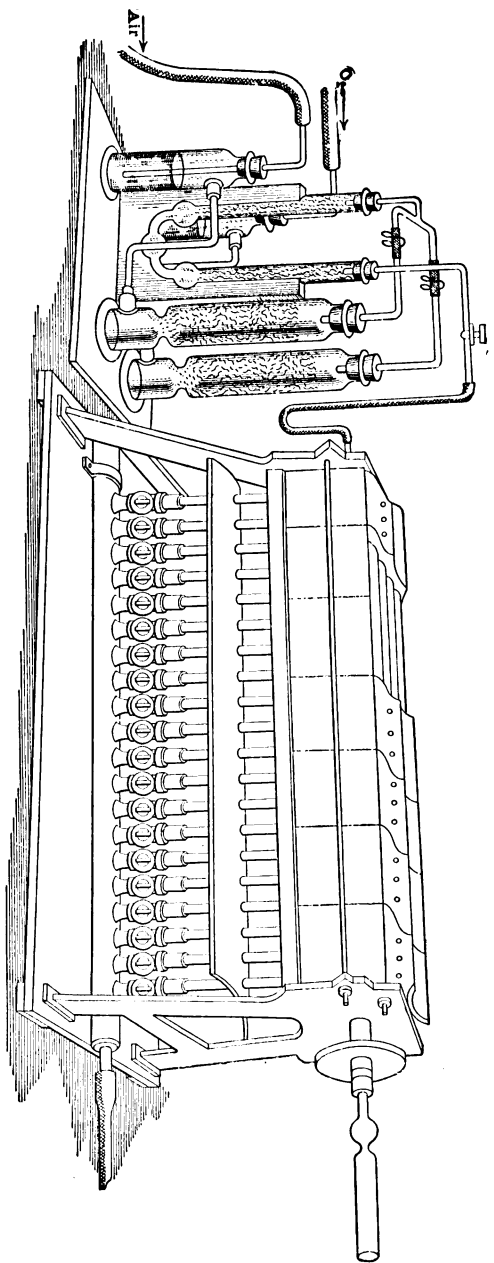
apparatus (see Fig. 11). It first bubbles through a strong solution of caustic potash, which removes most of the carbon dioxide; then passes through a large U-tube or drying-tower containing soda-lime or small pieces of NaOH, which removes the last traces of carbon dioxide; then through another U-tube containing calcium chloride, which removes
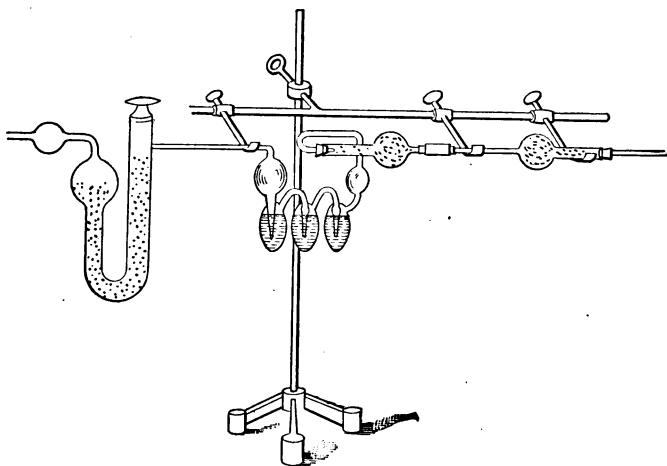
FIG. 12.

moisture.[1] The dry gas passes into the combustion-tube; when it reaches the fine copper oxide it aids the oxidation of the organic substances, and carries along with it the carbon dioxide and steam produced, also any volatilized material that has not

[1] To insure thorough drying the air is sometimes finally bubbled through sulphuric acid. In this case H_2SO_4 must also be used as the absorbent in the place of the calcium chloride tubes (see Fig. 12).

been oxidized, and brings them into contact with
the coarse copper oxide, which completes the oxida-
tion; thus the stream when it reaches the end of
the tube consists of air or oxygen containing car-
bon dioxide and water-vapor. In passing through
the calcium chloride tube of the absorption appara-
tus the water is absorbed, and finally in bubbling
through the caustic potash solution of the absorp-
tion bulbs the carbon dioxide is removed; the slight
amount of moisture picked up here is removed by
the straight calcium chloride tube (see Fig. 12).
The details of the method are given in the following
experiment.

EXPERIMENT. *Combustion analysis of salicylic
acid.* After the combustion-tube has been charged
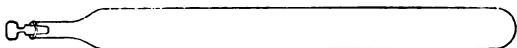
FIG. 13.

and thoroughly heated as directed above, remove
the stopper at the end nearest the air-tank, quickly
pour out the coarse oxide into a clean dry beaker,
pull out the short spiral, and finally pour out the fine
oxide into another beaker and replace the stopper.
Put the beakers and the spiral into a desiccator.
Weigh accurately a weighing-bottle containing about
0.2 gm. of pure salicylic acid that has stood in a
desiccator several days. Through a clean short-
stemmed funnel pour the salicylic acid into the mix-
ing-tube (see Fig. 13); add some of the fine oxide
carefully through the funnel in such a way that all
the crystals of salicylic acid are carried along with

the CuO into the mixing-tube. When the tube is half full, insert the stopper; hold the tube and stopper firmly and shake very vigorously. When well mixed, quickly empty the contents into the combustion-tube; rinse the mixing-tube by shaking successively with small portions of fine oxide until all the oxide has been transferred to the combustion-tube. Replace the spiral and pour in the coarse oxide. Replace the stopper, connect with the air-purifying apparatus, and start the air-stream. The $CaCl_2$ tube remains at the other end of the tube. Reweigh the weighing-bottle.

Begin lighting the burners at the end near the calcium chloride tube, starting one burner at a time and with the lowest flame possible, then very gradually increasing the flames in number and size. Do not heat near the fine oxide. In the meantime weigh the calcium chloride absorption-tube and the caustic potash bulb with its calcium chloride tube (remove the plugs before weighing), and attach them in place of the ordinary calcium chloride tube. When the coarse oxide has been brought to a dull red heat, the part of the tube that contains this having been covered with tiles, start the heating of the other end of the tube, very gradually, beginning at the far end. Stop the air-stream. When the fine oxide is heated, watch closely, and turn down the burners here if bubbles pass too rapidly through the potash bulbs. The bubbles should not go so fast that they cannot be easily counted (three in two seconds). Finally, bring the whole tube to a dull red heat (never hotter). When

bubbles cease to pass, combustion is practically complete; but continue the heating of the tube for thirty minutes (fifteen if oxygen is used) while passing a slow air-stream (which will give the proper rate of bubbles). Then begin to cool the tube by gradually turning down the burners from each end, but do not remove the tiles. Examine the end of the combustion tube for condensed water; if present, vaporize it by careful heating at that point. If oxygen is used, change to an air-stream at this point so as to clear oxygen out of the absorption tubes before reweighing. During the first fifteen minutes of cooling pass the air-stream more rapidly to sweep out of the tube all water-vapor and carbon dioxide. Disconnect the absorption tubes, put on the plugs, and allow to cool in the balance room for one hour. When cool, reweigh after removing the plugs. Do not forget to attach the calcium chloride tube in the place of the absorption apparatus. Before the combustion-tube is used for another analysis, it should be heated for an hour while dry air is passed through it. The KOH solution in the potash bulbs should not be used for more than two combustions.

The increase in weight of the U calcium chloride tube indicates the weight of the water produced by the combustion. One-ninth of this is hydrogen; therefore the per cent of hydrogen present in the substance burned can be obtained by the following formula:

$$\text{Per cent H} = \frac{\text{wt. of } H_2O \text{ produced} \times 100}{9 \times \text{wt. of substance burned}}.$$

The increase in weight of the potash bulb and straight calcium chloride tube is equal to the weight of the carbon dioxide produced. Carbon represents $\frac{3}{11}$ of this; therefore for calculating the per cent of carbon the formula used is:

$$\text{Per cent C} = \frac{\text{wt. of } CO_2 \text{ produced} \times 3 \times 100}{11 \times \text{wt. of substance burned}}.$$

The sum of the per cents of hydrogen and carbon deducted from 100 gives the per cent of oxygen.

If the substance contains *nitrogen*, oxides of nitrogen may be formed when the substance is oxidized as above. This necessitates a special modification of the method, because these oxides are absorbed by caustic potash. A long copper spiral (12–15 cm.), which has been reduced to pure copper by dipping it while hot into alcohol,[1] is put into the end of the tube nearest the weighed absorption apparatus in the place of part of the coarse oxide. When the nitrogen oxides come in contact with the hot reduced copper, they are deprived of their oxygen by the copper, and nitrogen is set free.

Of course a free stream of air or oxygen cannot be used in this case until combustion is complete, otherwise the reduced copper spiral would become oxidized and be rendered useless. The air-stream is used to clear carbon dioxide out of the tube at the start before the heat is applied to the reduced copper spiral; during combustion the air is shut

[1] By this treatment any oxide adherent to the copper yields up its oxygen to oxidize the alcohol to aldehyde.

off; when combustion is complete the air-stream is again turned on to remove all the products from the tube.

If halogens are present in the substance to be analyzed a silver spiral must be used in place of the reduced copper spiral. The silver combines with the halogens and prevents their passing into the absorption tubes, where they would be absorbed.

When sulphur or phosphorus is present lead chromate takes the place of the cupric oxide in the tube. The sulphur or phosphorus is fully oxidized, and is held in the tube as sulphate or phosphate of lead.

To estimate the nitrogen alone in an organic substance the same tube as that described above for nitrogenous substances can be employed, provided a stream of dried carbon dioxide gas, instead of air, is used for removing the gases, etc., produced by the combustion and for clearing out the nitrogen and oxygen contained in the tube before the heating is begun. The absorption apparatus in this case is a gas burette (a burette closed with a glass cock at the top) having some mercury in the bottom to act as a valve, and filled with a 40% solution of caustic potash (see Fig. 14). When bubbles no longer collect at the top of the burette and the latter remains full of caustic (i.e., when only carbon dioxide is passing out of the tube), the carbon dioxide is shut off and combustion is carried out by heating the tube gradually up to a red heat. When combustion is completed carbon dioxide is passed again until the tube is cleared of nitrogen, as shown by

the constancy of the volume of the gas in the burette. The caustic potash absorbs all the products of combustion except nitrogen. The burette is allowed to stand for an hour to come to room temperature, the alkali being leveled up in the apparatus. The caustic potash in the reservoir is brought to exactly the same level as that in the burette, and the number of cubic centimeters of gas is read off. The temperature of the nitrogen is found by placing a thermometer against the burette, with the bulb at the mid-level of the gas. The barometric reading (corrected for temperature) must also be taken. The results of the analysis are then computed by referring to specially prepared tables, which give in grams the amount of nitrogen corre-
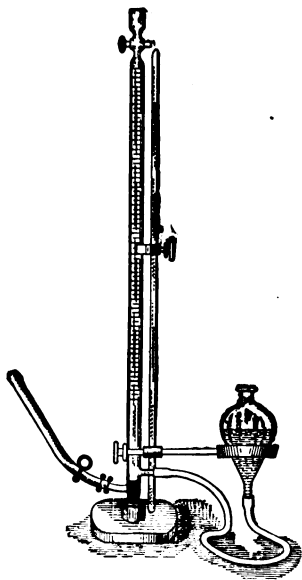
Fig. 14.

sponding to 1 c.c. of the moist gas in the burette, at various temperatures and under various pressures (see Appendix, p. 447). In order to use the table for nitrogen collected over alkali, add to the barometric pressure the difference between the vapor pressure of water and that of 40% potassium hydroxide at the temperature of observation (see Table VI, p. 450).

An easier method of nitrogen estimation is the *Kjeldahl method*, by which the nitrogen in the organic substance is converted into ammonia by heating with pure sulphuric acid.   The ammonium sulphate produced can then be treated with alkali, and the ammonia thus liberated distilled into a measured quantity of standard acid.   From the amount of this latter which is thus neutralized, the amount of nitrogen contained in the organic substance can readily be calculated.   A few organic compounds do not give a correct nitrogen estimation by the Kjeldahl method.   This method is extensively employed in biochemical analysis and will be found fully described in many of the laboratory manuals on that subject.

Oxygen is not estimated directly, but is calculated by deducting from one hundred the sum of the per cents of all the other elements present.

After the percentage composition is determined, a *provisional formula* for the compound may be found as follows: divide the percentage number of each element by its atomic weight, divide each of the resulting figures by the smallest of them (as the greatest common divisor [1]), and make use of these smaller figures, or the nearest whole number, to express the number of atoms of each element in one molecule.   The following example will illustrate this.   Alcohol was found by one analysis to contain 52.05% C, 13.13% H, and 34.82% O. Then

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[1] In many cases some other common divisor will have to be used.

C $\ 52.05 \div 12 = \ 4.337;$ $4.337 \div 2.176 = 1.993$
H $\ 13.13 \div \ \ 1 = 13.130;$ $13.130 \div 2.176 = 6.030$
O $\ 34.82 \div 16 = \ 2.176;$ $2.176 \div 2.176 = 1.000$

Therefore the formula may be C_2H_6O. The same percentage composition would, however, be shown by any substance having the formula $C_{2n}H_{6n}O_n$. It becomes necessary then to determine the number of atoms in the molecule by finding out the molecular weight; the value of n is thus discovered, so that it becomes possible to write the correct empirical formula.

CHAPTER IV

MOLECULAR WEIGHT DETERMINATION. THE NATURE OF SOLUTIONS. OSMOTIC PRESSURE. IONIZATION. SURFACE TENSION.' VISCOSITY. COLLOIDAL SOLUTIONS

MOLECULAR WEIGHT DETERMINATION BY ANALYSIS OF DERIVATIVES

THE molecular weight of a substance can be deduced from a *quantitative analysis of its derivatives*. This method is most easily applied to acids and bases. Take, for example, a simple acid, such as acetic. By analysis, its formula might be CH_2O, or any multiple thereof. By forming its silver salt and estimating the amount of silver in it, this will be found to be 64.6%. Now, knowing that the atomic weight of silver is 107.9 and that it is monovalent, and having ascertained that only one silver acetate occurs (showing that the acid is monobasic), we can see what formula agrees with this proportion of silver in silver acetate. Suppose this salt to have the formula $CHOAg$, then the per cent of Ag must be $\frac{107.9}{136.9} \times 100 = 78.8$. Obviously CH_2O cannot be the correct formula for acetic acid. If we take $C_2H_3O_2Ag$ as the formula, the per cent of silver will be $\frac{107.9}{166.9} \times 100 = 64.6\%$; therefore $C_2H_4O_2$ is the correct

formula. In the case of bases, their chlorplatinates have been found to be the most suitable compounds to form for this purpose.

MOLECULAR WEIGHT OF GASES AND VAPORS

In order to understand fully the physico-chemical nature of solutions and the subject of molecular weight determinations, it will be advisable briefly to review some of the fundamental points in chemistry that relate to these subjects. As we shall see later, gases and solutions in their physico-chemical behavior are very much alike, so that a clear conception of the gas laws, which are well known and readily tested, will enable us to study more satisfactorily the nature of solutions.

The three important gas laws are as follows:

1. *Gay-Lussac's or Dalton's law:* provided its pressure remains unchanged, every gas expands by $\frac{1}{273}$ *of its volume at* $0°$ for each degree of rise of temperature.

Thus a gas occupying a volume of 1 liter at $0°$ will occupy 2 liters at $273°$, if the pressure remains constant. In making calculations it should be remembered that the absolute temperature of $0°$ is $273°$, and therefore for any temperature above $0°$ the absolute temperature is that temperature plus $273°$. Another way of stating the law is that the volume of a gas (at constant pressure) varies directly with its absolute temperature.

2. *Boyle's law:* provided the temperature remains constant, the volume of a gas varies *inversely* as the pressure. Thus, if 1 liter of gas be compressed

into the space of 0.5 liter, the pressure has been doubled.

3. *Avogadro's hypothesis:* under the same conditions of temperature and pressure, equal volumes of all gases contain the same number of molecules.

The relative weights of equal volumes of different gases, under the same conditions of temperature and pressure, must represent the relative weights of the molecules (Avogadro's hypothesis). If, then, we take the weight of one gas as the standard, the molecular weights of other gases can readily be ascertained. Hydrogen is the gas thus chosen, and since its molecule contains two atoms, we ascribe to it a molecular weight of 2. Similarly, oxygen has a molecular weight of 32, being sixteen times heavier than hydrogen. Two grams of hydrogen at 0° and 760 mm. Hg pressure has a volume of 22.4 liters. But 2 is the molecular weight of hydrogen; therefore if we take the number of grams of any other gas equivalent to its molecular weight this amount of gas will also occupy a volume of 22.4 liters (at 0° and 760 mm.). Such a weight in grams corresponding to the figures for the molecular weight is called a *gram-molecule* or a *mole.* In consequence of Boyle's law it must follow that if we compress a mole of any gas at 0° to the volume of 1 liter, it will have a pressure of 22.4 atmospheres (i.e., 22.4×760 mm. Hg).

If, therefore, we know the volume, temperature, and pressure of a known weight of a gas, it is easy by applying the above laws to determine its molecular weight. As an example, suppose that 0.2

gm. of a dry gas has a volume of 50 c.c. at 10° and 740 mm. Hg; what is the molecular weight?

$$50 \times \frac{273}{273+10} \times \frac{740}{760} = 46.899 = \text{c.c at } 0° \text{ and } 760 \text{ mm.}$$

But a mole occupies 22,400 c.c. Then 0.2 gm. is $\frac{46.899}{22,400}$ of a mole, therefore the mole is 95.4 gm. The molecular weight is 95.4.

Vapors obey the same laws as gases. Substances, solid or liquid, that can be vaporized by heat submit to a molecular weight determination as readily as gases. In practice the determination is made either by weighing a known volume of the substance in the form of vapor, or by measuring the volume of the vapor produced from a known weight of the substance.

A known volume of vapor is weighed when *Dumas' method* is used. By this method an indefinite quantity of the substance is vaporized in a flask-like bulb by heating the bulb in an oil-bath. The neck of this flask-like bulb is drawn out to a fine tip. When all the air is displaced from the bulb, and the substance is completely vaporized, the tip is sealed off in a flame. The temperature of the bath is recorded, also the barometric pressure. After cooling, the weight of the substance in the bulb and the capacity of the latter are accurately determined, and from these data the molecular weight can be calculated. This method, while simple in principle, is nevertheless tedious in practice.

A much more useful method for general purposes is that of *Victor Meyer*, in which the volume of a known weight of vapor is ascertained by finding how much air is displaced in a closed apparatus when the substance changes to a vapor.

The apparatus,[1] as shown in the figure, consists of an elongated bulb continued above into a long neck closed at the top by a rubber stopper; from the neck passes a side tube, which is connected by heavy rubber tubing with a gas burette. The bulb is suspended in a wide tube having a bulb-like expansion at its closed end (the upper two-thirds of this tube should be wrapped with asbestos paper) and containing some liquid with a boiling-point 40°–50° above the vaporization temperature of the substance.

EXPERIMENT. Fill the bulb of the outer tube two-thirds full of distilled water; suspend the inner tube in it by means of a cork (this will have to be cut in two and then wired together again). By means of this cork also hang a thermometer in the steam-chamber and insert a bent glass tube as a steam-vent. Now boil the water (start the heating very gradually). When the thermometer registers a constant temperature, i.e., the boiling-point of

[1] An excellent modification of this apparatus has been made by Bleier and Kohn, by which, instead of measuring air-displacement, the increase of pressure (the volume of gas in the apparatus being constant) due to the vaporization is measured by means of a mercury manometer. Before making an estimation the air-pressure in the apparatus is lowered by a suction-pump.

the water,[1] connect the side tube with the gas burette and cork the inner tube tightly with a rubber stopper. Bring the water in the burette and in the reservoir to exactly the same level. If there is no variation from this level for 5–10 minutes, the apparatus is ready for making an estimation. The entire column of air in the narrow tube has now come to the temperature of the steam surrounding it. Remove the stopper of the inner tube and place in position (supported by the glass rod, which fits the extra branch tube and extends into the neck of the main tube, as shown in Fig. 15) a little sealed glass bulb containing a known weight of pure chloroform (the bulb having been weighed before and after filling). Fit the stopper tightly, and wait
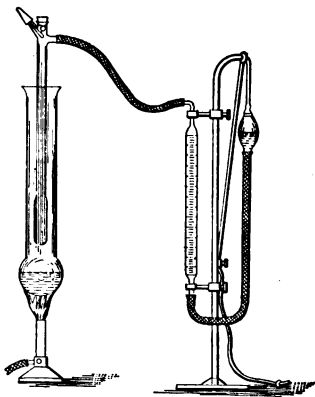
FIG. 15.

a few minutes to determine whether the volume of the air in the apparatus remains constant (as indicated by the level of the liquid in the burette). When constant, fill the burette exactly to the cock by raising the reservoir after having brought the burette into communication with the outer air by means of a two-way cock (either the cock of the

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[1] Boiling-point at 735 mm. barometric pressure is 99.1°, at 740 mm. 99.3°, at 745 mm. 99.4°, at 750 mm. 99.6°, at 755 mm. 99.8°, and at 760 mm. 100°.

burette or one specially inserted in the rubber tubing connection). Then close the cock, so that the burette communicates only with the air of the system. Now drop the bulb to the bottom of the Victor Meyer tube by pulling the rod. Some glass wool has been put into the bottom of the tube to prevent injury. Vapor forms and hot air is pushed over into the burette. Level up the water in the burette with that in the reservoir. When the level remains absolutely constant for a few moments, close the cock of the burette. After allowing sufficient time for cooling, measure the volume of the air displaced into the burette in exactly the same way as in nitrogen estimations (see p. 37), correcting for temperature, also for aqueous (see Appendix) and barometric pressure, and convert to the volume at 0° and 760 mm. (see p. 43). To make the calculation divide 22,400 (22.4 L.) by the number of cubic centimeters of air displaced, and multiply this quotient by the weight of the chloroform vaporized; the product gives the weight of a gram-molecule of the substance, and the same figures express the molecular weight.

THE NATURE OF SOLUTIONS. OSMOTIC PRESSURE

In their physical properties solutions are very different from gases. In attempting to apply gas laws to substances in solution, it is evident that other methods than those used in the case of gases must be adopted to measure the pressure of the dissolved substance. We measure the pressure of a

gas by means of a manometer, but it is obviously impossible to measure the pressure of a dissolved substance by the same means, for the only pressure which the manometer can record is that of the solution against the walls of its container.

By making use of membranes, however, much can be learned about the behavior of solutions. If a permeable membrane, for example, parchment paper, is arranged as a partition to separate a solution of some substance from pure solvent, the two liquids refuse to remain separate. The solvent passes through the membrane in both directions; but a more important fact is that the dissolved substance diffuses through the membrane into what was at the start pure solvent, and this process continues until the liquids on both sides of the membrane become solutions of the same concentration. The energy manifested in this process of dialysis is *diffusion pressure.*

If, however, a much less permeable membrane is used, diffusion of a solute through it is prevented; but the solvent readily passes through in both directions. Such a membrane is called a **semi-permeable membrane.** In a properly constructed apparatus this membrane can be used to demonstrate a kind of pressure different from diffusion pressure.

The best example of a semi-permeable membrane is a film of copper ferrocyanide. Since this film of copper ferrocyanide is too fragile to exist unsupported, it may be deposited in the pores of a

porous cell (such as is used for electric batteries), and the following method may be used in preparing it.

A fine-grained porous cell, about four inches long and one inch inside diameter, is closed with a perforated rubber stopper, through which passes a glass tube connecting with a suction-pump. The cell is set in water, and the water is sucked through the pores; then placed in acid, then in water again. By this means the pores of the cell are thoroughly cleaned, and air is removed. When clean, the cell is placed in a concentrated solution of copper sulphate, and suction is maintained until the pores are completely filled. The inside and the outside of the cell are then thoroughly washed with distilled water, after which it is filled with 3% potassium ferrocyanide solution and the outside is exposed to a solution of copper sulphate. The copper sulphate reacts with the potassium ferrocyanide in the pores of the porous pot, so that a fine gelatinous precipitate of copper ferrocyanide is deposited. After standing for a day the cell is washed in water.

If a solution of cane sugar is placed inside and the cell is suspended in water, water will pass into the cell and cause the volume of fluid in this to increase so that, by connecting a vertical glass tube with the cell by means of a rubber stopper, fluid will mount up in it to a very considerable height. If, however, the liquid in the cell is put under pressure, increase in the volume of the solution is prevented. When the system is in equilibrium because the

pressure is so regulated as to prevent change in volume, exactly as much solvent diffuses out as diffuses in. By connecting a manometer with the apparatus, the pressure can be determined by measuring the height of the column of mercury. Large pressures are reported as atmospheres pressure, 760 mm. of mercury constituting one atmosphere. The pressure thus demonstrated is called **osmotic pressure.**

No membrane has ever been prepared that is absolutely semi-permeable, that is, impermeable to all solutes. A carefully prepared membrane is truly semi-permeable to sugar solutions and to colloidal solutions.

The **law of osmotic pressure** as stated by van't Hoff and modified by Morse, is as follows: The osmotic pressure of a substance in dilute solution is the same amount of

FIG. 16.

pressure that the substance would exert, if it could exist in the form of a gas at the same temperature as the solution, and if it were confined to the same volume as that occupied by the pure *solvent.* If this law could be applied to concentrated solutions, it would mean that the osmotic pressure
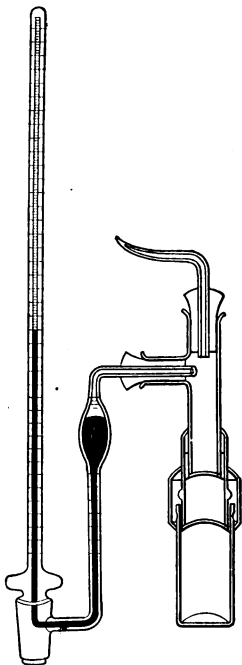
of all weight-normal[1] solutions at 0° must be 22.4 atmospheres,[2] because this is the pressure of a gram-molecule of gas when compressed to the volume of a liter.   On the basis of this, we can calculate what the pressure of any dissolved substance in solution will be.   Thus, the pressure x of a 1% solution of cane sugar may be calculated from the proportion: Molecular   solution : 1% solution :: 22.4   atmospheres : x.   Solutions which obey the laws of osmotic pressure most accurately are those that are not more concentrated than one-tenth gram-molecular.

Since a comparison has been made of osmotic pressure to gas pressure, it will be of interest to test the application of the gas laws to solutions.

1. According to Gay-Lussac's law, the osmotic pressure should be proportional to the absolute temperature.   That this is so is proved by observations like the following: A 1% solution of cane sugar at 14.2° has an osmotic pressure of 510 mm. Hg, and at 32° of 544 mm. Hg.   According to calculation it should be 540.6 mm. Hg (practically agreeing with the finding), thus

$$510 \times \frac{273+32}{273+14.2} = 540.6.$$

[1] By gram-molecular solution is meant the molecular weight of a substance in grams dissolved in an amount of solvent sufficient to make 1 L. of solution, while by weight normal is meant a solution in which the gram-molecular weight of substance is dissolved in 1000 gm. of solvent.

[2] The pressure should be 22.28 atmospheres according to Morse, because 1000 gm. of water at 0° has a volume greater than 1000 c.c.

2. According to Boyle's law, the osmotic pressure should be inversely proportional to the volume of the solution, or, in other words, directly proportional to the concentration. The osmotic pressures of glucose solutions of varying strengths (at the same temperature, 0°), have been found to be as follows:

Gram-molecules in 1000 gm. Water.	Osmotic Pressure in Atmospheres.	
	Observed.	Calculated.
0.1	2.40	2.23
0.2	4.65	4.45
0.3	7.01	6.68
0.4	9.30	8.91
0.5	11.65	11.14

It will be noticed that the pressures observed are almost proportional to concentration. Thus the pressure for the 0.4 molar solution is twice that for the 0.2, but that for the 0.2 is not quite twice that for the 0.1. The figures given above as calculated pressures are the gas pressures which the glucose would be under if in the form of a gas at 0° and confined to the same volume as the solvent. These values are a little lower than the actual osmotic pressure. Some would explain the variation as due to hydration of the sugar molecules.

3. According to Avogadro's hypothesis, all equi-molecular solutions (i.e., solutions in which the weights of the solutes in a given quantity of solution bear the same ratio to one another as the molecular weights of those substances) ought to

have the same osmotic pressure. This has been found to be the case.

Osmotic pressure is related to vapor pressure. When a substance is dissolved, the vapor pressure of the solvent is lowered. This lowering of vapor pressure explains why the freezing-point of a solution is lower, and the boiling-point higher than that of the pure solvent. Increase of osmotic pressure is proportional to decrease of vapor pressure, so that the osmotic pressure of a solution has been calculated from its vapor pressure. This was found to agree closely with the pressure that was actually measured in an osmotic apparatus.

The tendency of the pure solvent to diffuse through a membrane, so as to pass into the liquid having a lower vapor pressure, can be seen more clearly by considering the effect of a difference of vapor pressure in an experiment that does not involve the use of a membrane. Thus if pure water is put in one beaker and an aqueous solution in another, and both are set in a jar that is then tightly closed, vapor will pass off from the water, but will be taken up from the air of the jar by the liquid of lower vapor pressure, that is, by the solution. The transfer of water from one beaker. to the other is equivalent to distillation. If it were possible to subject the solution in the one beaker to pressure without at the same time cutting the liquid off from contact with the air of the jar, and also without changing the pressure on the pure water, the vapor pressure of the solution could be raised by the increasing hydrostatic pressure until

finally it equaled that of the pure water; and in consequence distillation would cease. It will be seen, therefore, that pressure can be used to bring two liquids into equilibrium with each other as regards vapor pressure. It is not at all improbable that the equilibrium brought about in an osmotic apparatus by exerting pressure on the solution in the cup, is due to the establishing of an equilibrium of the vapor pressures of the two liquids.

One of the recent theories as to the *method* of the passage of the solvent through the osmotic membrane supposes that the solvent is in the form of a vapor while passing through the capillary pores of the membrane. The vapor condenses, and is taken up by the solution on the other side of the membrane. According to this theory the pores do not become wet, and the process is simply distillation. If we accept this theory, we have no difficulty in understanding why the molecules of the dissolved substance do not diffuse through the pores of a perfect semi-permeable membrane.

The old-time theory that the membrane acts as a sieve, preventing the molecules of the solute from passing through the pores, is no longer tenable. It has been recently shown that an osmotic membrane can be prepared by partially blocking the pores of an unglazed porcelain plate by means of a fine non-gelatinous precipitate. When the diameter of the capillaries has been reduced to about 0.5μ, the plate can be used to demonstrate osmotic pressure (but the pressure will be only a fraction of the true osmotic pressure of a solution). But

the diameter of these capillaries is from 500 to 1000 times the diameter of the molecules of most solutes, so that it is evident that there is no sieve-like action involved.

A theory that is favored by some supposes that the solvent passes through the membrane by first dissolving in the substance of the membrane and then passing out of the membrane on the other side. This theory does not take those membranes into account that are known to have capillary pores. By using a non-porous membrane, as, for example, a rubber membrane, and by using solvents that dissolve in rubber, the osmotic pressure of solutions made with such solvents can be demonstrated. Such an experiment does not prove anything whatever about the mode of action of a membrane in the case of aqueous solutions. It may well be true that osmosis occurs through *some* membranes in accordance with this solution theory; but the theory certainly does not apply to all membranes.

Biological Methods for Measuring Osmotic Pressure. If, in the experiment with cane sugar solution, instead of placing the cell in water we had placed it in a solution of cane sugar weaker than that contained in the cell, then the osmotic pressure would not be so great as in the previous case, because water would pass into the cell only until the strength of the solution came to be the same as that outside it. This fact leads us to an important conclusion, viz.: that the relative strengths of two solutions can be ascertained by seeing whether osmosis occurs between them when they are separated from each other by a semi-permeable membrane.[1]

[1] This is true only for solutions of diffusible substances in the same solvent (water).

In the case of the copper ferrocyanide cell above described, we could determine this fact by measuring the pressure inside the cell. If, however, we employed a closed sac of some semi-permeable membrane filled with one of the fluids, then we could, by suspending this sac in some other fluid, tell if osmosis had occurred, by seeing whether the sac became distended or the reverse. In the case of the red blood-corpuscles we have a structure analogous to this. The envelope of the corpuscles acts like a semi-permeable membrane; it allows water to diffuse through it, but not salts.[1]

Now a corpuscle contains a solution of salts and hæmoglobin, and if it be placed in a fluid containing in solution the same number of molecules as is contained in the fluid inside the corpuscle, then no osmosis will occur in either direction and the corpuscle will remain unchanged in volume Such a fluid which is isosmotic with the fluid inside the corpuscle, is called an *isotonic* solution. If the corpuscle be placed in a solution which is weaker than that contained in the corpuscle, then water will diffuse in and the corpuscle will distend and may ultimately burst. Such a solution is said to be *hypotonic*. If the corpuscle be placed in a solution which is stronger than that of its fluid contents, then water will diffuse out of the corpuscle, so that the corpuscle will shrink. Such a solution is called *hypertonic*.

This change in the volume of the corpuscle may be observed under the microscope, and a quantitative expression also of the change in volume of the corpuscle may be obtained by using an instrument called a hæmatocrit. This consists of a graduated narrow capillary tube, about seven centimeters long. At one end the tube is widened so as to give space in which the fluids may be mixed. Blood is drawn into the capillary by means of a syringe, and its volume accurately measured. The pipette is then closed at each end by small,

[1] The corpuscles are, however, permeable for alcohols, free acids, and alkalies, ammonium salts, and urea. This explains why an isotonic NaCl solution remains isotonic after the addition to it of urea, in spite of the increase in osmotic pressure.

accurately fitting, metal plates held in position by a spring. The tube is then placed horizontally in a rapid centrifuge and rotated so that the corpuscles are thrown to the outer end. The graduation mark at which the column of corpuscles stands is then noted.

In another tube a drop of the same blood is mixed with an equal volume of the fluid the molecular concentration of which it is desired to determine. The exact amount of blood and fluid taken is read off from the graduations of the tube. The two fluids are then sucked into the wide part of the tube and mixed by means of a fine platinum wire. The tube is then closed and centrifuged. If the corpuscles stand at the same level as for blood alone, then we know that the solution is isotonic with the blood-corpuscles, which means that they must also be isotonic with the plasma. If the column of corpuscles be longer, then we know that their volume must have been increased, and that the fluid under examination is hypotonic. If the column of corpuscles be shorter, the solution is hypertonic.

Isosmotic solutions are isotonic to the same cells provided the cells are impermeable to the solutes. Solutions of corresponding concentration (as, one-tenth gram-molecular) of most organic compounds (except metallic salts, acids and bases) are isosmotic. Solutions of ionizable substances (p. 65) have a greater osmotic pressure than solutions of other substances, since each ion has the same effect as a molecule; a comparison is made in the following:

Cane sugar (not ionized)...... 1.00
Potassium nitrate............ 1.67
Sodium chloride.............. 1.69
Calcium chloride............. 2.40

These figures are the *isotonic* coefficients of the substances. The coefficient 1.69 for NaCl means that a 0.1 gram-molecular solution of salt has the same osmotic pressure as a 0.169 gram-molecular solution of sugar.

In the case of living cells it seems to be necessary to take into account selective permeability; for example, the tadpole when immersed in a hypertonic sucrose solution (as 8%) shrinks noticeably in twenty-four hours, there being no injury to the epithelium; on the other hand, a tadpole placed in hypotonic sucrose solution (3%) does not swell up, because the epithelial cells are not noticeably permeable to water passing in.

EXPERIMENTS. (1) *Osmotic Pressure Effects in a Vegetable Membrane.* With a sharp razor shave thin slices from a red beet, mount some on a slide, and examine microscopically. Now add a drop of saturated NaCl on the slice and observe that the red substance shrinks away from the wall of the cell, the hypertonic solution having caused *plasmolysis*.

(2) *Osmotic Pressure Shown by an Animal Membrane.* The large end of an egg contains an air space, open the shell at this point, removing it down to where the egg membrane joins the shell. Cross three strips of parchment paper five inches long over the membrane, and stretch them on to the shell; bind them down to the shell beyond the middle of the egg with a rubber band, bend the strips back on themselves and hold them fast with another rubber band. Coat the bands with

melted paraffin to keep them in position. The parchment gives support to the membrane. To the opposite end of the egg attach a small upright glass tube by applying melted paraffin, run a long needle down the tube and carefully drill a hole through the shell and egg membrane; or the shell may be nicked before fastening the tube in position, and a wire can be put down the tube to break the egg membrane. Immerse the egg in distilled water. After standing some time the egg contents will have swollen sufficiently to force egg white up into the tube.

(3) *Osmotic Pressure Shown by an Inorganic Membrane.* (*a*) Select a long narrow crystal of $CuSO_4$, tie a thread about the middle, and fasten the thread to a glass rod lying across the top of a small beaker so that the crystal hangs in potassium ferrocyanide solution. A copper ferrocyanide membrane forms, which becomes distended by the passage of water through it toward the copper sulphate.

(*b*) Fill the bent portion of a U-tube with melted agar solution, cool, and when solidified fill one limb with $CuSO_4$. solution, the other with potassium ferrocyanide solution. On standing several days a sharply defined area of copper ferrocyanide forms midway in the agar.

(*c*) Drop a small lump of $CaCl_2$ into a test-tube half filled with saturated potassium carbonate solution. On standing a membrane develops and *grows*, making plant-like forms.

MOLECULAR WEIGHT OF SUBSTANCES IN SOLUTION

Theoretically, the measurement of the osmotic pressure would be a simple enough way of determining the molecular weight, but, in practice, the method can seldom be used.

Is there then no easily measurable physical property of solutions which depends on their molecular concentration, and which will, therefore, bear a relationship to the osmotic pressure? The vapor pressure of a solution is proportional to its osmotic pressure, but the method of determining vapor pressure is a difficult one to carry out. It has been found that the temperature at which a solvent freezes is lowered when a substance is dissolved in it, and that the amount of this lowering, or *depression of freezing-point*,[1] is for dilute solutions proportional, not, in general, to the chemical nature of the substance, but to the number of molecules of substance dissolved in a given volume. (The same holds true for the elevation of boiling-point, which can be most easily demonstrated with the McCoy apparatus. This method, however, will not be described here.) This being so, it follows that all gram-molecular solutions in the same solvent must lower the freezing-point to an equal extent. The depression of freezing-point produced by a gram-molecular quantity of a substance dissolved in 1000 gm. of the solvent (weight normal solution) varies for different solvents:

[1] *Cryoscopy* is a name given to freezing-point determination.

	Depression of Freezing-point.
For water................	1.86°
" benzol...............	5.00°
" phenol...............	7.20°
" acetic acid...........	3.90°

These figures are called the constants[1] (or C) of the solvents. They correspond, therefore, to an osmotic pressure of 22.4 atmospheres. The osmotic pressure of solutions is commonly calculated from the depression of freezing-point.

The apparatus in which the freezing-point determinations are made is known as Beckmann's. This consists of a large test-tube, to contain the substance, suspended in a somewhat larger test-tube, so as to form an air-jacket between the two tubes. The outer test-tube is placed in a freezing-mixture of iced water and salt contained in an earthenware jar (which has been wrapped round with flannel to diminish the heat-conduction). The freezing-mixture is stirred with a loop of wire as represented in the diagram. In the inner test-tube is suspended the bulb of a Beckmann thermometer. This thermometer does not give absolute readings of temperature as does an ordinary thermometer. It is used only for demonstrating the difference in temperature at which two solutions freeze, or with certain modifications it may

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[1] The constants are not always exactly those given above. Some substances give a depression of freezing-point of water, indicating a constant of 1.84 or 1.85. The constant for benzol seems to vary from 4.85 to 5.15.

be used to tell the different temperatures at which
two solutions boil. Before the thermometer is
used for freezing-point determinations, the menis-
cus of the mercury column must be adjusted so that
it stands within the scale (high up) at the tempera-
ture at which the solvent used
freezes or crystallizes. To make
this adjustment the bulb of the
thermometer is placed in iced
water, and if it be found that
there is too much mercury to
bring the meniscus within the
scale, then the upper end of the
thermometer is tapped with the
fingers so as to cause the mer-
cury at the top of the reservoir,
which is connected with the
upper end of the thermometer
tube, to fall to the bottom and
so to become disconnected from
the mercury column in the
thermometer tube. Should the
meniscus of mercury stand be-
low 3.5° on the scale at the
freezing-point of water, or of

the other solvent used, then the thermometer must
be inverted, and, by tapping, more mercury can
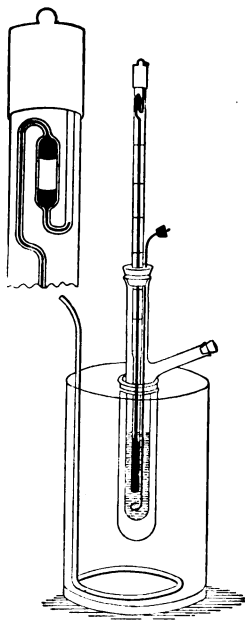be added to that in the tube.

For making the actual freezing-point determina-
tion the inner tube of the apparatus is partly filled
with the solution under examination so that the
latter comes a little above the bulb of the ther-

mometer (see Fig. 17).   The tube is then placed
directly in the freezing-mixture until the mercury,
having fallen to its lowest level, begins to rise
again, when the tube is removed quickly from
the freezing-mixture and placed in the larger test-
tube, as before described.   The cooling is then
proceeded with until the meniscus of mercury
stands at a constant level.   During cooling, the
fluid is kept constantly in motion by means of a
platinum wire, bent into a loop as shown in the
diagram.   The reading is taken whenever constant
and compared with the reading obtained when pure
water (or whatever other solvent is used) is frozen.
This difference is designated by Δ.[1]

Since this constancy of C, for any given solvent,
is the point on which the method depends, the
following experiment should be performed to
demonstrate that for water C has the value given
to it above.

EXPERIMENT.   Weigh out a quantity of pure
dry urea corresponding to one-tenth its molecular
weight in grams (i.e;, 6 gm.); dissolve this in 100

[1] Care should be taken that the supercooling is not excessive.
If this be so, a correction is necessary because the formation
of ice (pure water) lessens the volume of the solution, and there-
fore, the depression is greater than it would be if only a trace of
ice is present.   For aqueous solutions 1.25% of Δ is added to
the observed thermometer reading for each degree centigrade
of supercooling, and by deducting from the freezing-point
of water the true Δ is obtained.   For example, suppose the
freezing-point of water was at 3.9°, that of the solution at 2°,
and the point of supercooling at 0°. Δ is 1.9, then 1.9(2 × .0125)
= .047, 2 + .047 = 2.047;   3.9° − 2.047 = 1.853 = corrected Δ.

gm. of distilled water. Compare the freezing-point of this solution, corrected for supercooling, with that of pure water. Does it correspond to the constant? Also calculate the molecular weight of urea.

In determining the molecular weight of any substance we must first of all choose the most suitable solvent for it, and, in an accurately weighed quantity of this dissolve an accurately weighed quantity of the substance under examination. Knowing what C for our solvent is,—in other words, through how many degrees centigrade the freezing-point of our solution would be lowered were a gram-molecular quantity per 1000 gm. of solvent taken,—if we find the freezing-point actually lowered to a less extent than this, we know that less than a gram-molecule must have been dissolved, the actual amount less than this being proportional to the difference from C recorded by the thermometer. In other words, the depression observed, represented by Δ, is to C as the strength of the solution used $\left(\dfrac{\text{weight of substance}}{\text{weight of solvent}}\right)$ is to that of a gram-molecular solution (or rather a solution containing a gram-molecule dissolved in 1000 gm. of solvent).

$m = \dfrac{S}{L} \times \dfrac{C}{\Delta}$, where S equals the weight of substance used in grams; L, the weight of solvent in grams. $\dfrac{S}{L}$, when solved, gives a decimal fraction

expressing what part of 1 gm. of the substance is dissolved in 1 gm. of solvent; therefore, to calculate the gram-molecule (the amount dissolved in 1000 gm. of solvent), m must be multiplied by 1000, and M equals the *molecular weight* in the equation $M = \dfrac{S}{L} \times \dfrac{C}{\Delta} \times 1000$. For example, the Δ of a 1% cane-sugar solution is about 0.054°. The molecular weight of the sugar, therefore, is $\dfrac{1}{100} \times \dfrac{1.86}{.054} \times 1000 = 344$. According to the formula $C_{12}H_{22}O_{11}$, it should be 342.

The Δ of blood and of urine are sometimes determined. That of human blood is about 0.55°. In case of drowning the blood is diluted, therefore the Δ is much less; if a person were killed before being thrown into the water, the Δ would not be lessened.

IONIZATION

The method is not, however, applicable to all substances, even though they be readily soluble in the above-mentioned solvents. Weight normal solutions of certain substances give a depression of freezing-point greater than C. Practically all metallic salts and most acids and bases when in aqueous solution are included in this category. To demonstrate this let us determine the depression of freezing-point produced by a gram-molecular solution of sodium chloride.

EXPERIMENT. Weigh out one-tenth (one-twentieth is better) the molecular weight of pure sodium chloride in grams and dissolve, as in the

case of urea, in 100 c.c. of pure distilled water. Determine the depression of the freezing-point in Beckmann's apparatus. It will be found to be considerably greater than 1.86 (viz., about 3.35).

Knowing that 1.86 is Δ for a gram-molecular solution, it is easy to calculate how many gram-molecules per liter (X) a Δ of 3.35 will represent, thus:

$$1.86 : 1 :: 3.35 : X; \quad X = 1.8.$$

To ascertain the actual osmotic pressure of the sodium chloride solution we must accordingly multiply 22.4 atmospheres by 1.8. This gives us about 40 atmospheres.

What then is the cause of this deviation from the law? The answer to the question is furnished by comparing the *electrical conductivities* of the two classes of solutions. Solutions of those substances which obey the above law will be found to be bad conductors of electricity—*non-electrolytes*—whereas solutions of those substances which do not obey it will be found to be good conductors—*electrolytes*. This discovery, viz., that solutions which conduct electricity appear, from the determination of Δ, to have a greater number of molecules than those which do not conduct, has led chemists to the conclusion that certain of the molecules in such solutions must split up into smaller parts, called *ions*, and that it is only when this *dissociation* of molecules into ions takes place that it is possible for the solution to conduct electricity.

In fact, our whole conception of the conduction of electricity in solutions is based on this hypothesis. It is supposed that every molecule of substance is charged with positive and negative electricity, which in the intact molecules so neutralize each other that we do not appreciate either. When these molecules are suspended in solution, however, they show a greater or less tendency to split up into ions, one set of which carries positive electricity and the other negative electricity. These ions wander about the solution much as if they were independent molecules. Each ion has as much effect as a molecule on the vapor pressure, osmotic pressure and depression of freezing-point of a solution.

When an electrical current is passed through a solution that has undergone dissociation into ions, the ions tend to collect at the two poles and yield up their electrical charges. Those which collect around the positive element or anode are called *anions*, and those collecting around the negative element or cathode are called *cations*. Anions are charged with negative electricity, and cations with positive electricity. Examples of anions are OH and the acid portion of salts, for example SO_4, Cl, etc.; the cations include hydrogen and metals. The ionization is not dependent on the passage of an electrical current.

EXPERIMENT. Put some strong NaCl solution in a beaker, add a few drops of phenolphthalein solution, and immerse in the liquid a pair of battery

plates, consisting of a strip of sheet zinc and one of copper soldered together at one end and separated in the liquid. As the electric current passes, sodium ions travel to the copper plate and give up their electric charges, becoming metallic sodium, which attacks the water and forms NaOH in the region of the copper plate, therefore a pink zone (OH ions) appears at this point.

When solutions of acids undergo ionization, the cation H is that which confers the acidic properties on the solution. An un-ionized acid does not act like an acid; for example, H_2SO_4 dissolved in toluene does not ionize and will not give off hydrogen in the presence of zinc. (Also see experiment under Picric Acid, p. 342). On the other hand, hydrogen itself, as the gas or in solution, shows no acid properties. We must assume, therefore, that the hydrogen ion is something different from the hydrogen atom. The same is true for other ions: they are not the same as the free elements or groups of elements; they are particles with opposite electrical charges which behave like molecules. It is believed that the ions are hydrated, i.e., that they hold molecules of water intimately attached to them.

It is usual to designate the various ions by their symbols, affixed to which is the sign $\cdot$ for cations (e.g., $H\cdot$, $Na\cdot$, etc.) and $'$ for anions (e.g., Cl', NO'_3 etc.). Some ions, however, must carry two or more units of electrical charge, for otherwise in the case of such a substance as H_2SO_4 there would be an excess of positive electricity in the molecule.

The ion SO_4 must therefore carry two charges of negative electricity and be represented by the sign SO''_4. The valence of the ion usually agrees with the number of unit charges of electricity that it carries.

The coefficient of dissociation therefore indicates what proportion of the molecules have become split up into ions. For molecules that can yield only two ions it cannot be greater than 2, but for those splitting into more than two ions it may exceed this number. In the concentration of a 1% solution KCl has a coefficient of 1.82, KNO_3 1.67, K_2SO_4 2.11, Na_2CO_3 2.18 and NaCl 1.9.

The amount of dissociation that a salt or acid undergoes in solution depends very largely upon the dilution: the greater the dilution, the greater the dissociation.[1]

EXPERIMENT. To 1 c.c. of a saturated solution of cupric bromide add water gradually 5 drops at a time, and note the color changes. When the color is a pure blue, determine whether it is exactly the same color as that obtained by diluting solutions of cupric sulphate, nitrate and acetate. What is the blue color due to?

In a solution of an electrolyte there is a condition of equilibrium between molecules and ions. The molecules are continually dissociating, and simultaneously ions are uniting to form molecules. Re-

[1] For example, $\dfrac{N}{500}$ HCl is completely dissociated.

actions between electrolytes proceed rapidly, because as fast as ions are used up more molecules ionize in the effort to restore equilibrium. Even the trace of H and OH ions present in pure water (H ions amounting only to 0.0000001 gm. H per L at 22°) facilitates chemical reactions. Most organic compounds react slowly because of absence of ions.

EXPERIMENT. To two test-tubes add a few c.c. $AgNO_3$; to one add NaBr, and to the other C_2H_5Br.

Occasionally, when a substance is dissolved, instead of dissociation there occurs a fusion or *association* of several of the molecules. In such a case the freezing-point or boiling-point method would give too high a molecular weight. This tendency to form complex molecules most frequently manifests itself when the organic substances contain hydroxyl or cyanogen groups, and when chloroform or benzol is used as the solvent. For example, an 8% solution of phenol in benzol gives a depression of freezing-point indicating a molecular weight of 188, which is twice that called for by the formula, C_6H_5OH.

Many liquids polymerize, that is, their molecules *associate*. The condition of water is supposed to be represented by $(H_2O)_4$.[2] Liquid hydrocyanic acid is $(HCN)_6$. Next in order of association are formic acid and methyl alcohol. The greater the polym-

[2] H_2O, $(H_2O)_2$, and $(H_2O)_3$ are also present. Some chemists think that liquid water is a mixture of these three (but mainly dihydrol), and that ice is trihydrol, while steam is monohydrol.

erization of the solvent, the greater will be the dissociation of an electrolyte.

EXPERIMENT. Add a few drops of phenolphthalein solution to 25 c.c. of neutral ethyl alcohol, then one drop of concentrated NH_4OH; there is no color change. Dilute with water, and a pink color develops because ionization of the hydroxide takes place in the dilute alcohol.

HYDROLYTIC DISSOCIATION

Many salts when dissolved in water, undergo not only electrolytic dissociation, but also hydrolytic dissociation. The latter is induced by the action of water. Three classes of salts are hydrolyzed:

1. Salts formed by the combination of a weak base with a strong acid. The hydrolysis is illustrated in the following equation:

$$FeCl_3 + HOH = FeCl_2OH + (H + Cl).$$

2. Salts formed from a strong base and a weak acid:

$$KCN + HOH = (K + OH) + HCN.$$
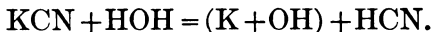
3. Salts formed from a weak base and a weak acid:

$$CH_3COONH_4 + HOH = NH_4OH + CH_3COOH.$$
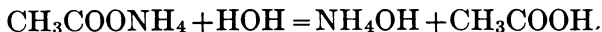
The condition of the solutions is not fully represented by the above equations, because only a certain fraction of the solute is hydrolyzed in each

case. In a one-thirtieth gram-molecular solution of aniline hydrochloride about 2.6% of the molecules are hydrolyzed to aniline and hydrochloric acid.

A solution of a salt of class 1 is acid in reaction because of the ionization of the strong acid set free (while the basic product of hydrolysis furnishes but few OH ions). A solution of a salt of class 2 is alkaline because the strong base liberated yields so many OH ions, but the weak acid hardly ionizes at all. A solution of a salt of class 3 will be neutral if both base and acid are equally weak, because the effect of the few H ions from the acid is neutralized by that of the correspondingly few OH ions from the base.

EXPERIMENT. Dissolve a little potassium citrate in 1 c.c. of distilled water. In similar manner prepare a solution of phenylhydrazine hydrochloride. Test each with litmus paper.

SURFACE TENSION

The molecules of a liquid are attracted to one another in all directions, these attractions neutralizing one another. At the surface, however, the molecules are attracted by the molecules below and at the sides, but as there is no counterbalancing attraction above there results a definite pressure called surface tension. The pressure crowds the molecules closer together. Surface tension is equivalent, then, to the stretching of an elastic membrane at the surface. Fine powders of such a nature that they do not readily take up moisture (as

sulphur) float when sprinkled on water; the par-
ticles rest on the surface exactly the same as if on a
membrane. If the surface tension is lowered, as
results when bile salts are dissolved in the water,
such particles will not be buoyed up, but will
sink. Surface tension is manifested also wherever
the liquid comes in contact with the supporting
vessel.

The effect of surface tension is very noticeable
in the case of small amounts of liquid under cer-
tain circumstances. If a little water is dropped
on an oily or paraffined surface, it will not spread
out in a film, but will gather together into drops.
The small drops are almost spherical, while the large
drops are flattened. Surface tension causes the
liquid to assume the form that has the least surface,
that is, the spherical. Unless the drop is very
small, the pull of gravity will modify the effect
of surface tension. When a drop forms at the tip
of a pipette, it appears to be exactly spherical while
small, but as it grows in size it assumes a some-
what bag-like shape. The drop falls when its
weight becomes great enough to overcome the
tension which has been holding it suspended.
The surface tension of a liquid may be determined
by finding the weight of the drops delivered from a
stalagmometer. For accurate estimations the tip
of the instrument must be of a certain diameter
and must have been standardized; also the drops
must form slowly and have a typical shape. A
correction must be made for temperature. Or-
dinarily it suffices to count the number of drops

produced by emptying a stalagmometer, and to compare with the number of drops of water delivered from the instrument at the same temperature. Allowance must be made for the density of the liquid. The formula for the calculation of the surface tension as dynes is as follows: Dynes per

$$\text{cm.} = \frac{\text{Number of drops of water}}{\text{Number of drops of liquid}} \times \text{specific gravity} \times 73.$$

The factor 73 is the surface tension of pure water in dynes, determined for a line at the surface of the water one centimeter in length.

Capillarity is due to surface tension. If a glass plate is suspended in water, the liquid will wet the glass for some distance above the surface of the water. This amounts to an increase in the total surface. But the force of surface tension combats an increase in surface, and tends to pull the surface into the least possible area. This it does by raising water at the junction of the surface with the glass, so that the surface curves upward on to the glass. The area of the surface along this curved portion is much less than the area of the surface in this region if it could lay flat plus the area of the vertical film of water on the glass plate. The weight of water raised is dependent on the length of contact of the water with the glass. The curved portion of the surface is called the meniscus.

If a number of glass tubes of different internal diameters are placed in water, the effect of capillarity seems to be different in the various tubes.

In a wide tube there is only the formation of a meniscus; this is exactly the same effect as with the glass plate, the only difference being in the curve of the glass wall. In a narrower tube the water is raised slightly, because the amount of water enclosed in the tube is greatly diminished in proportion to the number of vertical lines of contact, and there will not be a sufficient weight of water in a meniscus to balance the pull, therefore, a column of water must be raised to get the requisite weight. In the case of a tube having a capillary bore the amount of water available for the action of each line of contact is extremely small, and in consequence the water is raised to a considerable height. The relative surface tension of a liquid may be determined by measuring the height of the column of liquid in a capillary tube, and comparing with the height of the column of water when the same tube is used in water. The reading must be corrected for the specific gravity of the liquid, so that the comparison made will be of weights of liquids raised. The absolute surface tension can be calculated, if the diameter of the capillary is known. Many organic liquids, such as methyl and ethyl alcohols, ether, chloroform, glycerol, acetone, aniline, pyridine, phenol and certain organic acids, have a low surface tension; on the other hand when they are dissolved in water they lower the surface tension of the water.

EXPERIMENTS. (1) Fill a test-tube with water, and another with 0.1% solution of castile soap; on

the surface of each liquid dust a few very fine particles of sulphur. The sulphur sinks in the soap solution. Dilutions of the soap may be made to find how dilute a solution still shows marked lowering of surface tension.

2. Place a little paraffin on a small glass plate, and melt it by warming over a flame, so that a smooth layer is obtained. Attempt to spread water as a film over the paraffin. Observe the shape of small and of large drops of water that stand on the paraffin.

3. Pour about 10 c.c. of saturated K_2CO_3 into a test-tube, and add a few drops of chloroform. Notice that the latter forms a layer on the carbonate. Hold the test-tube obliquely, and pour down the wall about 5 c.c. of water, but do not mix the liquids. Why does the chloroform refuse to remain as a layer between the two aqueous liquids?

4. Count the drops delivered from a stalagmometer, using (in the order indicated) ether, chloroform, alcohol and water. Use suction to dry the tube before each filling. A 1 or 2 c.c pipette having a fine tip may be substituted for the stalagmometer, if necessary. In order to secure slow dropping, attach a piece of rubber tubing, and use a pinchcock to control the outflow. Do not handle the glass parts after filling; and keep the apparatus in a vertical position (since the size of the drops may be different if held in an inclined position). Calculate the surface tension of each liquid by means of the formula given above.

5. Compare the relative surface tensions of ether, chloroform, alcohol, and water, after having measured the height of the column of liquid raised in a graduated capillary tube of medium-sized bore. After using the tube in one liquid dry it by suction before placing it in another. Before comparing the results multiply each reading by the specific gravity of the liquid.

The surface of the liquid is that part in contact with the air; this may be called the air-liquid interface. As a matter of fact there are other surfaces. For instance, wherever the liquid comes in contact with the supporting vessel there is a surface, a solid-liquid interface. Also, if particles are suspended in the liquid, there is a solid-liquid interface about each particle. A liquid-liquid interface exists at the plane of contact of two immiscible liquids. If hydrated particles of substance in the liquid phase (emulsoid colloids, see p. 81) are present in suspension in water, there is a liquid-liquid interface about each particle.

Surface tension is not the same, quantitatively, at these various interfaces. It is stated that the surface tension at the solid-liquid interface is much greater than that at the air-liquid interface, while it is least at a liquid-liquid interface. Surface tension effects are of considerable importance in the case of colloidal particles.

Inorganic salts raise the surface tension of the water in which they are dissolved, while most dissolved substances lower it. At liquid-liquid

interfaces, however, all substances (including salts) lower the surface tension of the solvent.

Gases are more soluble in liquids of low surface tension, and the degree of solubility is almost proportional (inversely) to the surface tension. For example, the solubility at $0°$ of CO_2 in 1 c.c. of water, alcohol, and ether is 1.713, 4.33, and 7.33 c.c. respectively, while the surface tensions of these liquids are 73, 22 and 16 dynes.

VISCOSITY

The viscosity of a liquid depends upon its internal friction. The friction is due to the adhesion of the molecules of the liquid to one another. A measurement of this friction may be made by observing the time required for a certain quantity of liquid to pass through a capillary tube and comparing with the time required by an equal volume of water in the same apparatus. In the calculation account must be taken of the specific gravity of the liquid, because increase in the weight of the column of liquid increases the pressure and, therefore, increases the rate of flow.

We may suppose that the layer of liquid in contact with the wall is not moving, that the next layer is moving slowly, and that each layer moves faster the nearer it is to the center of the tube. The rate of flow of the liquid as a whole will depend upon the amount of friction between these successive layers, hence measurement of this rate gives a basis for calculating viscosity. When liquid particles push past one another in this way, work must be done,

and the amount of work necessary is dependent upon the internal friction.

Specific viscosity is the ratio of the viscosity of a liquid to that of another liquid that has been chosen as a standard. For example, compared with water as unity, the specific viscosity (at 25°) of 5% ethyl alcohol is 1.161, and of 5% ethyl acetate is 1.044.

It will not be necessary to discuss the determination of the *absolute viscosity* of a liquid.

The temperature of the liquid must be controlled when its viscosity is determined, since increase in temperature diminishes viscosity. The temperature should always be reported. The coefficients for change in viscosity for temperature are different for different liquids.

The viscosity of organic liquids belonging to an homologous series (see p. 104) increases in proportion to the increase in molecular weight.

The viscosity of the blood is of great physiological importance. Fluidity is the reciprocal of viscosity. In proportion as the viscosity is lessened, the fluidity is increased.

EXPERIMENTS. (1) Compare the viscosity of water, and of absolute alcohol in an Ostwald viscosity pipette. To do this pour about 5 c.c. of the liquid into the large tube and by suction from a suction-pump draw it into the small tube and bulb, filling above the upper mark; disconnect and prevent the liquid flowing back by sealing the end with the finger (as in using a pipette); draw off the excess of liquid in the large tube with a pipette.

Now releasing the finger start a stop-watch at the instant that the meniscus reaches the upper mark and stop the watch when it reaches the mark on the capillary tube.

2. Use a viscosimeter such as is used for commercial chemical work; Scott's is a simple apparatus. Try this with water and later with an oil at the same temperature (preferably at 20°). Each determination is made as follows: put 200 c.c. of the liquid into the viscosity cup, set a graduate under the cup to catch the outflow, press the lever which raises the plunger and at the same instant start the watch; when 50 c.c. has flowed out stop the watch and let the plunger fall. Dividing the time for the oil by the time for water gives the figure for the viscosity number [1] of the oil.

Now raise the temperature of the oil 20° and make another determination.

COLLOIDS

Dispersion of Substances in a Liquid. When sodium chloride dissolves in water, it forms what we call a true solution. The molecules of NaCl, and also the Na and Cl ions are uniformly distributed throughout the mass of the solvent. In

[1] In testing a vegetable oil for adulteration valuable evidence may be secured by determining the viscosity of the soap solution produced from the oil by saponification. The Ostwald viscosimeter is used, and care is taken to work at a temperature of exactly 20°. (See Sherman, Organic Analysis, 2nd edition, pages 182–184.)

the solution there is both *ionic* and *molecular dispersion*. In a true solution of a substance that does not ionize there is only molecular dispersion of the substance.

On shaking an insoluble powder (as talcum) with water the fine particles are scattered all through the liquid, and seem to be in uniform suspension. This condition is temporary, however, for, on standing, the liquid becomes clear and all of the solid substance is deposited at the bottom. In the case of some substances the particles may be fine enough to remain suspended for a long time. Such a mixture is a *suspension*, not a solution.

Insoluble liquids may be broken by shaking with water into minute droplets. As long as these drops remain suspended the mixture is an *emulsion*. In order to form a permanent emulsion it is generally necessary to use an emulsifying agent. This forms a film about the drop, so that it is kept separate from other drops. In cream the fat is present as a permanent emulsion, the microscopic drops being enclosed by films.

Intermediate between these coarse dispersions of solids and liquids in liquids, and the molecular dispersions of true solutions, there is another type of dispersion that is characteristic of colloidal solutions. The particles in a colloidal solution are larger than the largest molecules in a true solution, but smaller than the smallest particles in a suspension or emulsion. The colloidal particles remain permanently suspended. Some colloidal solutions are somewhat opaque or opalescent, but others are

practically as clear as true solutions. One of the distinguishing differences between colloidal solutions and true solutions is the fact that in all colloidal solutions the particles have surfaces of contact with the liquid, while in true solutions there are no surfaces of contact of the dissolved substance. These surfaces are an important factor in the behavior of colloids.

There are two kinds of colloids, *suspensoids* and *emulsoids*. Suspensoid particles are in the solid phase, while emulsoid particles are in the liquid phase. Suspensions and suspensoids are essentially of the same nature, differing only in the size of the particles. In appearance, however, they are distinctly different, since suspensions are invariably turbid, but suspensoid solutions may be quite clear, so that they seem to be free of solid particles.

Emulsions and emulsoids are not of the same nature, although both consist of liquid particles suspended in liquids. The liquid particles in an emulsion are practically insoluble, and have no affinity for the liquid in which they are dispersed. Emulsoids, however, readily take up the solvent, so that the particles become liquid particles. The solvent dissolves in the colloidal substance, and the latter, instead of becoming molecularly dispersed, breaks up into infinitely small liquid particles. In the case of colloidal solutions in water we may say that the emulsoid particles are hydrated.

Suspensions, emulsions, and colloidal solutions are heterogeneous mixtures, while true solutions are homogeneous.

In the following classification of dispersion mixtures the diameter of the particles is indicated.

<div align="center">HOMOGENEOUS DISPERSIONS</div>

Ionic dispersions
Molecular dispersions   0.1–1.0 $\mu\mu$ [1]

<div align="center">MICRO-HETEROGENEOUS DISPERSIONS</div>

Emulsoids   1.0–100 $\mu\mu$
Suspensoids   1.0–100 $\mu\mu$

<div align="center">COARSE HETEROGENEOUS DISPERSIONS</div>

Emulsions   greater than 100 $\mu\mu$
Suspensions   greater than 100 $\mu\mu$

We must warn against getting the idea that these forms of dispersion are rigidly separated from one another. It is believed that all substances can be brought into colloidal solution under proper conditions. Therefore, it is better to throw the emphasis on the *colloidal state,* and to avoid looking upon certain particular substances as distinctively colloidal. A true solution may spontaneously change to a colloidal solution. Thus, silicic acid, when first prepared, is in true solution, and on standing becomes mainly colloidal, finally changing to a typical colloidal gel (see p. 84). In some cases there may be a trace of substance in true solution, in equilibrium with that portion which is in colloidal solution. It is supposed that, if a substance has extremely large molecules, a molecularly dispersed

[1] A $\mu\mu$ is one-millionth part of a millimeter.

solution of it may have the properties of a colloidal solution. For instance, hæmoglobin is considered by some to have single molecules as the ultimate particles in solution, yet it is colloidal. As a rule, however, the very smallest particles in a suspensoid or emulsoid solution are clusters or aggregations of many molecules.

Behavior of Colloidal Solutions. Solutions of suspensoids do not gelatinize, are not viscid, and are coagulated by a small quantity of electrolytes. They are irreversible colloids, that is, after being evaporated the residue cannot be put into colloidal solution again. The surface tension of these solutions is practically the same as that of the pure solvent.

EXPERIMENT. Prepare colloidal Prussian blue as follows: measure into one test-tube 10 c.c. N/50 ferric chloride, into another 10 c.c. N/50 potassium ferrocyanide, and pour the two solutions simultaneously at the same rate into a clean beaker. A blue solution free of precipitate is secured. Shake some of the solution in a test-tube; it does not form a foam, there is no evidence of viscidity. Dilute about 5 c.c. with 25 c.c. of distilled water; there is no precipitate. To 5 c.c. of the diluted solution add 5 c.c. of magnesium chloride solution. On standing a blue precipitate forms. Save the more concentrated Prussian blue solution for a later experiment. To test reversibility evaporate 5 c.c. in an evaporating dish on the water-bath, and attempt to redissolve the residue.

Illustrations of suspensions are: colloidal gold, colloidal hydroxides of metals (as $Fe(OH)_3$), and colloidal sulphides of metals (as As_2S_3).

Emulsoid solutions are viscid, they tend to gelatinize, and they are not coagulated by small amounts of electrolytes. After evaporation the residue can be redissolved, so that they are reversible. They are also reversibly soluble after precipitation by alcohol or certain salts. Emulsoid solutions usually have a lower surface tension than the pure solvent.

EXPERIMENT. Pour about 5 c.c. of warm 5% gelatin solution into a test-tube. Shake well, the frothing indicates viscidity. Cool the tube with running tap water; the solution becomes a jelly. Warm the tube until the gelatin liquefies; pour part of it into an evaporating dish and evaporate to dryness on a water-bath; to the rest add an equal volume of magnesium chloride solution. Dissolve the residue in the evaporating dish with hot water. To a few c.c. of dilute gelatin solution add ammonium sulphate crystals, and shake. Filter off the precipitated gelatin, and dissolve it in hot water.

Illustrations of emulsoids are: silicic acid, tannin, soaps, many of the dyes, gelatin, albumin and other proteins.

A colloidal solution when in the liquid condition is called a *sol*, and when in the gelatinized state a *gel*. If the solvent is water the terms hydrosol and hydrogel may be used. When a solution " gelates," a structure or framework develops in the liquid. In some cases the structure is sponge-like, liquid

being interspersed throughout. In other cases (e.g., 13% gelatin) the liquid is held as separate droplets imprisoned in the solid gel substance.

Diffusion of Colloids. The rate of diffusion of typical colloids is only one-hundredth of that of the most rapidly diffusing electrolytes, and about one-tenth of that of cane sugar. Diffusion may be tested by bringing the solution and solvent together, but separated by an easily permeable membrane. Crystalloids diffuse into soft colloidal gels, passing along the liquid pathways of the gel almost as readily as they diffuse in a liquid. Colloids, however, diffuse very slowly into gels.

EXPERIMENT. Take two test-tubes containing 1% agar-agar solution in the gel state. Into one pour Prussian blue solution; into the other pour some ammoniacal copper hydroxide solution (to 5 c.c. concentrated copper sulphate solution add ammonia water until the precipitate is just redissolved). Let the tubes stand an hour or more; the Cu solution penetrates the agar, while the colloidal suspension does not. At the end of the session empty the tubes, leaving the agar in, rinse out; and note the condition of the agar. In which tube is agar colored blue?

Dialysis. Colloids will not diffuse through a gelatinous partition such as an animal membrane or parchment paper, but crystalloids pass through it quickly. Certain colloids are said to dialyze to a slight extent. It may be that in these cases there is a trace of the substance in true solution main-

tained in equilibrium with the colloidally dissolved substance; then it would be expected that more of the colloidal substance would go into true solution as fast as the molecularly dispersed part passes through the dialyzer membrane, so that slow continuous dialysis would take place.

Ultra-filtration. By impregnating pieces of filter-paper with gelatin of different concentrations from 2 to 10%, and then hardening the gel by exposure to formaldehyde, filter disks can be obtained in which there is a gradation in the size of the pores. The 10% gelatin produces a filter having the smallest size pores; this filter holds back almost all colloidal particles. Working with a set of these filters, results are obtained that enable one to arrange a list of colloidal solutions in the order of the size of their particles. In the following list Prussian blue has the largest, and dextrin the smallest particles

> Prussian blue.
> Colloidal ferric hydroxide (about 44 $\mu\mu$).
> Casein (in milk).
> Collargol (about 20 $\mu\mu$).
> 1 per cent gelatin.
> 1 per cent hæmoglobin.
> Serum albumin.
> Albumoses.
> Dextrin.

As a rule suspensoid particles are much larger than emulsoid particles.

Optical Properties. A microscope of the highest power (2250 magnifications) can detect a body 140 $\mu\mu$ in diameter. The particles in most suspensions and emulsions can, therefore, be seen. These microscopic particles have been named *microns*. Visual evidence of the existence of colloidal aggregations in a solution can be obtained by using the ultramicroscope. A microscope is used, but the illumination is from one side instead of from below. An intense beam of light from an arc lamp is passed through a special condenser, so that it is focused to a point within the solution directly under the lens of the objective. The colloidal particles diffract the light, so that some rays pass up through the microscope. This diversion of light is on the same principle as the Tyndall phenomenon observed in the scattering of light by dust particles, when a sunbeam passes into a darkened room. The light is polarized. The particles appear as dots or tiny specks of light on a dark background. Those that can be seen as separate points of light are called *submicrons*. In some solutions the particles are so small that they cannot be detected, but they cause a haze of light to be seen; these are called *amicrons*. The particles in colloidal solutions of metals have a greater power to diffract light than those in other colloidal solutions, so that particles of colloidal gold as small as 3–5 $\mu\mu$ (about 10 times the size of alcohol and ether molecules) have been detected.

In the case of emulsoids the particles exert so much weaker action in diffracting the light, that

they cannot be seen as submicrons unless their
diameter is at least 30 $\mu\mu$. Most emulsoid solu-
tions show a haze of light, and, therefore, have
amicrons. Submicrons have been observed in al-
bumin, gelatin, glycogen, and agar hydrosols.
Diluting a solution may cause amicrons to take the
place of submicrons. Heating some solutions (as
3% soluble starch or 0.01% gelatin) can change
submicrons to amicrons. In the presence of elec-
trolytes (or, in some cases, alcohol) the particles
are aggregated into larger clumps, and appear large
in the ultra-microscope.

Motion of the Particles. Colloidal particles are
constantly in motion (Brownian). Submicrons have
been observed to trace a zigzag course. The motion
of large particles is oscillatory. The premanency
of suspension of the colloidal particles is largely
due to their motion. Increase in the viscosity of
a solution lessens Brownian movement.

Surface Tension of Colloidal Solutions. Suspensions
and suspensoid solutions have practically the same
surface tension as the pure liquid. Emulsoids,
however, affect the surface tension; some increase
it (e.g., starch and gum arabic), and others lower
it (e.g., dextrin, gelatin, egg albumin, tannic acid,
fats, resins and soap). This difference in behavior
can be taken advantage of for the purpose of dis-
tinguishing emulsoids from suspensoids   Venetian
soap (olive oil soap) has a marked effect in high
dilution, thus a 0.004% solution has a very low sur-
face tension. The surface tension of emulsoid
solutions is changed by H ions, OH ions, and by

salts. Rise of temperature decreases surface tension. Surface tension effects take place within all colloidal solutions, since there is a surface of the liquid presented to the surface of each particle in the solution.

How important this is in a consideration of colloidal solutions will be understood by noticing the enormous increase of surface exposure when a substance is divided into fine particles. A compact sphere of substance one mm. in diameter (surface area of 0.0314 sq. cm.), if broken up into particles of uniform size, corresponding to the size of the largest suspensoid particles (0.1μ), will acquire a surface area of 314 sq. cm. If a colloidal solution is purified, that is, freed of other dissolved substances, the surface tension about the particles becomes higher, and as it becomes higher, the difference in potential increases and the particles divide into smaller particles.

Viscosity of Colloidal Solutions. Suspensoid solutions have a viscosity but slightly different from that of the pure solvent. A 3.85% solution of a colloidal silver compound was found to be only 1% more viscid than pure water. Some emulsoids (as agar-agar) show great viscosity in low concentrations. Most emulsoid solutions, if stronger than 1%, have increased viscosity.

Traces of acid or of alkali increase the viscosity of some emulsoids. There is a point of maximum viscosity; for example, with gelatin solution the maximum viscosity with HCl is secured when $\dfrac{N}{256}$

is present. The maximum viscosity with NaOH is the same, but is obtained when $\frac{N}{128}$ is present.

Increase of temperature lessens the viscosity. But in the case of albumin solutions a marked increase in viscosity has been observed at a temperature slightly below that at which heat coagulation occurs.

Osmotic Pressure of Colloids. Osmotic pressure has been demonstrated with some colloidal solutions. Hæmoglobin in 3% solution gave 12 mm. mercury pressure, and in 6% solution 22 mm. The osmotic pressure of 1.5% gelatin was found to be 8 mm., and that of 1.5% egg albumin was 25.6 mm. For these determinations a dialyzing membrane was used as the osmotic membrane, so that the effect of impurities was neutralized, since these dialyzed until there was exactly the same concentration of them in the liquids on both sides of the membrane. Apparently the colloidal particle exerts the same effect in causing osmotic pressure as a molecule of a crystalloid. The number of molecules aggregated together into a colloidal agglomerate is variable and may be different at different times in the same solution. Whenever the colloidal clumps become larger the osmotic pressure is lessened.

Molecular Weight of Colloids. The true molecular weight cannot be calculated from the osmotic pressure, because the number of molecules in the colloidal particle can not be determined. Exactly the same difficulty applies to molecular weight deter-

mination by the freezing-point method. The read-
ings for depression of freezing-point are too low to
be made use of, since a solution which has an osmotic
pressure of 50 mm. gives only 0.005° depression.
In the case of hæmoglobin the smallest possible
molecular weight can be calculated from the con-
tent of iron on the supposition that each molecule
contains one atom of iron; but it does not necessarily
follow that this minimum is the correct molecular
weight.

Electrical Charges of Colloids. The particles in
a colloidal solution carry positive and negative
charges of electricity; and, since the charges are
all of the same kind, the particles repel one another.
This repulsion is a factor of importance in main-
taining the stability of a colloidal solution. When
a current of electricity is passed through a colloidal
solution, the particles travel to one electrode, to
the cathode if they are electro-positive, but to the
anode if they are electro-negative. This process
is called *cataphoresis* or electrophoresis. The nature
of the electrical charge is determined by this method.

Most suspensoids are electro-negative, but a
few (as the hydroxides) are electro-positive. Prac-
tically all emulsoids that are of importance physio-
logically are electro-negative. Hæmoglobin, how-
ever, is electro-positive. An albumin solution, that
had been purified so as to free it of electrolytes to
the highest degree, showed no cataphoresis; but
when acid was added to the solution, the colloid
became electro-positive (effect of H ions), and,
when alkali was added, it became electro-negative

(effect of OH ions). Some favor the view that most emulsoids would be found to be electrically neutral, if sufficiently purified. In their natural environment in vegetable and animal tissues, emulsoids would never be electrically neutral. Many of the dyes are emulsoids, some being electro-positive, and others electro-negative.

Precipitation of Colloids. If two suspensoids of opposite electrical sign are mixed in such proportions that there are just as many positive as negative charges present in the mixtures, maximum mutual precipitation occurs. The oppositely electrified particles attract each other, and when they meet the charges are neutralized. This change in electrical condition lowers the surface tension about the particles, so that larger colloidal clumps must necessarily be formed. The agglomeration of the colloidal masses progresses steadily until they are large enough to separate out as a precipitate. The Brownian movement aids in bringing the masses together after the factor of electrical repulsion has been eliminated. Emulsoids of opposite electrical sign can cause mutual precipitation. In this case, also, there must be the proper relative proportions of the two colloids.

EXPERIMENT. To 1 or 2 c.c. of colloidal arsenious sulphide solution [1] add gradually, a drop at a time,

[1] Arsenic sulphide may be prepared in colloidal solution by pouring a boiling hot saturated solution of arsenious acid into an equal volume of cold water that has been saturated with H_2S. Continue the passage of the H_2S until the mixture retains

colloidal ferric hydroxide (Merck's dialyzed iron containing 5% Fe_2O_3); let it stand a few minutes after each addition. Finally a decided precipitate will be obtained. It is difficult to regulate the proportions just right. Maximum precipitation is secured when the mixture contains 24 parts by weight of As_2S_3 and 13 parts of Fe_2O_3.

Precipitation by Salts. Suspensoids are precipitated by ions of opposite electrical sign; electro-positive colloids, as ferric hydroxide, are precipitated by anions, as Cl, SO_4, while electro-negative colloids, as arsenious sulphide, are precipitated by cations, as H, K, Mg. The colloidal particles attract the ions carrying an opposite electrical charge; their electrical charges are thus neutralized. In consequence precipitation occurs for the reason explained above. The precipitating power is proportional to the concentration of the ions. Thus a 0.7 gram-molecular solution of acetic acid and a 0.0038 gram-molecular solution of hydrochloric acid have the same concentration of H ions, and have the same degree of precipitating action on colloidal arsenious sulphide.

The precipitating ions are held by the colloidal masses (adsorption, see p. 95) while the other ions remain in solution.

Emulsoids are not precipitated by small quanti-

the odor of the gas after thorough shaking. Now remove the free H_2S by passing hydrogen through the solution. An opaque yellow liquid is secured. If there is any precipitate remove this with the aid of a centrifuge.

ties of electrolytes; the latter, however, have an effect on the solution. When an electrolyte is added to a solution, it concentrates at the interfaces between the colloidal particles and the solvent, just as it does at the air-liquid interface. Salts lower surface tension at liquid-liquid interfaces (see p. 76); and, since the surface tension about the colloidal particles is lessened, the particles must come together to form larger clumps so as to restore the balance in potential. If an emulsoid solution, that shows only amicrons, is treated with an electrolyte, submicrons will be seen in it with the ultra-microscope. Addition of more electrolyte increases the size of the particles.

Precipitation of emulsoids occurs when large amounts of very soluble salts are added; this is generally referred to as a salting-out process. The explanation offered is that such concentrations of salts act to abstract water from the hydrated colloidal particles, so that the latter are reduced to the solid phase, and, therefore, become suspensoid particles, which are easily precipitated.

In contact with water most insoluble substances acquire negative charges of electricity. For example, the fibers of filter-paper, wool, cotton and asbestos become electro-negative. This is true also of the particles in most suspensions, very few being electro-positive (e.g., barium carbonate). Suspensions of some fine powders, as lamp-black or kaolin, are precipitated by electrolytes in a similar manner as suspensoids. Acids can diminish the negative charge, completely neutralize it, or even impart a positive charge; this effect is undoubtedly due to adsorption (see below) of the positive H ions.

Adsorption. Colloidal particles attract ions having opposite electrical charges, and hold them, but not by entering into chemical combination. This physical union is described as surface condensation; and the process is called adsorption.

Other substances besides ions are adsorbed. Emulsoids adsorb to suspensoid particles, particularly if the colloids have opposite electrical charges. For example if $Fe(OH)_3$ (electro-positive suspensoid) is mixed with a faintly alkaline solution of protein (electro-negative emulsoid), on adding a salt both iron and protein are completely precipitated.

EXPERIMENT. To 10 c.c. of blood serum add 70 c.c. of water, then 15 c.c. of colloidal ferric hydroxide solution and add powdered sodium sulphate, shaking after each addition, until a gelatinous precipitate forms. Filter, and test the filtrate for protein (biuret test, p. 282) with NaOH solution and a drop of dilute $CuSO_4$.

Enzymes are supposed to be emulsoids. The substrate (the substance that is to be acted on) condenses on the surface of the enzyme particle, and the rate of enzyme action at any particular moment is proportionate to the degree of adsorption. Other substances adsorb to enzymes, so that it is practically impossible to separate enzymes in pure condition.

The humus of the soil is an emulsoid colloid; it plays an important part in holding soluble salts in the soil by adsorption.

Dyes adsorb to the fibers of cloth (see p. 407).

Crystalloids, enzymes, and colloids adsorb to insoluble particles suspended in a liquid. The high surface tension at the liquid-solid interfaces about the particles probably accounts for the intensity of the adsorption process. Finely powdered animal charcoal is one of the most effective agents for removal of substances from solution by adsorption. It is used extensively for decolorizing liquids. The rate of adsorption is increased by shaking, also by heating; but the total amount adsorbed is less in a hot than in a cold liquid. Adsorption is reversible, since the adsorbed substance may be removed, at least in part. For instance, lactose that has adsorbed to charcoal may be recovered by treating the charcoal with acetic acid, the more easily adsorbable acetic acid dislodging the lactose and being adsorbed in its stead.

In some cases not all of the substance is adsorbed, the mixture coming to an equilibrium when a certain proportion has been adsorbed. Some solutions should not be filtered, because the dissolved substance adsorbs to the paper too readily.

In some cases chemical reaction follows adsorption. This is undoubtedly what takes place in the manufacture of leather; tannin being first adsorbed to the tissue substance of the hide, and later forming insoluble compounds.

Protective Colloids. When an emulsoid is added to a suspensoid solution, it exerts a protective action, preventing or hindering the precipitation of the suspensoid by electrolytes. This effect is believed to be due to adsorption of the emulsoid on the sus-

pensoid, so that the latter acquires the character of an emulsoid.

EXPERIMENT. (a) To 5 c.c. of N/20 silver nitrate solution add three drops nitric acid and 5 c.c. of N/20 sodium chloride; a curdy precipitate is obtained.

(b) Into one test-tube put 5 c.c. N/20 silver nitrate, 3 drops nitric acid and about 1 c.c. gelatin. Into another put 5 c.c. NaCl and 1 c.c. gelatin. Empty both simultaneously and at the same rate into a beaker. An opalescent solution (milky) which resembles glycogen solution is obtained. Now dilute and note carefully absence of precipitate.

Photographic plates are made by taking advantage of the protective action of gelatin, which prevents precipitation of the silver salt.

The therapeutic agent, *collargol* is a colloidal silver preparation, in which albumin acts as the protective agent. There being no Ag ions it is not toxic; bacterial action, however, changes it to ordinary silver and the ions act antiseptically.

Swelling of Colloids. Many plant and animal tissues, also other gels (as starch, agar, gelatin, and other proteins) have the power of taking up water, so that they swell. In certain optimum concentrations acids and alkalies increase greatly the amount of water imbibed.

CHAPTER V

FORMULÆ EMPIRICAL AND STRUCTURAL. ISOMERISM

A KNOWLEDGE of the percentage composition and of the molecular weight of a substance, as we have seen, enables us to assign to it a formula indicating the number of .atoms of each element present in the molecule. This is called the *empirical formula.* But it often happens that several organic substances with very different properties may have the same empirical formula. For example, there are no fewer than eighty-two compounds having the empirical formula $C_9H_{1:}O_3$. Such bodies having the same empirical formula are called isomers. It is evident, therefore, that a more detailed formula is necessary —a formula, namely, in which the relations of the various atoms to one another (i.e., the grouping of the atoms) are indicated. Such a formula is called the *structural formula.* It is ascertained by acting on the substance with reagents which decompose it into simple bodies that can be identified; in other words, we must tear the molecule apart. After some knowledge has been gained as to what simpler groups of atoms the body is composed of, an attempt is made to build up the substance by causing the simpler groups to unite, i.e., by synthesizing the sub-

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stance. If the synthesis is successful, the structure of the molecule is proved.

We see then that the structural formula is not only a graphical expression of the actual number of the various atoms present in a molecule of the substance, but it is also an epitome of the more important reactions of the substance.

In the chapters that immediately follow this one, the methods by which the various facts indicating the structure of the molecule are discovered will be fully explained (see especially acetic acid, p. 164). When we come to study the more complex substances, we shall find that even the structural formula does not always suffice to differentiate the substance, since, indeed, there may be several bodies having the same structural formula. In such cases it is supposed that the cause of the difference lies in the order of arrangement of the atoms in space. This subject will be found described in connection with lactic and tartaric acids (pp. 214 and 222).

Before starting with a systematic study of the compounds of carbon, the student should bear in mind the extreme importance of the structural formula; he should never allow one to pass him without thoroughly understanding why it is so written. If he conscientiously follows this advice, he will soon find that organic chemistry is by no means the uninteresting and disconnected subject so many students think it to be.

SYNOPSIS OF CHAPTERS I–V.

Determination of the Chemical Character of an Organic Compound

1. PURIFICATION.
   a. Methods.
   b. Tests of purity.

2. IDENTIFICATION.
   a. Physical properties.
   b. Elementary analysis.

3. EMPIRICAL FORMULA.
   a. Elementary analysis.
   b. Molecular weight determination.

4. STRUCTURAL FORMULA.
   a. Reactions to detect the relative placing of atoms and groups of atoms in the molecule.
   b. Synthesis of the molecule.

Physical Chemistry Topics

1. Osmotic pressure.
2. Electrolytic dissociation.
3. Hydrolytic dissociation.
4. Surface tension.
5. Viscosity.
6. Colloids (including adsorption).

CHAPTER VI

PRELIMINARY SURVEY OF ORGANIC CHEMISTRY

BEFORE attempting to study the various organic substances individually, it is essential that we possess a general idea of their relationships to one another. Their number is so great that, did we attempt to remember the properties and reactions of each organic substance separately, we should utterly fail, and should, moreover, probably overlook one of their most important characteristics in contrast with inorganic substances, viz., their transmutability into other organic compounds. In inorganic chemistry it is impossible to convert the compounds of one element into those of another element, except by substituting the elements. Each element has its own fixed chemical properties and compounds. In organic chemistry, on the other hand, as remarked above, we may consider all our substances as compounds of the element carbon and as being, therefore, convertible into one another.

As is natural, we select as our basis of classification the very simplest organic substances, namely, those which contain carbon along with one other element. From our studies in inorganic chemistry we know that there are several elements with which carbon may be thus combined, e.g., with oxygen in CO_2, with sulphur in CS_2, etc. We do not, however, consider these as organic compounds, the

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simplest organic compounds being those in which carbon is combined with hydrogen or with nitrogen.

In union with nitrogen, carbon forms *cyanogen* (which is the lowest member of a group of compounds including hydrocyanic acid, HCN, cyanic acid, HCNO, sulphocyanic acid, HCNS) and the substituted ammonias.

In union with hydrogen, carbon forms the so-called *hydrocarbons* (i.e., hydro[gen] carbons). Practically all the remaining carbon compounds may be considered as derived from these.

The quantitative relationship between C and H in hydrocarbons is variable, so that we are enabled to subdivide hydrocarbons into several groups. If we express the hydrogen in terms of its proportion to carbon, we shall find that all the hydrocarbons group themselves into several series, four of which are of importance. The general formulæ for the four series or groups are as follows:

(1) C_nH_{2n+2} (3) C_nH_{2n-2}

(2) C_nH_{2n} (4) C_nH_{2n-6}

(in the case of the fourth series n is at least 6.)

It will, moreover, be found that it is to the first and fourth of these groups that the great majority of hydrocarbons belong.

If, now, we investigate the behavior of the members of these four groups towards hydrobrom'c acid, we shall find that members of the first and fourth groups do not readily react, whereas those of the second and third do; and indeed, that these directly combine with the reagent by addition, i.e.,

without chemical substitution. We may, therefore, further subdivide our four groups into two, viz., *saturated* (1st and 4th) and *unsaturated* [1] (2d and 3d.)

Of the two *saturated* groups it will be found that many members of the 4th group have an aromatic odor, whereas those of the 1st do not. The members of the 4th group are hence often styled *aromatic compounds*, and on account of the fact that the members of the 1st group are very resistant toward chemical reagents, they are called *paraffins* (*parum affinis*).

On account of their properties, then, we may amplify our classification into paraffins (1st group), unsaturated compounds (2d and 3d), and aromatic bodies (4th).[2] Compounds of the first three groups make up the ALIPHATIC OR FATTY DIVISION of organic chemistry.

The compounds and derivatives formed by the various hydrocarbons of each of these groups are, in general, analogous, although the reactions by which they are produced may differ somewhat. If we understand the chemistry of the most important derivatives of one hydrocarbon in each group, we shall be able to infer approximately what the derivatives and reactions of all the other members of the group will be; and further, when we come to study the hydrocarbons of the other groups, we shall find many of their compounds quite similar to those already met with.

[1] Only unsaturated compounds can form addition products.
[2] The groups are also sometimes named from the lowest member of each, e.g., methane group, benzene group, etc.

From these preliminary remarks it will be evident
that we must first of all take one group, and, having
shown the relationship of its various members to
one another, then study carefully the derivatives of
some one or two of these members.

Let us take the **paraffins**. They have the general
formula $C_n H_{2n+2}$. The following is a list of the most
important members:

Methane, CH_4 Butane, C_4H_{10}
Ethane, C_2H_6 Pentane, C_5H_{12}
Propane, C_3H_8 Hexane, C_6H_{14}

It will be noticed that each differs from the one
preceding it by CH_2. They all form the same kind
of derivatives, differing from one another again by
CH_2; thus the hydroxide or alcohol of methane has
the formula CH_3OH, and of ethane C_2H_5OH.
Such a series is called an *homologous series* (cf.
nitrogen oxides series).

Let us consider why it should be that the increase
of complexity is by CH_2. To understand this we
must remember that C is considered to have a
valence of four; that, in other words, an atom of
it can combine with four atoms of a monovalent
element such as H, and that each of these valence
bonds has exactly the same combining value. We
may therefore write the structural formula for
methane as follows:

$$H-\overset{\displaystyle H}{\underset{\displaystyle H}{\overset{|}{\underset{|}{C}}}}-H.$$
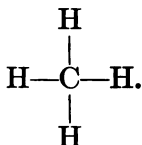
When two methane molecules fuse together a hydrogen atom of each disappears and the liberated valence bonds unite as represented in the formula

$$
\begin{array}{c}
\quad H \quad H \\
\quad | \quad\ | \\
H - C - C - H. \\
\quad | \quad\ | \\
\quad H \quad H
\end{array}
$$
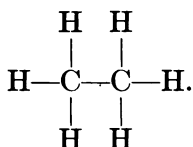
Since each of the four valence bonds of C has the same value, it will be obvious that only one propane can exist: that we can write only one structural

formula for it, viz.,

$$
\begin{array}{c}
\quad H \quad H \quad H \\
\quad | \quad\ | \quad\ | \\
H - C - C - C - H. \\
\quad | \quad\ | \quad\ | \\
\quad H \quad H \quad H
\end{array}
$$

But we may
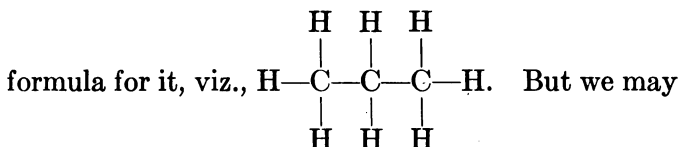
have two varieties of the next member of the series, viz., butane, for, in adding an extra CH_3 group to propane, we may . add it either to the central C atom of the chain or to one of the end ones,

$$
\begin{array}{cc}
\quad\quad\ H & \\
\quad\quad\ | & \\
\ H\ \ H - C - H\ \ H & \quad H \quad H \quad H \quad H \\
\ |\quad\ |\quad\quad\ | & \quad | \quad\ | \quad\ | \quad\ | \\
H - C - C - C - H, \quad or \quad & H - C - C - C - C - H \\
\ |\quad\ |\quad\quad\ | & \quad | \quad\ | \quad\ | \quad\ | \\
\ H\quad H\quad\quad\ H & \quad H \quad H \quad H \quad H
\end{array}
$$
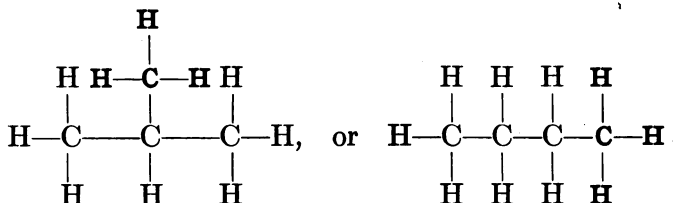
and the properties of the corresponding body will vary accordingly; in other words, it makes a difference when the extra CH_3 group is tacked on to a C atom in union with two H atoms (as is the case

with the central atom), and when on to one with three H atoms (as in the case of an end atom). When the substitution occurs in the center of the chain the resulting body is called an *iso*-compound; when at the end it is *normal*. Such an *iso*-compound therefore contains a branched chain. Now, this *isomerism* applies not only to the methyl derivatives of propane—for butane may be considered as such—but also to all its derivatives, e.g., chlorides, hydroxides, etc.

By using models instead of formulæ these points

Ethane   Propane

Normal butane   Isobutane
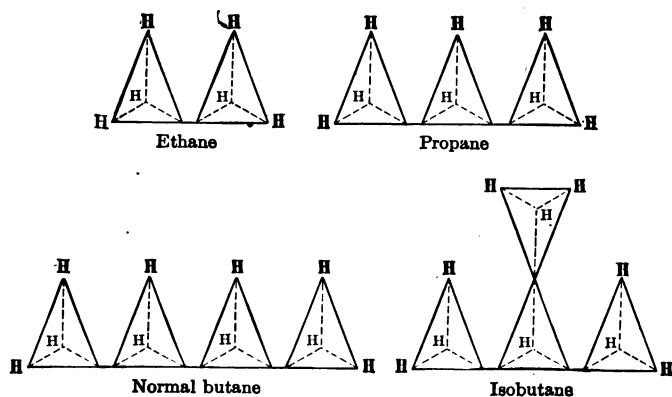
can be still more clearly demonstrated: thus we may consider C as occupying the core of a tetrahedron (made of wood), the four solid angles of which represent monovalent combining affinities, these angles being covered in the model by pyramidal tin caps representing H atoms (see Fig. 22, p. 223). By removing an H cap from two models of methane and joining the two tetrahedra by the

bared angles, we obtain the model of ethane. And, if by removing another H cap from ethane we unite three such tetrahedra, we obtain the model of propane. It does not matter which of the H caps we remove in these manipulations; the resulting ethane or propane models are always the same. When we proceed to add another tetrahedron to propane, however, it will be evident that this can be done in either of two ways, by attaching it either to one of the end tetrahedra or to the central one; in the former case the model will represent normal butane, and in the latter isobutane; and so with the other homologues.

We may also describe this progression from one hydrocarbon to the next higher as being due to the replacement of the H atoms of the former by the group CH_3, called *methyl*.

Now we may proceed with the **derivatives of the paraffins.** These are produced by the replacement of one or more of the H atoms of the simple hydrocarbons by various elements or groups of elements. Since, as explained, these derivatives are, in general, the same for each member of a series, we may choose any one of these and confine our attention for the present to its derivatives, remembering always that the corresponding derivative of any other member of the series will differ from it by just as many CH_2 groups as did the original hydrocarbons differ from one another.

In inorganic chemistry the halogen compounds, the oxides, and the hydroxides are among the most important compounds of an element, and the same

applies to the hydrocarbons: each has halogen
derivatives, oxides (ethers), and hydroxides (al-
cohols).   Beyond these, however, the analogy breaks
down, for whereas an inorganic hydroxide is an
ultimate product and cannot be further oxidized,
an organic hydroxide (or alcohol) can be oxidized
so as to yield various substances according to the
extent of the oxidation and the nature of the alco-
hol started with.   We may, therefore, classify our
derivatives thus:

> Halides.
> Oxides or ethers.
> Hydroxides or alcohols.
> Oxidation products of alcohols.

Halides.   When the paraffins are brought into
contact with chlorine, substitution of one or more
of the H atoms occurs.   Thus, taking methane,
we may have monochlormethane, dichlormethane,
trichlormethane (chloroform), and tetrachlorme-
thane.   In connection with the monohalogen sub-
stitution products it should be pointed out that
they may be considered as derived from a halogen
acid, the H of the acid having been replaced by a
hydrocarbon minus one of its H atoms.   The
general term for all such groups is *alkyl*, and the
specific names for the alkyls are methyl (CH_3-),
ethyl (C_2H_5-), propyl (C_3H_7-), and so on.   An
alkyl is, therefore, analogous with a monovalent
element or with NH_4-.

Halogen atoms may likewise displace one or more
of the H atoms of the alkyl radicle when this latter

is already in combination with some other substituting group. Thus, chloral is trichloraldehyde, CCl_3CHO, aldehyde being CH_3CHO.

Oxides (or ethers). Since oxygen combines with two atoms of a monovalent element, as in sodium oxide, Na_2O, the lowest alkyl oxide will have the formula $\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!\!O$. To this group belong the ethers, common ether being $\begin{matrix} C_2H_5 \\ C_2H_5 \end{matrix}\!\!>\!\!O$.

Hydroxides (or alcohols). When one of the H atoms of methane is replaced by hydroxyl, OH, methyl alcohol is formed. Thus

$$H-\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}-H$$

becomes

$$H-\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}-OH,$$

and it does not matter which of the H atoms is thus replaced, the resulting compound being always the same.

The same is true for ethane and its alcohol, ethyl alcohol, CH_3-CH_2OH.

When we come to form the alcohol from propane, however, we encounter conditions analogous with those which exist when butane is formed from propane (see p. 106); we may add the OH group to a C atom of propane that is in combination with three hydrogen atoms or to one in union with two such, and the resulting product, as we have seen,

will exhibit different properties. Consequently we have two forms of propyl alcohol. Of these the OH group in the one is attached at the end of the chain, CH_3—CH_2—CH_2OH; in the other it is attached in the middle of the chain,

$$CH_3—\overset{\overset{\displaystyle OH}{|}}{C}H—CH_3.$$

The former is called a *primary alcohol*, the latter a *secondary alcohol*.

In the case of butane, we may have the hydroxyl radicle at the end of the chain, CH_3—CH_2—CH_2—CH_2OH (primary butyl alcohol); or attached to a C atom in the center of the chain with one other H atom attached to it, CH_3—CH_2—$CH\!\!\underset{\diagdown CH_3}{\overset{\diagup OH}{}}$ (secondary butyl alcohol); or—a third possibility—the hydroxyl radicle may be attached to a C atom that is not directly combined with any other H atom, thus

$$CH_3—\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}—OH$$

(tertiary butyl alcohol).

There are, therefore, three varieties of these alcohols:

1. Primary, containing the group —CH_2OH
2. Secondary, containing the group —$CHOH$—
3. Tertiary, containing the group $—\overset{|}{\underset{|}{C}}—OH$

The essential chemical difference between these is that when oxidized they yield different products.

In all these alcohols only one hydroxyl radicle is

present; they are analogous with hydroxides of monovalent elements such as sodium (thus $NaOH$ is analogous with CH_3OH). Just as in inorganic chemistry, however, we may have hydroxides with two hydroxyls, e.g., $Ca{<}^{OH}_{OH}$, so may we have alcohols with two hydroxyls, e.g., CH_2—OH. Simi-
$\qquad\qquad\qquad\qquad\qquad\qquad |$
$\qquad\qquad\qquad\qquad\qquad CH_2$—OH
larly, there are alcohols containing three hydroxyl
$\qquad\qquad\qquad CH_2$—OH
$\qquad\qquad\qquad\quad |$
groups, e.g., CH —OH, which are analogous with
$\qquad\qquad\qquad\quad |$
$\qquad\qquad\quad CH_2$—OH

$Al{<}^{OH}_{OH}$ —OH.
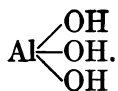
Alcohols, like hydroxides in general, have the power of neutralizing acids to form salts. Thus, sodium hydroxide reacts with HCl in accordance with the equation $NaOH + HCl = NaCl + H_2O$; and taking an alkyl hydroxide (alcohol) instead of an alkaline hydroxide, we have $ROH + HCl = RCl + H_2O$ (R = alkyl).[1] They can react in this way with organic acids, the resulting body being known as an ethereal salt or ester (see p. 173). These organic salts differ widely from metallic salts in their chemical behavior.

An alcohol with only one hydroxyl group is called

[1] Alcohols, however, are not really basic in the same sense as are metallic hydroxides.

monacid,[1] because it can react with only one molecule of a *monobasic* acid; those with two such groups are called *diacid*[2] those with three are called *triacid*. The monacid alcohols are by far the most numerous; there is only one diacid alcohol (glycol) of importance and one triacid alcohol (glycerol).

Oxidation Products of Alcohols. As has been mentioned (p. 110), the division into primary, secondary, and tertiary alcohols is warranted by the difference of their behavior on oxidation:

> Primary alcohols yield on oxidation aldehydes and acids.
>
> Secondary alcohols yield ketones.
>
> Tertiary alcohols, when oxidized, break up into lower compounds.

The oxidation products that we must consider are, therefore, aldehydes, acids and ketones.

A. **Aldehydes.** When methyl alcohol, CH_3OH, is oxidized, one of the H atoms of the methyl radicle becomes replaced by hydroxyl, so that a body having the formula $CH_2(OH)_2$ would tend to be formed. But such a body having two hydroxyls directly attached to a C atom cannot exist, and it immediately breaks up, giving off water, thus:

$$H-\overset{\overset{\textstyle H}{|}}{C}\diagup^{\text{O}\boxed{\text{H}}}_{\diagdown\boxed{\text{OH}}}$$, leaving a body having the formula

$$H-C\diagup^{H}_{\diagdown O}.$$ This is an aldehyde, and the group

---
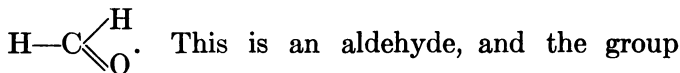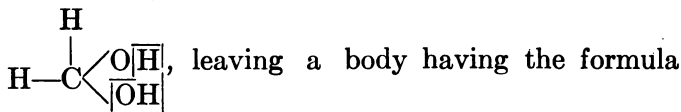
[1] The terms mon*atomic* and mono*hydric* are also used; but the best designation would be *monohydroxylic.*

$-C\begin{smallmatrix} H \\ \diagdown O \end{smallmatrix}$ is known as the *aldehyde group*. The CO portion of this group is called *carbonyl*. Each hydrocarbon has a corresponding aldehyde.

B. **Acids.** When an aldehyde is further oxidized it absorbs oxygen and forms a body having the group COOH, which is called the *carboxyl group* (from carb[onyl hydr]oxyl), and is the characteristic acid group of organic compounds:

$$H-C\begin{smallmatrix} H \\ \diagdown O \end{smallmatrix} + O = H-C\begin{smallmatrix} OH \\ \diagdown O \end{smallmatrix}.$$

(Formic aldehyde)   (Formic acid)
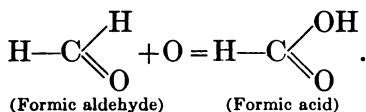
The H atom of this carboxyl group can be replaced by an atom of a monovalent metal to form a salt, thus: $H \cdot COONa$, sodium formate. Instead of a metal, an alcohol radicle may replace this H atom, the resulting compound being called an ethereal salt, thus: $H \cdot COOC_2H_5$, ethyl formate. Such an acid can form only one salt; it is *monobasic*.

If two carboxyl groups are present, the resulting acid is *dibasic*. The lowest dibasic acid corresponding to the simplest diacid alcohol is oxalic,

having the formula $\begin{smallmatrix} COOH \\ | \\ COOH. \end{smallmatrix}$ Like dibasic acids in

general, these acids can form two series of salts, in one of which only one carboxyl group reacts,

$\begin{smallmatrix} COOK \\ | \\ COOH \end{smallmatrix}$ (acid potassium oxalate), and in the other,

COOK

both, | (neutral potassium oxalate).   *Tribasic*
COOK

organic acids also exist, but are less important.

C. **Ketones.**   When   a   secondary   alcohol   is
oxidized, it forms a body having the group —CO—,
which is called a ketone:

$$CH_3—CHOH—CH_3 + O = CH_3—CO—CH_3 + H_2O.$$
<div style="text-align:center">(Secondary propyl alcohol)   (Acetone)</div>
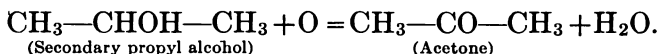
OTHER DERIVATIVES OF ALCOHOLS.

The hydroxy-acids contain one or more hydroxyls
besides that in carboxyl.

The carbohydrates are complex compounds con-
taining alcohol groups.   Many have an aldehyde or
ketone group.

THE NITROGEN DERIVATIVES of most importance
are cyanogen and ammonia compounds, and ni-
trites.

As we have inorganic cyanides, as KCN, so we
have **organic cyanides,** as $CH_3 \cdot CN$, methyl cyanide.

There are several kinds of **ammonia derivatives.**
One hydrogen atom of NH_3 may be replaced by
an organic radicle, leaving the group NH_2, which is
called the *amido-* or *amino-group*.   Two hydrogen
atoms may be displaced, leaving NH, called the
imido-group.   All three hydrogen atoms may be
displaced, leaving only N; such compounds are
called *tertiary bases*.   Or we may have the hydrogens
of ammonium (NH_4) in NH_4OH displaced, as in
the *quaternary bases*.

Several organic **nitrites** are of importance.

The amino-acids contain both the NH_2 and the

COOH groups. **Acid amides** have the OH of carb-
oxyl replaced by an NH_2 group.

SULPHUR DERIVATIVES. In these, sulphur may
take the place of oxygen in an alcohol or ether,
giving **sulphur alcohols** (mercaptans), as CH_3SH,
and **sulphur ethers,** as $CH_3—S—CH_3$.

Sulphonic acids contain the group SO_3H instead of
carboxyl.

Finally, UNSATURATED HYDROCARBONS, having the
linkings $C=C$ and $C\equiv C$, and their derivatives,
will conclude the chemistry of fatty compounds.

The last great division of organic chemistry, that
of the AROMATIC OR BENZENE COMPOUNDS, can be
considered but briefly in this book.

SYNOPSIS

I. Fatty or Aliphatic Compounds.

A. SATURATED HYDROCARBONS.

Paraffins, C_nH_{2n+2}.

Paraffin derivatives.

1. *Halogen substitution products.*
2. *Oxides or ethers.*
3. *Hydroxides or alcohols, and derivatives.*
    a. Monacid alcohols.
    1. Primary alcohols, group—CH_2OH.
       Oxidation { Aldehydes, —CHO.
       products { Acids, —COOH.
    2. Secondary alcohols, —CHOH.
       Oxidation { Ketones, —CO—.
       product {
    3. Tertiary alcohols, —COH.
    b. Diacid alcohols.
       Oxidation { Aldehydes.
       products { Acids.

       c. Triacid to hexacid alcohols.

             Oxidation $\left\{\begin{array}{l}\text{Aldehydes.}\\ \text{Acids.}\end{array}\right.$
             products

       d. Hydroxy-acids.

       e. Carbohydrates.

    4. *Nitrogen derivatives.*

       a. Cyanogen combinations.

       b. Ammonia combinations (amido-group, NH_2; imido-group, NH, etc.).

       c. Nitrites.

       d. Amino-acids, acid amides, and other similar compounds.

    5. *Sulphur derivatives.*

B. UNSATURATED HYDROCARBONS.

    1. *Ethylenes,* C_nH_{2n} ($-C\!\!=\!\!C-$).

    2. *Acetylenes,* C_nH_{2n-2} ($-C\!\!\equiv\!\!C-$).

C.[1]

II. Aromatic Compounds.[2]

    A. BENZENE HYDROCARBONS, C_nH_{2n-6}.

    Benzene derivatives (see synopsis, p. 423).

[1] As will be explained later, the group of cyclic hydrocarbons and the terpenes (see p. 309) is really an intermediate class of compounds between the fatty and the aromatic, and it would naturally be inserted in the synopsis after C. To avoid confusion we say nothing about these compounds in this chapter.

[2] A more scientific classification of organic compounds groups fatty compounds as *acyclic* (not closed-chain structure), benzene derivatives as *isocyclic* (closed chain of C atoms), and certain other aromatic compounds as *heterocylic* (closed chain in which N, S, or O takes the place of one or more of the C atoms of the chain).

CHAPTER VII

SATURATED HYDROCARBONS. THE METHANE SERIES.

METHANE (CH_4) can be synthesized from the elements in several ways:

(1) A small quantity of CH_4 can be produced directly from the elements by passing a stream of hydrogen between the glowing carbon tips of an electric arc-light (see acetylene, p. 304).

(2) By producing carbon disulphide (CS_2) and hydrogen sulphide (H_2S), and allowing a mixture of them to act on heated copper:

$$CS_2 + 2H_2S + 8Cu = CH_4 + 4Cu_2S.$$

(3) By the action of water on aluminium carbide:

$$Al_4C_3 + 12HOH = 3CH_4 + 4Al(OH)_3.$$
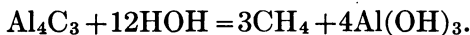
THE PARAFFINS OR MARSH-GAS SERIES, C_nH_{2n+2}.

Having obtained methane, we may build up the other members of the series from it by first of all producing its halogen substitution products and then reacting on these with metals, thus:

$$CH_3 I + Na + Na + I CH_3 = CH_3 \cdot CH_3 + 2NaI,$$
(Methyl iodide) (Ethane)

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$$CH_3 \overline{\underline{I+Na}} + \overline{\underline{Na+I}} C_2H_5 = CH_3 \cdot CH_2 \cdot CH_3{}^1 + 2NaI;$$
(Methyl iodide)   (Ethyl iodide)   (Propane)
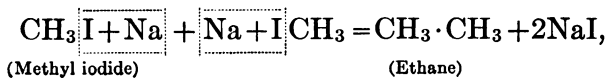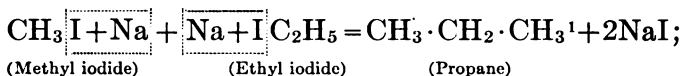
also with zinc methyl, thus:

$$2CH_3 \overline{\underline{I+Zn}} (CH_3)_2 = 2CH_3 \cdot CH_3 + ZnI_2,$$
(Zinc methyl)

$$2C_2H_5 \overline{\underline{I+Zn}} (CH_3)_2 = 2CH_3 \cdot CH_2 \cdot CH_3 + ZnI_2.$$
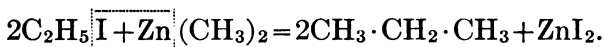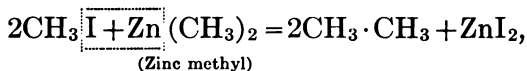
The paraffins may be prepared for general pur-
poses (1) by decomposing the proper substitution
product with nascent hydrogen,[2] or (2) by heating
an acid derivative with an excess of soda-lime:

$$CH_3I + 2H = CH_4 + HI,$$
(Methyl iodide)

$$CH_3 \cdot COONa + NaOH = CH_4 + Na_2CO_3.$$
(Sodium acetate)
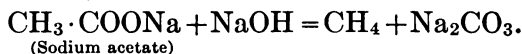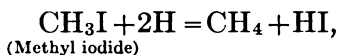
Methane (marsh-gas), CH_4, occurs in nature (1)
as a gas arising from stagnant water where decom-
position of vegetable matter is going on, (2) as the
so-called fire-damp in coal-mines, and (3) as one of
the constituents of natural gas. Its production by
decomposition of vegetable matter can be brought
about in the laboratory by inoculating water
containing small suspended pieces of filter-paper

[1] C_2H_6 and C_4H_{10} are also formed.

[2] The nascent hydrogen for such reactions as this may be
obtained from a copper-zinc couple (made by heating together
one part of powdered copper with three parts of powdered
zinc and then cooling in a closed vessel). In the presence
of a trace of acid (H_2SO_4) the couple readily yields nascent
hydrogen. In the above reaction a mixture of the methyl
iodide with alcohol and a drop of H_2SO_4 is brought into contact
with the couple, drop by drop.

(cellulose) with the microörganisms contained in sewage. It forms an explosive mixture with air, hence the danger of having bare flames in coal-mines and the necessity for using the Davy safety-lamp. Fortunately its kindling temperature, (i.e., the temperature at which it explodes) is high.

Natural gas has about 95% methane; it also contains a little nitrogen, ethane, hydrogen and only a trace of carbon monoxide. There are two hypotheses as to the production of natural gas, one that it is the result of decomposition of vegetable or animal matter, and the other that it is due to the action of water on metallic carbides (cf. aluminium carbide reaction). *Coal gas* contains 30 to 40% of methane.

Water gas is the most poisonous illuminating gas that is used, because of its large content of carbon monoxide (about 30%). Coal gas is also very dangerous, containing 4 to 10% of carbon monoxide. This poison acts by combining with the hæmoglobin of the blood, thus interfering with the oxygen-carrying power of the blood. The water gas prepared from crude oil and steam has nearly the same composition as coal gas. *Pintsch gas* (produced from oil) contains very little carbon monoxide, but a large amount of methane and other hydrocarbons.

Methane is a colorless, odorless, stable gas. When mixed with chlorine and exposed to direct sunlight it explodes:

$$CH_4 + 4Cl_2 = CCl_4 + 4HCl,$$
(Carbon tetrachloride)
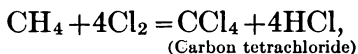
or when exposed to diffused sunlight it forms a mixture of monochlor- (CH_3Cl), dichlor- (CH_2Cl_2), trichlor- ($CHCl_3$), and tetrachlor-methane (CCl_4). The last is also called carbon tetrachloride.

EXPERIMENT. Dehydrate some sodium acetate by heating it in an evaporating dish with a small flame. Cool, powder in a mortar and mix 10 gm. with 10 gm. of soda-lime, and heat in an iron retort. A large test-tube could be used instead of a retort. By means of a delivery tube fitted to the retort, collect the evolved methane over water in the usual manner. Test its inflammability, also its lightness compared with air.

Ethane (C_2H_6), **propane** (C_3H_8), and **butane** (C_4H_{10}) are also gases at ordinary temperatures. The other paraffins are liquids or solids. Above butane the name indicates the number of carbon atoms in the formula. There is a regular gradation of physical properties from the lowest to the highest members of the paraffin series: the boiling-point, the specific gravity, and the melting-point increase as we ascend the series.

	Boiling-point.	Specific gravity.	Melting-point.
Methane, CH_4	$-164°$	0.415 (at $-164°$)	$-184°$
Ethane, C_2H_6	$-84.1°$	0.446 (at $0°$)	$-172.1°$
Propane, C_3H_8	$-44.5°$	0.535 (at $0°$)	$-45°$
Butane, C_4H_{10}	$+1°$	0.600 (at $0°$)	
Pentane, C_5H_{12}	$36.3°$	0.627 (at $14°$)	
Hexane, C_6H_{14}	$69°$	0.6603 (at $20°$)	
Tetradecane, $C_{14}H_{30}$	$252°$	0.775 (at $4°$)	$4°$
Hexadecane, $C_{16}H_{34}$	$287°$	0.7758 (at $18°$)	$18°$
Octodecane, $C_{18}H_{38}$	$317°$	0.777 (at $28°$)	$28°$

The heat of combustion of a gram molecule of a paraffin hydrocarbon is about 158 large calories greater than that of the next lower hydrocarbon; this is the heat of combustion value of the CH_2 group.

The members of the series after methane are met with mainly in petroleum. American petroleum also contains a few sulphur derivatives. California petroleum contains some benzene hydrocarbons. To secure products suitable for commercial purposes, petroleum is subjected to crude fractional distillation. Some of the oils thus obtained are purified by successive treatment with sulphuric acid, caustic soda solution, and water. The lower fractions are distilled with steam; the distillate between 40° and 150° is *gasoline* (or naphtha), and that between 150° and 300° is *kerosene*. Gasoline and its products are mostly mixtures of C_6H_{14}, C_7H_{16}, and C_8H_{18}. From low-boiling gasoline there can be obtained, by careful fractional distillation, cymogene (a gas), rhigolene (b. pt. 18.3°), *petroleum ether* (40–70°), gasoline (70–90°), naphtha (80-110°), ligroin (80–120°) and benzine (120–150°). High-boiling gasoline, called also benzine,[1] is used as a solvent in many industrial processes. Kerosene contains the paraffins from C_9H_{20} to $C_{16}H_{34}$. It should contain no gasoline as the vapor of the lower hydrocarbons in a lamp would form an explosive mixture with air. Its flashing-point, tested in a manner similar to that described in the experiment below, tells us whether

[1] Carefully distinguish from *benzene* (p. 318).

it contains any gasoline. The minimum flashing-point is regulated by law, varying in different States and countries from about 38° to 49°. The residual tar, after kerosene is removed, is distilled. By strongly cooling the distillate (paraffin oil) and filter-pressing it, crude paraffin is separated; and the liquid that is pressed out is fractionally distilled (with steam), giving the various grades of lubricating oil. Purified *paraffin* is a white waxy solid. *Vaseline* and *liquid petrolatum* are made by a special process from selected crude oil. Pennsylvania petroleum yields 16.5% naphtha, 54% kerosene, and 17% lubricating oils. The fuel value of gasoline is greater than that of an equal weight of kerosene, because of the greater percentage of hydrogen present.

EXPERIMENT. Place the flashing-point apparatus

FIG. 18.

(see Fig. 18) containing 20 c.c. of kerosene in a large beaker two-thirds full of water. Suspend a thermometer so that the bulb is in the kerosene. Heat the beaker slowly. Bubble air through the oil at frequent intervals, and test the vapor with a lighted match. Note the temperature when the *vapor* takes fire (the burning temperature of the oil is 40–50° above the flashing-point).
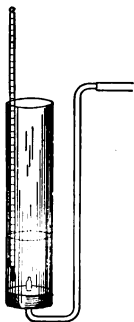
There are many isomers of the paraffins (see p. 106). These *iso-compounds* are represented in their formulæ as having branched chains of carbon atoms

instead of straight chains as in the normal com-
pounds, and they possess properties quite different
from those of the normal paraffins.

Isobutane is the iso-compound having the·fewest
carbon atoms (see p. 106):

$$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_3 \rightarrow CH_3 \cdot CH \cdot CH_3$$
<div align="center">(Normal butane)</div>

$$CH_3$$
<div align="center">(Isobutane)</div>
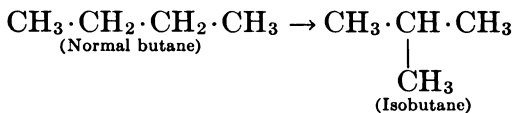
Isopentanes. There are several pentanes:

$$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_3; \quad CH_3 \cdot CH \cdot CH_2 \cdot CH_3;$$
<div align="center">(Normal pentane)</div>

$$CH_3$$
<div align="center">(Isopentane)</div>

$$
\begin{array}{c}
CH_3 \\
| \\
CH_3 - C - CH_3 \\
| \\
CH_3
\end{array}
$$
<div align="center">(Neopentane)</div>
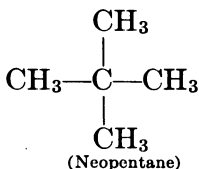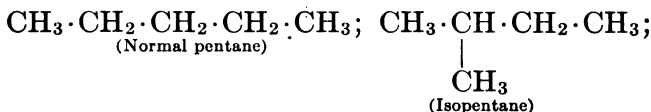
The newer nomenclature designates these isomers
as derivatives of methane; thus, isopentane is
dimethylethyl-methane, and neopentane is tetra-
methyl-methane.

In the case of hexane still another kind of iso-
hydrocarbon is possible, in which there are two
branches attached to different (inside) *C* atoms of
the chain.

HALOGEN SUBSTITUTION PRODUCTS OF THE PARAFFINS

IF only one hydrogen atom of the hydrocarbon is replaced by a halogen atom, the compound is called an alkyl halide (or alkyl halogenide), because it consists of a halogen atom linked to an alkyl radicle, e.g., CH_3—Cl (see p. 108).

The **alkyl halides** derived from methane are: methyl chloride or monochlormethane, CH_3Cl; methyl bromide or monobrommethane, CH_3Br; methyl iodide or monoiodomethane, CH_3I.

General Methods of Preparation. (1) The chloride and bromide can be produced from methane by mixing chlorine or bromine with it and exposing the mixture to diffused sunlight.

(2) All may be secured by acting on methyl alcohol with the proper halogen acid, in accordance with the following equations:

$$CH_3OH + HCl = CH_3Cl + H_2O,$$

$$CH_3OH + HBr = CH_3Br + H_2O,$$

$$CH_3OH + HI = CH_3I + H_2O.$$
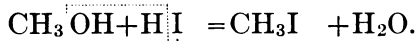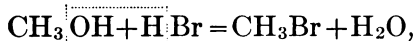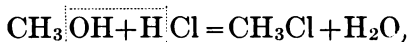
(3) Another method of obtaining them is by the action on methyl alcohol of PCl_3, PBr_3, and PI_3:

$$3CH_3OH + PCl_3 = 3CH_3Cl + P(OH)_3,$$

$$3CH_3OH + PBr_3 = 3CH_3Br + P(OH)_3,$$

$$3CH_3OH + PI_3 = 3CH_3I + P(OH)_3.$$
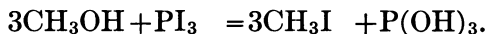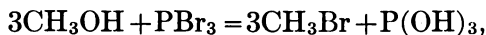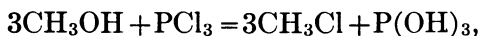
In a manner exactly similar to the last two methods the ethyl halides can be derived from ethyl alcohol.

Some of the More Important Alkyl Halides.

Methyl chloride (monochlormethane), CH_3Cl, is a gas under ordinary conditions. It is readily liquefied, the liquid boiling at $-23.7°$.

Ethyl chloride (monochlorethane), C_2H_5Cl, is a liquid boiling at $12.2°$. It is put up in glass or metal tubes, and is used for local anæsthesia by spraying the liquid on the skin. The rapid evaporation causes the abstraction of enough heat from the skin to result in freezing the latter. Its vapor is very inflammable. It can be used also as a general anæsthetic,[1] being administered as a vapor by inhalation.

Ethyl bromide (monobromethane), C_2H_5Br, is a liquid resembling chloroform in odor, density, and physiological effect. It boils at $38.37°$ (at $37.1°$–$37.4°$ under 737 mm. pressure), and its specific gravity is 1.468 at $13°$. It may be obtained by any of the general methods, but is best prepared by the action of ethyl sulphuric acid on potassium bromide, as in the following experiment.

[1] In this book brief pharmacological statements are frequent. For full information on these points consult the excellent pharmacology text-books by *Cushny* and by *Sollmann*.

EXPERIMENT. Into a 250, c.c flask put 55 c.c. of concentrated sulphuric acid; add quickly 55 c.c. of ethyl alcohol, shaking at the same time. Cool the flask by holding it in running water, add 38 c.c. of iced water, and cool again. Meanwhile set up a condenser having an adapter attached. Use a rapid stream of water in the condenser. Put into the flask 50 gm. of powdered potassium bromide,
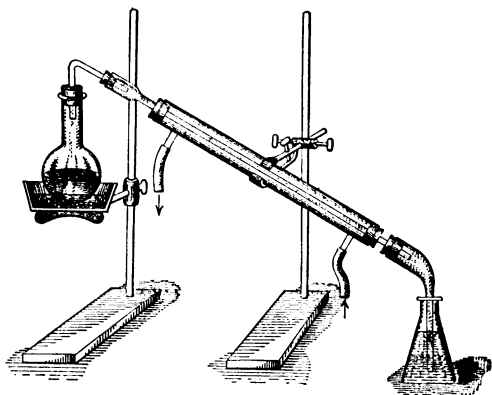
FIG. 19.

then place the flask on a sand-bath and attach to the condenser. Fill an Erlenmeyer flask one-third full of ice-water and have the adapter dip below the surface of the water. Place this receiving flask in a bath of cold water. Heat rapidly and continue heating as long as any distillate comes over. Watch that the contents of the receiver be not sucked up into the condenser. If this is threatened turn the adapter so that air can enter it.

Decant most of the water from the ethyl bromide,

then add ice-water and agitate. Decant the water. Wash several times in this manner. Finally shake the washed ethyl bromide with a dilute sodium carbonate solution; do not, however, cork the flask. Transfer the bromide to a separating funnel, and run out the bottom layer into a dry flask. Add dry calcium chloride, cork tightly, and let it stand in a cool place. After a day or so distill from a small fractionating flask, using a water-bath. Place an empty receiving flask in cold water. Note the boiling-point. Take the specific gravity in a small picnometer holding 5 or 10 c.c. The following equations will explain the reactions:

$$C_2H_5OH + H_2SO_4 = CH_3 \cdot CH_2 \cdot HSO_4 + H_2O,$$
(Ethyl alcohol)   (Ethyl sulphuric acid)

$$CH_3 \cdot CH_2 \cdot HSO_4 + KBr = CH_3 \cdot CH_2Br + KHSO_4.$$
(Ethyl bromide)   (Acid potassium sulphate)
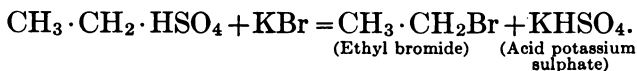
Other halogen derivatives (besides the alkyl halides) are illustrated by the following compounds: dichlormethane, CH_2Cl_2; dibrommethane, CH_2Br_2; diiodomethane, CH_2I_2; trichlormethane, $CHCl_3$; tribrommethane, $CHBr_3$; triiodomethane, CHI_3; and tetrachlormethane, CCl_4.

Of the many compounds thus derived from the paraffins the three trihalogen substitution products of methane are the only ones of importance.

Chloroform (trichlormethane), $CHCl_3$, is a liquid having a pleasant odor and a sweetish taste. Its boiling-point is 61° at 731 mm. Its specific gravity is 1.498 at 15°, 1.5039 at $\frac{11.8°}{4°}$. It is slightly soluble in

water, one liter of water dissolving 8 gm. of chloroform, while, on the other hand, one liter of chloroform can take up 3 gm. of water. It is a good solvent for many substances. Chloroform is a very useful general anæsthetic, but is considered much less safe than ether. Since it is not inflammable, it can be used at night as an anæsthetic where only lamp or gas-light is available. Chloroform vapor should not be allowed to come in contact with a flame, as noxious gases are produced. It is not a stable compound, as exposure to light, air, and moisture causes some decomposition, thus furnishing the poisonous impurities, chlorine, hydrochloric acid, and carbon oxychloride or phosgene ($COCl_2$). These impurities can be readily detected, since chloroform containing them gives a precipitate when shaken with silver nitrate solution. Pure chloroform or other halogen substitution products do not immediately give a precipitate with silver nitrate, because they furnish no halogen ions (see p. 69). The addition of alcohol to chloroform, to the extent of 0.6%, prevents decomposition. The method of its preparation is given in the following experiment. Chlorine (from bleaching-powder), acts to chlorinate acetone, and from the product by the action of the calcium hydroxide present in the mixture, chloroform is produced. Alcohol may be used instead of acetone.

EXPERIMENTS. (1) *Preparation.* Into a liter flask put 150 gm. of bleaching powder (calcium hypochlorite) and 450 c.c. of water, and mix them

thoroughly. Add *slowly* a mixture of 16 c.c. of acetone and 35 c.c. of water. Connect the flask with a steam generating flask and with a condenser, as for steam distillation (p. 16). Pass steam as long as droplets of chloroform appear with the water at the end of the condenser. Transfer the distillate to a separating funnel, draw off the chloroform and wash it with several *small* portions of water. Run the chloroform into a dry flask, add calcium chloride, cork, and let it stand a day or so. As the yield is small, it need not be redistilled, but can be sealed up in sample bottles. The following equations will explain the reaction:

$$CH_3 \cdot CO \cdot CH_3 + 6Cl = CCl_3 \cdot CO \cdot CH_3 + 3HCl,$$

$$2CCl_3 \cdot CO \cdot CH_3 + Ca(OH)_2 = 2CHCl_3 \\ + (CH_3 \cdot COO)_2Ca.$$
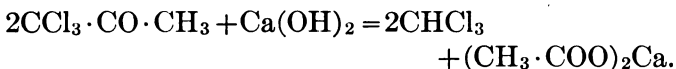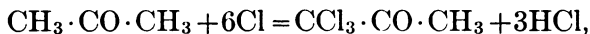
(2) To 1 c.c. of chloroform add half a test-tube of distilled water and shake vigorously. Remove the water with a pipette. Wash three times in this manner, testing the last wash-water with silver nitrate solution; if no precipitate appears, add silver nitrate to the washed chloroform. Let it stand, observing whether a precipitate forms later.

Bromoform (tribrommethane), $CHBr_3$, is a liquid which boils at 146° at 751 mm. On cooling it becomes solid, melting at 8°. Its specific gravity is 2.885 at 15°. It has been used as a medicine.

Iodoform (triiodomethane), CHI_3, is a yellow crystalline solid, the crystals having the form of hexagonal plates. Its odor is peculiar and charac-

teristic. It melts at 119°. Its specific gravity is
4.008. It is used in surgery as an antiseptic, the
action being probably due to iodine which is freed.
It is manufactured from acetone by the action of
iodine and potassium carbonate. Its method of
preparation is illustrated in the following experi-
ment:

EXPERIMENTS. (1) Dissolve 5 gm. of sodium
carbonate in 30 c.c. of warm water, add 5 c.c. of
alcohol, heat in a water-bath to 70–80°, and add a
little at a time 3 gm. of powdered iodine, shaking
frequently. If the liquid has become brown, add
just enough sodium carbonate solution to change it
to a pale yellow. After cooling, filter and wash the
crystals. After being dried in a desiccator, a melt-
ing-point determination may be made.

The reactions involved are doubtless the produc-
tion of iodal, $CI_3 \cdot CHO$, by the action of NaIO;
then the conversion of iodal by the action of the
alkali present into iodoform and sodium formate.

(2) Make a yellow solution of iodoform in alcohol,
and set it aside loosely covered; by slow evaporation
of the alcohol hexagonal crystals of considerable
size are formed.

This reaction, besides being given by alcohol, is
given by aldehyde, acetone, and other compounds
that contain the group $CH_3 \cdot CO$—, provided the CO
is not part of a carboxyl group. On account of
its characteristic strong odor, the production of
iodoform in this manner is often used as a test for

the presence of alcohol or other substances containing the above group.

Iodoform Substitutes. Because of the unpleasant odor of iodoform many antiseptic preparations have been put on the market which disguise or eliminate the bad odor. Such are *eka-iodoform* (iodoform with paraformaldehyde), *iodoformin* (iodoform with hexa-methylenetetramine), *iodoformogen* (protein com-pound of iodoform), and *anozol* (iodoform and thymol). *Iodol* (see p. 414) and possibly *aristol* (see p. 344) liberate iodine in the tissues, so that they are suitable substitutes for iodoform. *Diiodoform* is tetraiodoethylene, C_2I_4 (see ethylene, p. 299).

Tetraiodomethane, CI_4, is a solid, having a very high specific gravity, 4.32.

Similar to the alkyl halides are the alkyl combinations with metals, as zinc methyl, $Zn(CH_3)_2$, and sodium methyl, $NaCH_3$. Both of these are important reagents.

CHAPTER IX

ETHERS

THE alkyl oxides are called ethers. They consist of two organic radicles linked to an oxygen atom, as methyl ether, $CH_3—O—CH_3$; ethyl ether, $C_2H_5—O—C_2H_5$.

A general method of *synthesis* is shown by the following equations:

$$CH_3 \cdot O \;|\overline{Na+I}|\; CH_3 = CH_3—O—CH_3 + NaI,$$
(Sodium methylate) (Methyl iodide) (Methyl ether)

$$C_2H_5 \cdot O\overline{|Na+I|}C_2H_5 = C_2H_5—O—C_2H_5 + NaI.$$
(Sodium ethylate) (Ethyl iodide) (Ethyl ether)
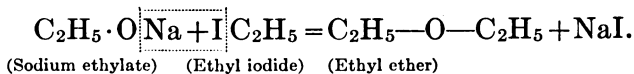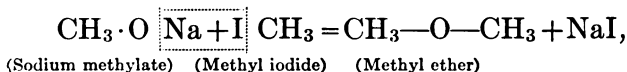
Methyl ether is a gas and is unimportant.

Ethyl ether is common ether. Pure ether is a liquid, boiling at 35° (33.6° at 734 mm. barometric pressure) and having a specific gravity of 0.718 at 15.6° and 0.7079 at $\frac{25°}{4°}$. It dissolves to a certain extent (about 6.5%) in water; it also takes up about $1\frac{1}{4}\%$ of water. If ether is allowed to stand for some time over magnesium bromide both water and alcohol will be abstracted from it by the salt. To obtain absolute ether, it is necessary to treat

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the ether with metallic sodium and then distill
($Na + H_2O = NaOH + H$).   It vaporizes readily, and,
when rapidly evaporated, abstracts enough heat to
freeze water if the latter is contained in a small
vessel surrounded by the ether.   The vapor is
heavier than air and consequently falls.   It is
very inflammable, and should therefore be kept
away from a flame.   Ether is a solvent for a great
number of substances.   It is extensively used as an
anæsthetic, being reasonably safe when properly
administered.   Heat is liberated when chloroform
and ether are mixed in certain proportions.

Because of the use of sulphuric acid in its produc-
tion, it is sometimes called sulphuric ether.   To pre-
pare it, ethyl alcohol is allowed to flow slowly into
heated ethylsulphuric acid (see p. 127) contained in
a flask.   The following experiment will make clear
how this is done:

EXPERIMENT.   In a liter Jena flask mix 165 c.c.
of C.P. H_2SO_4 with 210 c.c. of alcohol.   Fit a cork,
pierced with three holes, into the mouth of the flask,
One hole is to admit the bent tube connecting with
the condenser, another holds a thermometer, and
the third is for a dropping funnel which contains
ethyl alcohol.   The bulb of the thermometer is
immersed in the liquid.   A better arrangement is
to introduce alcohol into the ethylsulphuric acid
in the form of vapor.   For this it is necessary to
have an extra flask in which to boil alcohol, which
is connected with a tube extending to the bottom of
the ether generator flask.   When all is ready,

place the flask on a sand-bath and connect with the condenser. Submerge the receiving flask in a cold bath and use an adapter (cf. ethyl bromide, p. 126). Heat rapidly until the ethylsulphuric acid has a temperature of 140°, at which point it must be kept for the rest of the process. Run in a *very little* alcohol from the funnel, or vapor from the alcohol flask. At intervals, i.e., when the amount of ether vapor diminishes, add more alcohol, a few cubic centimeters at a time. Keep flames away from the vicinity of the receiving flask. Watch the apparatus constantly. When sufficient distillate has been secured, wash it with dilute NaOH solution in a separating funnel, then with several small portions of water; draw off the water, pour the ether into a dry flask, add calcium chloride, and cork tightly. Redistill after a day or so, using a water-bath. The following equations will explain the reaction:

$$C_2H_5OH + H_2SO_4 = C_2H_5 \cdot HSO_4 + H_2O,$$

(Ethyl alcohol)   (Ethylsulphuric acid)

$$C_2H_5O\,\overline{H + HSO_4}\cdot C_2H_5 = C_2H_5\!-\!O\!-\!C_2H_5 + H_2SO_4.$$
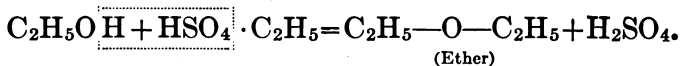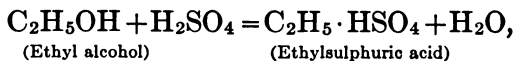
(Ether)

Mixed ethers contain two different organic radicles linked to the same oxygen atom, as methyl ethyl ether, $CH_3\!-\!O\!-\!C_2H_5$. They may be formed by a synthetic process similar to that described above for simple ethers, thus:

$$CH_3 \cdot O\,\overline{Na + I}\,C_2H_5 = CH_3\!-\!O\!-\!C_2H_5 + NaI.$$
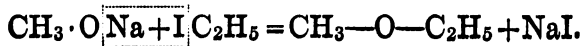
It is interesting to note that the boiling-point of methyl ethyl ether (11°) is intermediate between that of dimethyl ether, $(CH_3)_2O$ ($-23.6°$), and that of diethyl ether, $(C_2H_5)_2O$ (34.6°).

The ethers are very stable, not being affected by boiling with alkali or dilute acid.

PRIMARY ALCOHOLS

AMONG the most important classes of organic compounds are the alcohols. The empirical formula of a monacid alcohol can be derived from the formula of the paraffin hydrocarbon containing the same number of carbon atoms, by attaching an atom of oxygen, thus: $C_nH_{2n+2}O$.

Alcohols, however, are not oxides of the hydrocarbons. They are *hydroxides*. A primary alcohol is an *alkyl hydroxide*. Alcohols cannot be obtained by direct oxidation of the hydrocarbons. *That the oxygen atom is present in hydroxyl* is proved by the following reactions:

(1) $CH_3|OH + H|Cl = CH_3Cl + HOH$
(Methyl alcohol)   (Methyl chloride)

(cf. $K|OH + H|Cl = KCl + HOH$),

(2) $3CH_3OH + PCl_3 = 3CH_3Cl + P(OH)_3$
(Phosphorus   (Phosphorous
trichloride)   acid)

(cf. $3HOH + PCl_3 = 3HCl + P(OH)_3$),

(3) $CH_3OH + H_2SO_4 = CH_3HSO_4 + HOH$

(cf. $KOH + H_2SO_4 = KHSO_4 + HOH$).

(4) $CH_3OH + CH_3 \cdot COOH = CH_3 \cdot COO \cdot CH_3 + HOH$
(Acetic acid)   (Methyl acetate)

(cf. $KOH + CH_3 \cdot COOH = CH_3 \cdot COOK + HOH$).
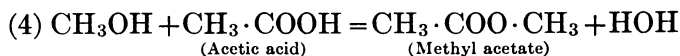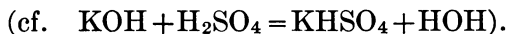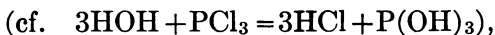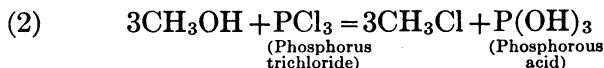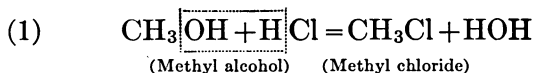
The striking similarity between the reactions of alcohol and the most typical of all hydroxides (viz., KOH and H_2O) is clearly shown by these reactions.

The reaction of potassium and sodium [1] with alcohols shows further that one particular hydrogen atom of the latter has a different linking from that of the other three hydrogen atoms:

$$CH_3OH + Na = CH_3ONa + H$$
(Sodium methylate)

(cf. $HOH + Na = NaOH + H$).
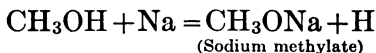
Finally, the structure of an alcohol is settled beyond a doubt by its *synthesis* from an alkyl halide by the action of a strong hydroxide:

$$CH_3 Cl + K OH = CH_3OH + KCl.$$
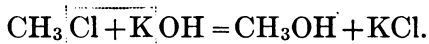
Inorganic hydroxides are strong bases, because they furnish many hydroxyl ions when dissolved in water (see p. 172). Alcohols, on the other hand, *are not bases;* they ionize very slightly, if at all. It is to be noted that the change of one hydrogen atom of the hydrocarbon molecule into hydroxyl greatly alters the chemical behavior of the compound; the paraffin is very stable and enters into reaction with few reagents, whereas the alcohol is *reactive*, being readily affected by many reagents. The heat of combustion of an alcohol is less than that of the corresponding hydrocarbon. This is just what we should expect since there is oxygen in the alcohol molecule.

[1] The higher alcohols are hardly affected, the fewer the C atoms in the alcohol the more vigorous is the sodium action.

MONACID PRIMARY ALCOHOLS.

These comprise the most important group of alcohols. They form an homologous series beginning with methyl alcohol. There is a regular increase of specific gravity and boiling-point from the lowest to the highest members of the series.

Methyl alcohol (methanol, carbinol), $H \cdot CH_2OH$ or CH_3OH, is obtained from the distillate produced by the destructive distillation of wood (see p. 162). The crude alcohol is therefore called wood alcohol. It is also secured by destructive distillation of vinasse, which is the residue left after ordinary alcohol has been distilled off from fermented beet sugar molasses.

Fractional distillation does not suffice to free the methyl alcohol from the acetic acid, acetone, and other constituents of crude wood spirits. A crystalline compound, methyl oxalate $(CH_3)_2C_2O_4$, can be formed by treatment with oxalic acid. The purified crystals can then be decomposed by boiling with ammonia water, yielding pure methyl alcohol.

If the crude alcohol be treated with calcium chloride, $CaCl_2 \cdot 4CH_3OH$ is formed; this is not affected by heating to 100°, but acetone is driven off. Treatment with water sets the alcohol free, and distillation completes the purification.

Methyl alcohol boils at 66° and its specific gravity at $\frac{15.6°}{15.6°}$ is 0.7931 (at $\frac{20°}{4°}$ it is 0.7913). Its melting-point is higher than that of ethyl alcohol, $-93.9°$. Electrolytes dissolved in methyl alcohol

ionize readily. It mixes readily with water, exhibiting the phenomena of contraction of volume and liberation of heat. It is a useful solvent; in consequence, the crude alcohol is used in the preparation of paints. It is intoxicating if taken internally; wood alcohol is dangerous, having caused many deaths when used as a substitute for ethyl alcohol. Wood alcohol burns with a blue flame, hence its use in alcohol lamps.

Ethyl alcohol (ethanol), $CH_3 \cdot CH_2OH$ or C_2H_5OH, is common alcohol. Its relation to methyl alcohol is seen when it is considered as methyl alcohol in which one hydrogen atom is replaced by the methyl radicle:

$$H \cdot CH_2OH \rightarrow CH_3 \cdot CH_2OH.$$
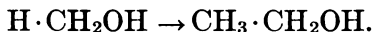
The name *methyl carbinol* expresses this relation. Similarly the higher alcohols are called carbinols (the prefix in each case indicating the groups attached).

Alcohol is produced by fermentation of dextrose (glucose) by means of yeast.

$$C_6H_{12}O_6 = 2CO_2 + 2CH_3 \cdot CH_2OH.$$
(Dextrose)
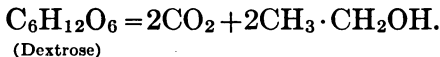
About 5% of the dextrose forms by-products, such as amyl alcohol, glycerol (i.e., glycerine), and succinic acid. It has been thought that lactic acid is an intermediate product of yeast fermentation; and that it is converted into acetaldehyde and formic acid, the latter in turn giving up H (and evolving CO_2), which adds itself to the aldehyde

molecule, and thus ethyl alcohol results. This
theory has not been proved, and is rather discoun-
tenanced by the fact that yeast will not produce
alcohol from lactic acid, nor from an equimolecular
mixture of formic acid and acetaldehyde (even when
these are gradually set free in the reaction mixture).
Another theory advances pyruvic acid as the first in-
termediate product of yeast action.   No theory has
as yet sufficient experimental evidence in its favor.
Alcoholic beverages are obtained by fermentation
of fruit juices containing sugar, as wine from grapes,
or of malted grain, as beer from barley.   Fermenta-
tion is inhibited when the alcohol content reaches
about 17% (by volume). Malt liquors contain
from 2 to 8% of alcohol.   Wines contain 8 to 15%.
Stronger wines are made from these by adding
alcohol.   Brandy is obtained by distillation of wine,
whiskey by distillation of fermented grain; both of
these contain 40 to 60% of alcohol   Many liquors
require aging in order that the by-products, which
are disagreeable and injurious, as for instance fusel-
oil, may be converted into ethereal compounds of
pleasant taste and odor.   The amount of alcohol
present in a liquor can be readily estimated by
distilling 100 c.c. of the liquor (diluted with 50 c.c.
of water); when 100 c.c. of distillate has been
collected, its specific gravity is determined.   The
percentage of alcohol is found by referring to tables
of specific gravities (see Appendix, p. 445).

Preparation.   Commercial alcohol is made from
the cheapest forms of starch, potato or corn.   The
ground or mashed raw material is heated until the

starch is thoroughly cooked. After cooling malt [1] is added and the mixture is kept at 60–62°. Malt contains a ferment, *diastase*, which changes starch into the sugar maltose, and, to the extent of about 20%, into dextrin. The sugar solution is diluted, and yeast is added.

The yeast furnishes a ferment that splits or inverts the maltose molecule into two dextrose molecules, and also a ferment that decomposes the dextrose into alcohol and carbon dioxide. These ferments can be extracted from the yeast cells by grinding the latter with fine quartz sand, subjecting the mass to a very high pressure (up to 300 atmospheres), and finally filtering the extract through porcelain. This filtrate contains no yeast cells, but it inverts maltose into dextrose and changes dextrose into alcohol.

The ferment in this extract from yeast cells is called *zymase*. Similar intracellular ferments can be obtained from certain bacteria. Ferments are often called *enzymes*.

The weak alcoholic solution (not over 13%) obtained by this process of fermentation is distilled in an apparatus containing a fractionating column. The crude distillate (90% alcohol) is filtered through animal charcoal, which removes many impurities. It is then redistilled, the product being *ordinary alcohol* (95%). This is apt to contain some aldehyde. The strongest alcohol obtainable by the most careful fractionation contains 4.5% by weight

[1] Malt is obtained by allowing barley to germinate to a certain stage.

of water. Commercial absolute alcohol contains about one-half of 1% of water. It is obtained by digesting alcohol with quick-lime and then distilling $(CaO + H_2O = Ca(OH)_2)$. More nearly absolute alcohol is secured by treating with metallic sodium and distilling. In Europe potatoes are used for alcohol production, but in this country corn starch is the material used, 2.7 gallons being secured from one bushel of corn. The cost of the *process* of manufacture exclusive of the cost of the raw material is said to be very low, less than five cents per gallon.

Properties. *Chemically absolute alcohol* is almost unknown, because it takes up moisture so rapidly when exposed to the air. Absolute alcohol has a specific gravity of 0.79365 at $\frac{15.56°}{15.56°}$, 0.79357 at $\frac{15°}{4°}$, and boils at 78.3° (corrected) (at 734 mm. pressure it boils at 77.7°). It solidifies at −112°. It has much less odor than common alcohol. Commercial absolute alcohol (*dehydrated alcohol*) contains 99% by weight, and has a specific gravity of 0.798 at 15°. Alcohol containing 95.57% by weight has the lowest boiling-point of any alcohol preparation, 78.15° at 760 mm. Alcohol is of great service as a solvent. Alcohol burns with a colorless flame. When mixed with water, rise of temperature and contraction of volume are observed. It is an intoxicant; the detrimental effect of alcoholic liquors, however, is due *in part* to other compounds besides the alcohol. *Methylated* or *denatured* alcohol is alcohol to which wood alcohol or nauseous substances have been added to render it unfit to drink. In the United

States 10 parts of wood alcohol and 1 or 2 parts of benzine, or else 2 parts of wood alcohol and 1 or 2 parts of crude pyridine per 100 parts of alcohol, are used. Such alcohol can be sold duty-free in many countries.

EXPERIMENT. Into a large bottle or flask put 500 c.c. of 10% glucose solution, and add some crumbled yeast. Through a cork that tightly fits the bottle or flask, pass a glass tube bent so as to extend down into a small bottle containing some baryta water, the tip of the tube just reaching the surface of the latter; through a second hole in its cork the baryta bottle is connected with a tube or tower of soda-lime. Thus CO_2 cannot enter the apparatus from without. Let it stand a few days, after which a copious precipitate of $BaCO_3$ is obtained.

Experiments with 95% *alcohol.* (1) Shake 10 c.c. in a test-tube with anhydrous $CuSO_4$ and let it stand (corked) one hour; the $CuSO_4$ becomes bluish (with absolute alcohol no blue color appears). Explain what takes place.

(2) Take 52 c.c. of alcohol and 48 c.c. of water, each being at a temperature of 20°, mix them in a 100-c.c. graduate, and note the maximum temperature, cool to 20°, and read off the volume (about 96.3 c.c. instead of 100 c.c.).

When miscible liquids are mixed a change in volume is generally noticed, usually a decrease (sometimes an increase). Heat may be either absorbed or given off.

(3) Put 10 c.c. of alcohol in a test-tube, and add as a bottom layer 5-c.c. of concentrated sulphuric acid. Throw in a number of small crystals of potassium permanganate. Flashes of fire will occur in the liquid in the zone of contact of the alcohol and acid (probably due to ozone production, and intense oxidation of a derivative of alcohol).

Propyl alcohol is a primary alcohol having the formula, $CH_3 \cdot CH_2 \cdot CH_2OH$.

Normal butyl alcohol is $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2OH$.

Primary isobutyl alcohol is $CH_3 \cdot \underset{\underset{CH_3}{|}}{CH} \cdot CH_2OH$.

As with hydrocarbons the branching of the chain lowers the boiling-point.

Normal amyl alcohol is

$$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2OH.$$
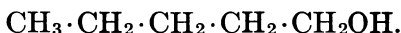
Primary isoamyl alcohol, called isobutyl carbinol, is $CH_3 \cdot \underset{\underset{CH_3}{|}}{CH} \cdot CH_2 \cdot CH_2OH$; this is the main constituent of *fermentation amyl alcohol.* Both of these amyl alcohols are contained in fusel-oil and in certain liquors, especially recently distilled brandy and whiskey. There are three isoamyl alcohols having the same structural formula,

$$\begin{array}{c} CH_3 \\ CH_3 \cdot CH_2 \end{array}\!\!\!\Big\rangle C \Big\langle\!\!\!\begin{array}{c} H \\ CH_2OH. \end{array}$$
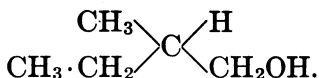
Their chemical and physical properties are identical, except that their action on polarized light is different.

One rotates the beam of light to the left, another rotates it to the right—these are the *active amyl alcohols;* the third does not cause rotation and is called *inactive amyl alcohol.*[1] There is also another amyl alcohol containing the primary alcohol group,

$$CH_3\!\!\diagdown \qquad \diagup CH_3$$
$$\qquad\quad C$$
$$CH_3\!\!\diagup \qquad \diagdown CH_2OH.$$
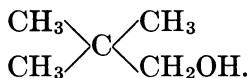
There are four secondary amyl alcohols, two normal and two isoamyl alcohols.

There is a **tertiary isoamyl alcohol**

$$CH_3\!\!\diagdown \qquad \diagup OH$$
$$\qquad\quad C$$
$$CH_3\!\!\diagup \qquad \diagdown CH_2\!\!-\!\!CH_3,$$
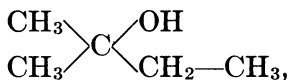
which has been used as a hypnotic under the name **amylene hydrate.**

Fusel oil contains normal propyl alcohol, primary isobutyl alcohol, primary isoamyl alcohol and the optically active (primary) isoamyl alcohol.

Solubility of alcohols. The hydroxyl group tends to render a compound soluble in water; the fewer the carbon atoms the more soluble the alcohol. Methyl, ethyl and propyl alcohols mix with water readily, while 30 parts of butyl alcohol and only 6 parts of amyl alcohol dissolve in 100 parts of water.

[1] For a discussion of this form of isomerism, see p. 214.

ALDEHYDES

IF a primary alcohol be oxidized, the first product is an aldehyde:

$$CH_3 \cdot CH_2OH + O = CH_3 \cdot CHO + H_2O.$$
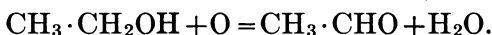
Two atoms of hydrogen have been removed from the alcohol molecule, hence the name *al(cohol) dehyd(rogenatus)*. The reaction is more accurately indicated as follows:

$$CH_3 \cdot CH_2OH + O = CH_3 \cdot CH \diagdown \begin{matrix} O \\ \end{matrix} \boxed{\begin{matrix} OH \\ -H \end{matrix}}$$
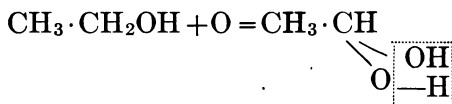
Two hydroxyls become attached to the same carbon atom, but, as is the rule [1] in organic compounds, such a combination is too unstable to persist and H_2O splits off.

It is to be noticed that the *aldehyde group*—CHO *contains no hydroxyl*. This can be proved experimentally. If alcohol or any other hydroxyl-containing compound be treated with phosphorus pentachloride, the place of each hydroxyl group is taken by one chlorine atom:

$$CH_3 \cdot CH_2OH + PCl_5 = CH_3 \cdot CH_2Cl + POCl_3 + HCl.$$

[1] There are three well-known exceptions to this rule—chloral hydrate, mesoxalic and glyoxylic acid.

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But if an aldehyde is similarly treated, a dichlor-compound is obtained:

$$CH_3 \cdot CHO + PCl_5 = CH_3 \cdot CHCl_2 + POCl_3.$$
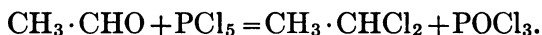
Therefore the aldehyde group must be written CHO, or $CO \cdot H$. Nascent hydrogen converts an aldehyde into the corresponding primary alcohol.

The aldehydes are named from the acids they produce when oxidized: thus, $H \cdot CHO$ is formic aldehyde or formaldehyde, and $CH_3 \cdot CHO$ is acetic aldehyde or acetaldehyde.

Aldehyde reactions. (1) All aldehydes are strong reducing agents, because they readily take up oxygen to form acids. The common tests for sugar are really aldehyde reactions, as practically all sugars contain the CHO group. The reduction of silver and copper salts is illustrated by the experiment below.

(2) The linking $C{=}O$ in the aldehyde group causes aldehydes to act like unsaturated compounds, for they readily form addition compounds, thus:

$$CH_3{-}C{\overset{O}{\underset{H}{\diagup}}} + HCN = CH_3{-}C{\overset{O{-}H}{\underset{H}{<}}}CN,$$

(Acetaldehyde)   (Acetaldehyde cyanhydrin)

$$CH_3{-}C{\overset{O}{\underset{H}{\diagup}}} + NH_3 = CH_3{-}C{\overset{O{-}H}{\underset{H}{<}}}NH_2,$$

(Aldehyde ammonia)

$$CH_3{-}C{\overset{O}{\underset{H}{\diagup}}} + NaHSO_3 = CH_3{-}C{\overset{O{-}H}{\underset{H}{<}}}SO_3Na.$$

(Sodium acid sulphite)   (Aldehyde bisulphite)
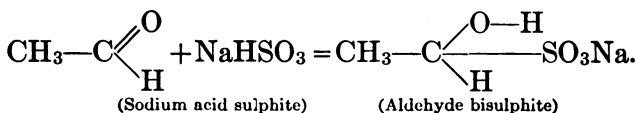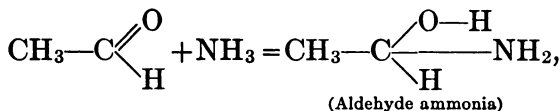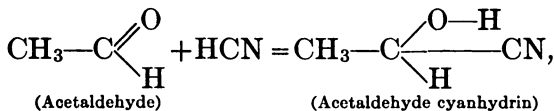
(3) Phenylhydrazine can combine with an aldehyde by removing O of the carbonyl group, a *hydrazone* being formed.

(4) Aldehydes (except chloral hydrate) cause a violet-red color to appear when added to a solution of fuchsin which has been decolorized by sulphurous acid. This reaction is due to the formation of condensation products (see acetaldehyde). Dextrose does not give this test because, as in the case of chloral hydrate, it does not contain a $C = O$ group; however, in the case of both of these compounds the aldehyde character appears under the influence of the strong reagents (and the heat) used for other tests.

Formaldehyde (methanal), $H \cdot CHO$, is a gas. It is very soluble in water. Commercial *formalin* is a 40% solution. Formaldehyde is prepared by bubbling air through methyl alcohol, which is kept at about 50°; then the mixture of air and vapor is passed through a heated tube containing platinized asbestos: $H \cdot CH_2OH + O = H \cdot CHO + H_2O$. It is also produced by burning methyl alcohol in a special lamp in which the supply of air is limited, so that incomplete combustion occurs; part of the alcohol is oxidized to formaldehyde and escapes. This lamp can be used for disinfection of rooms, but is not very satisfactory.

Formaldehyde has a tendency to form *polymers*. A polymer has a molecular weight which is an even multiple of that of the original substance, and it has the same percentage composition as the latter. Thus **paraformaldehyde** (trioxymethylene) is $(H \cdot CHO)_3$. Its graphic representation is
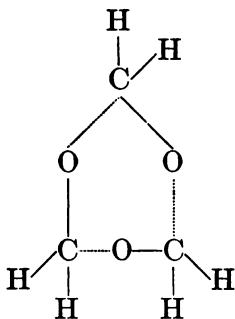
Paraformaldehyde (paraform) is a white sub-
stance, which, on being heated, is converted into
formaldehyde. It is sold in the form of tablets
or candles for disinfecting purposes.

With ammonia, formaldehyde does not form a
simple addition compound as do other aldehydes,
but a complex substance, hexamethylentetramine
(see p. 264).

Formaldehyde is an efficient germicide, and is
therefore used extensively for disinfecting pur-
poses. It is used either as the gas or in dilute solu-
tion. It is very irritating to the eyes and mucous
membranes. The dilute solution also hardens al-
buminous substances, and is consequently used to
prepare tissues for histological examination. It
converts a solution of gelatin into a hard insoluble
mass.

Glutol is a substance produced by the action of
formaldehyde on gelatin. In the form of a
dry powder it is used as a surgical dressing for raw
surfaces. It is said to act as an antiseptic because
of slow liberation of formaldehyde.

EXPERIMENTS. (1) To a few cubic centimeters of concentrated H_2SO_4 in a test-tube add a few drops of ferric chloride solution; with a pipette run in about 5 c.c. of milk containing 5 drops of 1 : 5000 formaldehyde solution as a top layer, avoiding mixing with the H_2SO_4. A violet zone forms between the two layers.

(2) Set in a desiccator an evaporating dish containing 5 c.c. of formalin. Leave several days until a white solid, paraformaldehyde, is obtained. When this is secured, heat some of it in a dry test-tube. It volatilizes completely, passing away as formaldehyde gas. Note the odor. Be careful not to get strong fumes into the eyes or nostrils, as the gas is very irritating.

(3) To 10 c.c. of milk in a large evaporating dish add a little formaldehyde and 10 c.c. of concentrated hydrochloric acid containing one drop of 5% ferric chloride. Heat over the flame, holding the dish in the hand and maintaining a rotary motion. At about 90° the mixture acquires a violet color.

(4) Add 4 drops of methyl alcohol to 3 c.c. of water in a test-tube. Make a spiral of copper wire that will easily slip into the tube. Heat the wire until red hot and plunge it into the solution. Repeat this several times. Cool the liquid, add 1 drop of 0.5% resorcinol solution, and with a pipette run in a bottom layer of 5 c.c. of concentrated sulphuric acid. A red zone develops. Why is formaldehyde produced by this procedure? This is used as a test for small quantities of methyl alcohol.

Acetaldehyde (ethanal, aldehyde), $CH_3 \cdot CHO$, can be obtained in similar manner as formaldehyde by the oxidation of ethyl alcohol vapor, induced by heated platinum. The oxidation is generally effected, however, by the use of sulphuric acid and sodium or potassium dichromate, as described in the experiment below. Acetaldehyde boils at 20.8° and has a specific gravity of 0.780 at 20°.

Acetaldehyde can be changed into the polymers, **paraldehyde,** a liquid boiling at 124°, and **metaldehyde,** a solid. Both have the formula $(CH_3 \cdot CHO)_3$. It is supposed that the difference in their structural formulæ is a stereomeric difference (see p. 214), that is, a difference in the arrangement in space of a CH_3 group in relation to the rest of the molecule. Paraldehyde is a hypnotic.

Aldehyde molecules can be made to fuse together, forming a "condensation" product, *aldol.* Zinc chloride will effect this change:

$$2CH_3-C \diagup_H^O \rightarrow CH_3-\overset{\overset{\displaystyle O-H}{|}}{C}H-CH_2-C\diagup_H^O$$
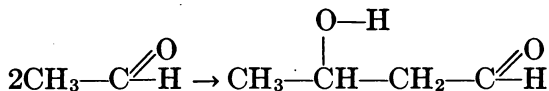
It has been suggested that the production of starch and sugar by plants is due to condensation and polymerization of formaldehyde, the latter being synthesized from CO_2 and H_2O. A sugar can be made from formaldehyde by condensation under the influence of lime-water (see p. 232).

EXPERIMENTS. *Preparation.* (1) Mix in a large flask 100 c.c. of water and 30 c.c. of C.P. H_2SO_4.

Fit a cork having two holes, one for the bent tube connecting with a condenser, the other for a dropping funnel. Have the tip of the dropping funnel about 3 cm. above the liquid. Connect with the condenser, and place the receiving flask in ice-water. Heat the flask over wire gauze to the boiling-point. Now add through the funnel, in a slow stream, a solution of sodium dichromate (100 gm. of dichromate dissolved in 100 c.c. of water,
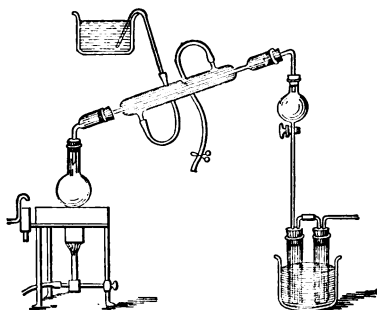
Fig. 20.

and mixed with 53 c.c. of alcohol). Remove the flame as soon as distillation is well started. If vapor passes through uncondensed, slacken the stream. If aldehyde ceases distilling, heat again with the flame. When all of the solution has been added, redistill the distillate. Save a portion of the crude distillate for making the aldehyde tests given below. In redistilling tilt the condenser upward, as shown in the diagram. Circulate through it water heated to 30°, using a reservoir or large funnel. Connect the condenser with a drop-

ping funnel, which dips into the ether in the first wash-bottle. Put 25 c.c. of dry ether into each wash-bottle. As aldehyde will not condense at 30°, while most of the alcohol and water will, only aldehyde passes into the ether, which absorbs it. Keep the ether bottles in a bath of ice-water. When the aldehyde seems to have all passed over, transfer the ether to a beaker, which is placed in a freezing-mixture. Now bubble into it ammonia gas (secured by heating NH_4OH in a flask), which has been dried by passing through a tower of soda-lime. A mass of white crystals of aldehyde ammonia will finally appear. Filter, wash the crystals with ether, and let them dry. From this product pure aldehyde may be obtained by dissolving some of it in an equal weight of water, adding $3\frac{1}{2}$ times as much 50% H_2SO_4, and then distilling. Put some of the crystals in a sample bottle, hold the bottle obliquely, bottom up, and fill with ammonia gas; cork and seal with sealing wax.

$$Na_2Cr_2O_7 + 4H_2SO_4 = 3O + Cr_2(SO_4)_3 + Na_2SO_4$$
$$+ 4H_2O,$$

$$CH_3 \cdot CH_2OH + O = CH_3 \cdot CHO + H_2O,$$

$$CH_3 \cdot CHO + NH_3 = CH_3 \cdot C{\overset{\displaystyle H}{\underset{\displaystyle NH_2}{\big\langle}}}OH.$$
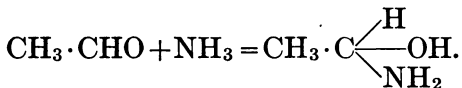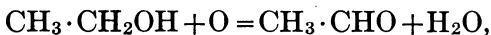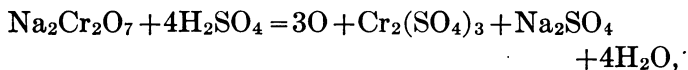
(2) *Aldehyde tests.* (*a*) Add a little of the crude distillate to 5 c.c. of dilute Fehling's solution in a test-tube; boil until Cu_2O is precipitated.

(*b*) Add another small portion to a few cubic centimeters of ammoniacal $AgNO_3$ solution in a

perfectly clean test-tube; and heat gradually. A mirror of silver is deposited.

(*c*) To 1 c.c. of dilute rosaniline (fuchsin) solution add a solution of sulphurous acid until almost decolorized. Add some aldehyde solution and shake, a violet-red color appears. Schiff's reagent is very convenient to use for this test.[1]

Chloral (trichloraldehyde), $CCl_3 \cdot CHO$, is a chlorine derivative of acetaldehyde. It is produced by passing dried chlorine gas into absolute alcohol for several days. Aldehyde and HCl are the first products of the chlorination. The final product is chloral alcoholate, $CCl_3 \cdot CH {\overset{\displaystyle OC_2H_5}{\underset{\displaystyle OH}{\Big\langle}}}$, an addition compound of chloral with alcohol. Chloral is liberated from this by the action of concentrated sulphuric acid.

Chloral is an oily liquid, boiling at 97.7° and having a specific gravity of 1.512 at 20°. It gives the aldehyde reactions. When it comes into contact with water it forms chloral hydrate crystals.

Chloral hydrate, $CCl_3 \cdot C {\overset{\displaystyle H}{\underset{\displaystyle OH}{\Big\langle}} OH}$, is believed to have two hydroxyls attached to the same carbon atom, contrary to the general rule. It may be considered an addition compound of the aldehyde with water. One reason for believing that a typical

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[1] Prepare the reagent by saturating with SO_2 gas a solution of 2.2 gm. of rosaniline in 10 c.c. of water. Cork tightly and let it stand until light yellow or colorless. Dilute with 200 c.c. of water and keep in a dark-colored bottle well stoppered.

CHO group is not contained in it is the fact that it does not give the fuchsin test.

Chloral hydrate is extremely valuable as a medicine, being used as a hypnotic. It is very soluble in water and in alcohol. It melts at 57°. Alkaline solutions decompose both chloral and chloral hydrate to chloroform and formic acid:

$$CCl_3 \cdot CHO + KOH = CCl_3H + HCOOK.$$
<div align="center">(Potassium formate)</div>
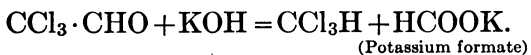
EXPERIMENTS. (1) Try the aldehyde tests (see acetaldehyde) with a solution of chloral hydrate.

(2) Warm a few cubic centimeters of chloral hydrate solution; after adding NaOH, notice the odor of chloroform.

(3) Boil a few cubic centimeters of chloral hydrate solution; then test part of it with $AgNO_3$; it gives no precipitate. Now add some zinc powder to the original solution and boil two minutes. Filter; test the filtrate with $AgNO_3$; it gives a white precipitate of AgCl. The zinc decomposes water; the nascent hydrogen produced takes chlorine from the chloral hydrate, forming HCl (which combines with the zinc).

(4) To 2 gm. of chloral hydrate in a dry test-tube add 5 c.c. of C.P. H_2SO_4, and warm gently while shaking. An oily liquid (chloral) separates as a top layer. Cool the tube to room temperature, and add 5 c.c. of chloroform which is free of alcohol and water. Draw off the top layer with a dry pipette, and allow the chloroform to evaporate; the residue in the dish will take up moisture from

the air, until finally chloral hydrate crystals are formed.

Chloral Substitutes.   Many derivatives of chloral have been synthetized with the object of correcting the tendency which chloral hydrate has to depress the circulation.   Such are:

Butyl-chloral hydrate (croton chloral),

$$CH_3 \cdot CHCl \cdot CCl_2 \cdot CH(OH)_2.$$

Chloralformamide, (chloralamide),

$$CCl_3 \cdot CH {\Large\langle} {}^{OH}_{NHOCH},$$
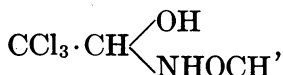
is a combination of chloral hydrate with formamide. $HCONH_2$.

Chloralose (chloral + glucose), $C_8H_{11}Cl_3O_6$.

Hypnal (chloral + antipyrin).

Dormiol (chloral condensed with amylene hydrate)

Isopral, trichlorisopropylalcohol,

$$CCl_3 \cdot CH {\Large\langle} {}^{OH}_{CH_3}.$$
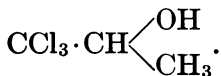
FATTY ACIDS AND ETHEREAL SALTS. FURTHER OBSERVATIONS IN PHYSICAL CHEMISTRY

ACIDS

Acids are defined as substances which, when dissolved in water, dissociate in such a way as to furnish hydrogen ions (see p. 67). Most organic acids dissociate but feebly; they are therefore weak acids as compared with inorganic acids (see p. 173). The majority of organic acids contain the carboxyl group.

A general method of production of carboxylic acids is by *hydrolysis* [1] of a cyanide (see experiment under acetic acid):

$$HCN + 2H_2O = H \cdot COONH_4,$$
(Ammonium formate)

$$CH_3CN + 2H_2O = CH_3 \cdot COONH_4.$$
(Ammonium acetate)
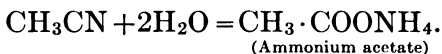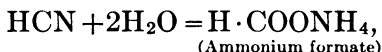
The acids to be studied at this point are called **fatty acids,** because common fats contain some members of this series of acids (in combination with glycerol). They are monobasic, i.e., they contain only one displaceable hydrogen atom in the acid group. They conform to the general formula,

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[1] Hydrolysis means introducing H_2O into the molecule of the substance to be hydrolyzed, the result being a product quite different from the original substance.

$C_nH_{2n}O_2$. They are the end products of the oxidation of primary alcohols, of the methyl alcohol series, since they can be obtained by oxidation of aldehydes:

$$H \cdot CHO + O = H \cdot COOH.$$
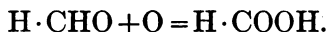
The OH of carboxyl can be proved to be hydroxyl by the reaction with PCl_3 (see pp. 136 and 146), thus:

$$3CH_3 \cdot COOH + PCl_3 = 3CH_3 \cdot COCl + H_3PO_3.$$
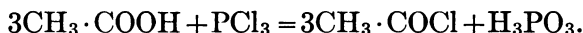
It would be desirable to call this series of acids the *formic acid series,* since the term fatty is misleading.

The boiling-points of these acids increase steadily with increase in the number of carbon atoms. For some unexplained reason a similar statement is not true of the melting-points, but on the contrary the acids having an odd number of carbon atoms have each a lower melting-point than the next acid having one less carbon atom.

Formic acid (methanoic acid), $H \cdot COOH$, is a liquid.

(1) It can be made by oxidation of formaldehyde by hydrogen peroxide in alkaline solution:

$$H \cdot CHO + H_2O_2 + KOH = H \cdot COOK + 2H_2O.$$

The acid can then be liberated from the potassium formate.

(2) Moist CO is absorbed by soda-lime at 190°–220°, forming sodium formate:

$$CO + NaOH = H \cdot COONa.$$
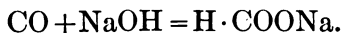
(3) Moist CO_2 coming in contact with metallic potassium forms potassium formate and potassium bicarbonate:

$$2K + 2CO_2 + H_2O = HCOOK + KHCO_3.$$
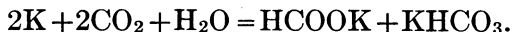
(4) Oxalic acid when heated with glycerol (glycerine) decomposes to formic acid and carbon dioxide (see exp.).

Formic acid occurs in red ants, and in stinging nettles. It is very irritant, causing blisters when applied to the skin. Formic acid boils at 101°; it solidifies at a low temperature, and melts at 8.3°. Its specific gravity is 1.2187 at 20°. It is a strong reducing agent, reducing silver and mercury compounds to the metal (see exp.). The full structural formula, $H—C{=}O$, shows that it con-
$$O—H$$
tains the aldehyde group overlapping the acid group, carbonyl being common to both. It oxidizes to carbon dioxide and water. It is a stronger acid than acetic acid. When treated with concentrated sulphuric acid it is decomposed, with evolution of carbon monoxide (see exp. 3).

EXPERIMENTS. (1) Prepare formic acid as follows: Into a half-liter flask put 50 c.c. of anhydrous glycerol (which has been heated at 170° for an hour); add 50 gm. of crystallized oxalic acid. Suspend a thermometer in the cork, so that its bulb is in the liquid. Heat gradually on a sandbath. Connect with a condenser. Carbon dioxide

is evolved, and formic acid begins to distill at about 115° (temperature of the liquid). When the temperature reaches 150°, cool the mixture to about 50°, then add 50 gm. of oxalic acid. Heat again up to 150°. If the mixture is overheated, acrolein (p. 302) will be produced, which is a very disagreeable gas. Test some of the acid distillate for formic acid as below. Dilute the rest of the distillate to a volume of 200 c.c. In the meantime copper hydroxide has been prepared by treating $CuSO_4$ solution with KOH until slightly alkaline, diluting and filtering. In similar manner, prepare lead hydroxide from lead nitrate solution. Add to half of the formic acid copper hydroxide, warming the mixture. When copper hydroxide no longer dissolves, filter and set away for slow evaporation. To the rest of the acid add lead hydroxide and proceed as with the copper formate.

$$C_3H_5(OH)_3 + (COOH)_2$$
(Glycerol)   (Oxalic acid)

$$= C_3H_5(OH)_2OCHO + H_2O + CO_2$$
(Monoformin or
glyceryl monoformate)

$$C_3H_5(OH)_2OCHO + H_2O = H \cdot COOH + C_3H_5(OH)_3.$$
(Formic acid)   (Glycerol)
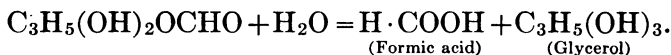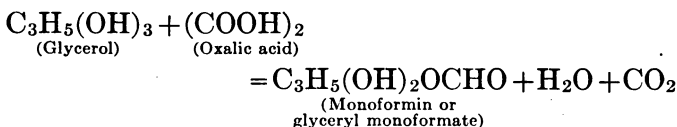
(2) Test for formic acid in the distillate as follows: Warm a few c.c. to 50°, add HgO, and shake vigorously. Filter and boil the filtrate one minute a gray precipitate of mercury develops:

$$HgO + H \cdot COOH = Hg + CO_2 + H_2O.$$
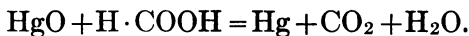
(3) Into a test-tube put 3 c.c. of undiluted formic acid; add slowly 6 c.c. of H_2SO_4. Cork quickly

with a cork through which passes a bent delivery-tube the end of which is to dip into a few cubic centimeters of dilute hæmoglobin solution in another test-tube. The hæmoglobin is changed to carbon-monoxide-hæmoglobin, which has a cherry-red tint. The hæmoglobin solution is made by adding a drop of blood to a little distilled water.

Acetic acid, CH_3COOH. There are various ways by which ethyl alcohol may be oxidized to yield acetic acid. In the laboratory, the addition of spongy platinum to alcohol contained in an open vessel causes the atmospheric oxygen to attack the alcohol, oxidizing it and producing acetic acid. The spongy platinum itself undergoes no change; it is a *catalytic* agent, merely transferring the oxygen to the alcohol.

Pure alcohol or alcohol diluted with pure water does not spontaneously become converted into acetic acid when exposed to the air, but does so if the dilute alcoholic solution contains nitrogenous matter. This is because of the growth in the latter solution of a microörganism derived from the air (*Mycoderma aceti*), which, like spongy platinum, transfers atmospheric oxygen to the alcohol. Nitrogenous matter is necessary for the life of this organism. It is in this way that wine becomes converted into vinegar. Mere exposure of wine or cider to air would, however, occupy too much time to produce sufficient vinegar to meet the demands of commerce, and consequently the above process has to be accelerated. This is done by allowing the wine to percolate slowly

through freely perforated barrels filled with beech shavings previously sown with the mycoderma by soaking them in strong vinegar. A slight amount of heat is generated during the oxidation; this creates currents of air, which enter the barrels through the perforations in their sides, and in this way a sufficiency of oxygen for the process is supplied. Other alcoholic solutions besides wine may be used for the purpose, e.g., cider or beer, and frequently some alcohol obtained by fermenting glucose is added to these. The amount of alcohol in such solutions should not, however, be over 10%. The resulting vinegars contain about 5% of acetic acid, besides various aromatic bodies.

To obtain acetic acid in a pure state, fermentation of alcoholic liquids is, however, not employed. For this purpose hard wood is subjected to what is known as *destructive distillation*. It is heated at low temperature (200°) in an iron retort from which air is excluded, and the vapors condensed. The resulting distillate consists of a mixture of a tarry material and a watery liquid known as pyroligneous acid. This latter contains, besides acetic acid (4–10%), various other organic substances, particularly acetone (0.5%) and methyl alcohol (1–2%). By fractional distillation several of these are separated, the second fraction, which contains most of the acetic acid, being neutralized with quicklime and evaporated; the resulting calcium acetate is then freed of impurities by heating and treated with hydrochloric acid so as to liberate the acetic acid, which is then distilled. This first distillate contains

about 36 to 50% of acetic acid. To purify it further, this dilute acid is passed through charcoal, and then redistilled over potassium dichromate. The final distillate, however, still contains water. To remove this, the solution is cooled down to a low temperature, when most of the acid solidifies and the water can be drained off. Since pure acetic acid solidifies on cooling, it is often called *glacial acetic acid;* this should not contain over 1% of water.

Acetic acid is a colorless liquid, boiling at 118.1° (corrected) and with a specific gravity of 1.055 at 15°. By dilution with water the specific gravity rises, attaining the maximum when an acid of 80% is obtained (see table in Appendix, p. 450). When glacial acetic acid is cooled it solidifies, the crystals again melting at 16.6°. It has a characteristic odor and, in dilute solution, a pleasant acid taste.

EXPERIMENTS. (1) Into a small fractionating flask put 6 gm. of powdered potassium dichromate and 10 c.c. of concentrated H_2SO_4; connect with a condenser; then, by means of a dropping funnel suspended by the cork of the flask, add drop by drop 12 c.c. of 20% alcohol. Heat until enough distillate is secured for the following tests.

(2) *Acetic acid tests.* (a) To 5 c.c. of the solution add 1 c.c. of H_2SO_4 and a few drops of alcohol. Shake, and note the odor of ethyl acetate on warming.

(b) Neutralize 5 c.c. with sodium carbonate solution. When neutral add a few drops of ferric chloride solution. The mixture becomes brownish

red; on boiling a colored precipitate separates out. Filter; the filtrate is colorless.

(3) Cool some glacial acetic acid in a large test-tube by means of ice-water, stirring with a thermometer. Melt the crystals with the heat of the hand, keeping the thermometer in motion. Note the temperature at which the acid melts.

In all its reactions acetic acid conforms with the structural formula CH_3COOH. Since, in our practical exercises, we shall perform nearly all the reactions that have enabled chemists to ascribe this formula to acetic acid, it may be advantageous, when describing these reactions, to indicate how they bear out the structural formula. To illustrate clearly just exactly *how a structural formula is arrived at* by the chemist, let us suppose that we are working with an unknown substance which, by elementary analysis and molecular weight determination (see Chapter III and p. 40), we have found to possess the empirical formula $C_2H_4O_2$.

For the sake of clearness of comprehension of the steps of the argument for the structural formula, a tabulated statement will be given before the detailed discussion.

(1) $C_2H_3O_2$—**H**, proof: monobasic acid.

(2) C_2H_3O—**OH**, proof: phosphorus chloride reaction.

(3) **CH₃**—(OC)—OH, methyl group proved by production of CH_4 from an acetate.

(4) **CH₃**—**COO**—H, proof: the addition of CO_2 to CH_3Na forming an acetate.

(5) *Synthetically* by the building up of methyl cyanide from CH_4, and the hydrolysis of the cyanide to acetic acid.

(1) In testing the reaction of this substance we shall have found it acid, and on neutralizing it with monacid bases and evaporating, crystalline salts will be obtained, which on analysis will be found to contain one H atom less than the acid itself. These facts indicate that the acid dissociates into a cation of hydrogen, $H\cdot$, and an anion represented by the remainder of the molecule, $C_2H_3O'_2$. In other words, one of the four H atoms must be represented in the structural formula as different from the others: $C_2H_3O_2$—H.

The hydroxides that may be employed to neutralize the acid are conveniently divided into metallic and organic.

Metallic salts of acetic acid—the acetates—are very numerous. *Sodium and potassium acetates* $(C_2H_3O_2K; C_2H_3O_2Na)$ are extensively used for various purposes in the laboratory. *Lead acetate*, $Pb(C_2H_3O_2)_2$, on account of its possessing a peculiar sweetish taste, is known as sugar of lead. It is used in medicine as an astringent. When it is mixed with lead oxide the compound is known as *basic lead acetate*. In the presence of carbonic acid, basic lead acetate forms densely opalescent solutions on account of the insoluble lead carbonate that is formed. In boiled distilled water the solutions are nearly clear. The lead acetates are valuable precipitating reagents and are extensively

employed for this purpose in biochemistry. *Copper acetate* is a well-known salt and is used as a reagent. All these acetates are most simply prepared by dissolving the metallic hydroxides in acetic acid.

Ethereal Salts of Acetic Acid. In studying alcohol we saw that its hydroxyl group (OH) is replaceable, for example, by halogens (Cl, Br, or I), or, as in the case of ethereal salts, by the organic acid radicle $C_2H_3O_2$. Since the ethereal salts are of considerable importance and are numerous, we shall postpone their consideration till later.

(2) So far we have seen that one of the H atoms in acetic acid differs considerably from the others. By another set of reactions we can show that this same H atom must be intimately connected with one of the O atoms, the resulting group, which we have already met with in alcohols, being hydroxyl. This hydroxyl is, as we have seen, replaceable by halogens. Thus, when acetic acid is treated with PCl_3, the following reaction ensues: $3C_2H_3O_2H + PCl_3 = 3C_2H_3OCl + H_3PO_3$. The hydroxyl group is evidently substituted by Cl, just as in the case of water or alcohol:

$$3HOH + PCl_3 = 3HCl + P(OH)_3.$$
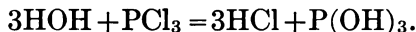
We must therefore assume that acetic acid can under certain conditions be caused to split up into C_2H_3O and OH. The former of these is called the *acetyl group.* An acid radical of this kind is called an *acyl.*

Acetyl chloride, C_2H_3OCl, belongs to the class of *acid chlorides* (or acyl halogenides) and may be pre-

pared by the method described in the following experiment:

EXPERIMENT. Put 25 c.c. of glacial acetic acid into a fractionating flask. Suspend a dropping funnel by the cork. Attach the flask to a con-
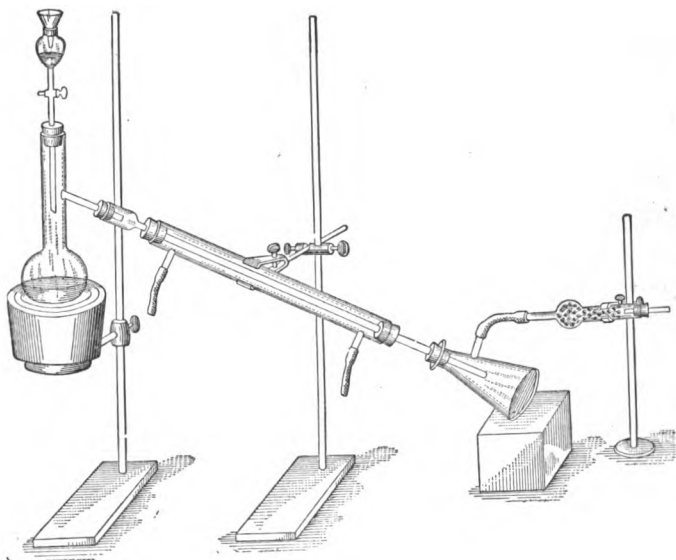
FIG. 21.

denser. As a receiver, fit a filtering flask to the condenser-tube with a cork (see Fig. 21), and attach to the side tube of the filtering flask a calcium chloride tube. All moisture must be carefully excluded in this manner. Add to the acid through the dropping funnel 20 gm. of phosphorus trichloride, the flask being immersed in a bath of ice-water.

When it has cooled, substitute a warm bath at 40°–
50°. Keep the temperature at this point until
the evolution of HCl ceases (having the apparatus
under a hood). Bring the water of the bath to
active boiling and distill the acetyl chloride.

It is a colorless volatile fluid, boiling at 51°. In
the presence of water it readily decomposes, as re-
presented in the following equation:

$$C_2H_3O|Cl + H|OH = C_2H_3OOH + HCl.$$
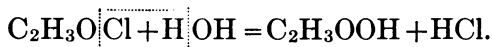
The atmospheric moisture is sufficient to cause this
reaction, so that when acetyl chloride is exposed to
the air it fumes, the fumes being very suffocating and
disagreeable. (It should be kept in tightly stoppered
bottles.) The H of the hydroxyl group of alcohols
reacts similarly with acetyl chloride, thus:

$$C_2H_3O|Cl + H|OC_2H_5 = C_2H_3OOC_2H_5 + HCl,$$
<div style="text-align:center">(Ethyl acetate)</div>
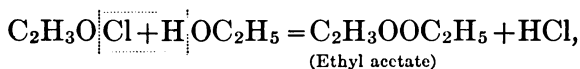
the ethereal salt of acetic acid with the radicle of
the alcohol used being formed. On this account
acetyl chloride is an invaluable reagent for the
detection of alcoholic hydroxyl; if we find that a
substance when treated with acetyl chloride forms
an ethereal acetate, we may conclude that the sub-
stance contains hydroxyl other than the hydroxyl
of carboxyl.

EXPERIMENT. To 3 c.c. of absolute alcohol add
slowly 3 c.c. of acetyl chloride. HCl is evolved.
Cool the mixture and neutralize with NaOH. Note
the odor of ethyl acetate.

The above experiments therefore, justify our writing the formula $C_2H_3O—OH$. Further corroboration of this is found in the fact that two molecules of acetic acid can be made to unite with the loss of a molecule of water, thus:

$$\left.\begin{array}{l} C_2H_3OO|H \\ C_2H_3O|OH \end{array}\right| = \left.\begin{array}{l} C_2H_3O \\ C_2H_3O \end{array}\right\rangle O + H_2O,$$
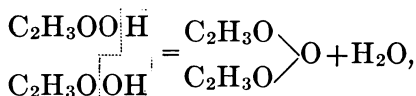
the resulting body being **acetic anhydride.** For practical purposes acetic anhydride may be prepared by acting on acetyl chloride with anhydrous sodium acetate, thus:

$$\left.\begin{array}{l} C_2H_3OO|Na| \\ + \quad | \\ C_2H_3O \; |Cl| \end{array}\right| = \left.\begin{array}{l} C_2H_3O \\ C_2H_3O \end{array}\right\rangle O + NaCl.$$
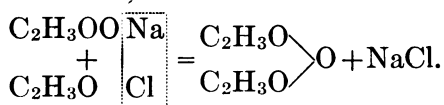
It is a fluid giving off a suffocating vapor. Added to water, it sinks to the bottom of the vessel, but gradually becomes reconverted into acetic acid. Its readiness to re-form acetic acid causes it to attack the hydroxyl group of alcohols and other hydroxyl compounds, one of the acetyl groups becoming thereby attached in place of the OH group, thus:

$$C_2H_5|OH \quad \quad OC_2H_3| = C_2H_5OOC_2H_3 + C_2H_3OOH.$$
$$+ O \big< $$
$$OC_2H_3$$

(Ethyl acetate)   (Acetic acid)
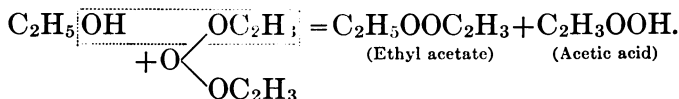
Like acetyl chloride, it may therefore be employed for ascertaining whether a substance contains hydroxyl not in carboxyl, and if so, how many such groups it contains (see p. 206).

(3) There remains for us to find out *how the acetyl radicle* C_2H_3O *is composed*. A clue to this is furnished by the observation that methane, CH_4, and a carbonate are obtained by heating anhydrous sodium acetate with soda-lime (see exp., p. 120):

$$C_2H_3OONa + NaOH = Na_2CO_3 + CH_4.$$

This must mean that the two carbon atoms are of different value and that one of them exists in combination with hydrogen as methyl, CH_3.

Further corroboration of this is furnished also by the fact that the three H atoms which belong to the methyl group can be separately replaced by chlorine atoms, thus forming the substitution products *mono-*, *di-*, or *tri-chloracetic acid*:

$$C_2H_3O \cdot OH + Cl_2 = C_2H_2ClO \cdot OH + HCl,$$

$$C_2H_2ClO \cdot OH + Cl_2 = C_2HCl_2O \cdot OH + HCl,$$

$$C_2HCl_2O \cdot OH + Cl_2 = C_2Cl_3O \cdot OH + HCl.$$
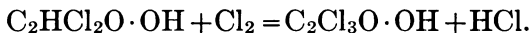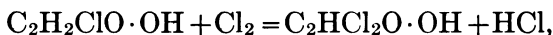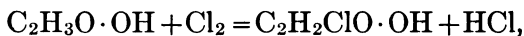
The resulting substitution products retain the acid properties of acetic acid, such as the power of forming ethereal salts, anhydrides, etc. The chloracetic acids are much stronger than acetic acid, and the acid power increases with the number of chlorine atoms.

(4) If we represent acetic acid as containing a methyl group, its formula must be written CCH_3OOH, $COCH_3OH$, or CH_3COOH: which of these is correct? The valence of carbon prevents C of CH_3 from having more than one linking to the rest of the molecule; and for the other C to satisfy

its valence, it is necessary that it be linked to both oxygen atoms as well as to C of CH_3; therefore the structure must be CH_3COOH. *Further evidence that the group* COOH *does actually exist in acetic acid* is given by the following observations:

(*a*) The formation of sodium acetate by treating sodium methyl with CO_2:

$$CH_3Na + CO_2 = CH_3COONa.$$
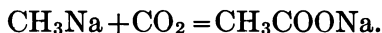
(*b*) The result of electrolysis of acetic acid. The cation H· is liberated at the cathode; the anion CH_3COO' passes to the anode, where it is liberated as CO_2 and ethane (the two methyl (CH_3) groups from two molecules having united).

(5) By synthesis, as shown by the equations:

$$CH_4 + Br_2 = CH_3Br + HBr.$$

$$CH_3Br + KCN = CH_3CN + KBr.$$

$$CH_3CN + 2H_2O = CH_3COOH + NH_3 \text{ (p. 256)}.$$
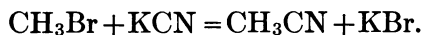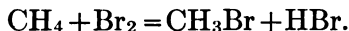
EXPERIMENT. Take 2 gm. of acetonitrile (prepared as directed in the experiment under methyl cyanide, on p. 255) and mix with 10 c.c. of 60% KOH in a small flask. Attach the flask to an upright (reflux) condenser. Heat for forty-five minutes. Note the ammonia escaping from the top of the condenser. Neutralize the resulting fluid with HCl and test for acetic acid (see previous experiments):

$$CH_3CN + 2H_2O = CH_3 \cdot COONH_4,$$

$$CH_3 \cdot COONH_4 + KOH = CH_3 \cdot COOK + NH_3 + H_2O$$
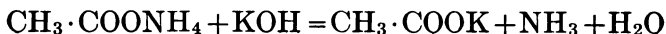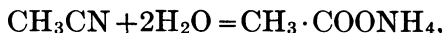
It is important to understand what it is that con-
stitutes the strength of an acid or alkali. This
obviously cannot be gauged by titration with
indicators: a normal solution of *any* acid will be
neutralized by an equal volume of a normal solution
of any alkali, and yet such acids as HCl, H_2SO_4,
etc., are far more *reactive*—are stronger, in other
words—than such acids as acetic, lactic, etc. This
difference in strength is explained by the fact that
only a certain fraction of any acid or alkali is effect-
ive, the value of this fraction being proportional
to the strength of the acid or alkali. The effective
fraction of an acid is that portion of it which becomes
ionized. In solution, acids ionize into a cation of
hydrogen or hydrion (which being charged with +
electricity is often called the positive ion) and
an anion of the rest of the molecule (see p. 66).
In the case of solutions of strong acids a much
greater proportion of acid ionizes in this way than
in the case of an equimolecular solution of weak
acids. We may therefore state that the *active*
acidity of a solution of an acid depends on the concen-
tration of the hydrogen ions.

In the case of bases, e.g., KOH and NH_4OH,
dissociation in solution into cations of the metal or
its equivalent (K,NH_4) and into anions of hydroxyl
occurs. It is the concentration of the *hydroxyl ions*
(hydroxions) which determines their strength (cf.
Amines, p. 260).

In a solution of HCl, for example, there exist: (*a*) undissociated HCl, (*b*) cations of H·, and (*c*) anions of Cl′. A solution of acetic acid contains (*a*) undissociated $CH_3 \cdot COOH$, (*b*) cations of H·, and (*c*) anions of $CH_3COO′$. The amount of (*a*) in the two cases will be very different, there being much less dissociation in the case of acetic acid than in the case of hydrochloric acid. In every acid, therefore, there must exist a certain proportion between the undissociated and the dissociated portions. This will, of course, vary at different dilutions, for it will be remembered that dissociation increases with dilution (see p. 68). Since it is known that the electrical conductivity of a solution depends on the amount of dissociation of the electrolyte dissolved in it, we may obtain a value for this proportion by measurement of electrical conductivity. In decinormal HCl solution 91% of the molecules are ionized, as compared with 1.3% in decinormal acetic acid. In decinormal NaOH solution 84% of the molecules are ionized, but only 1.4% in decinormal NH_4OH. (Consult the tables, p. 451).

ETHEREAL SALTS. ESTERS.

Corresponding to the salts of inorganic chemistry there are derivatives of organic acids in which the hydrogen of carboxyl is replaced by some hydrocarbon radicle. Thus ethyl acetate has the formula $CH_3COO \cdot C_2H_5$, from which it is seen that the two constituent radicles are linked together through an oxygen atom as in the ethers (see p. 132). On this

account such compounds are usually called *ethereal salts*, or more briefly *esters*. In a looser sense, compounds of mineral acids with organic radicles, as ethyl nitrate, $C_2H_5ONO_2$, and ethyl sulphate, $(C_2H_5)_2SO_4$, are included in this group; but since such as these have been considered elsewhere, we shall study at present only those salts in which organic acids are in combination.

Inorganic salts are immediately formed when solutions of an acid and a base are mixed, for, both of these being ionized, the hydrogen ion of the acid immediately unites with the hydroxyl ion of the base to form water:

$$(\overset{\cdot}{B} + OH') + (\overset{\cdot}{H} + Z') = (\overset{\cdot}{B} + Z') + H_2O.[1]$$
$$\text{(Base)} \qquad \text{(Acid)} \qquad \text{(Salt)}$$
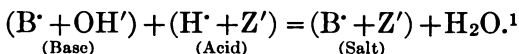
Esters are, however, not thus readily formed, for the reacting hydroxide, being an alcohol, is not ionized, but remains as a molecule, and on this the acid only slowly acts:

$$R \cdot OH + (\overset{\cdot}{H} + Z') = R \cdot Z + H_2O.$$
$$\text{(Alcohol)} \qquad \text{(Acid)} \qquad \text{(Ester)}$$
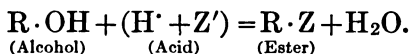
Inorganic are distinguished from ethereal salts not only in their ease of formation but also in their dissociability in solution, the former being usually entirely dissociated in solution, the latter not at all so. In this connection it is of great importance to point out that salts of organic acids with metals do undergo dissociation in solution, and to about

[1] This equation will serve as an example of how ions are represented in a reaction.

the same extent as inorganic salts. Thus in a solution of ethyl acetate there are no free ions, whereas in one of sodium acetate dissociation into Na˙ and CH_3COO' ions occurs.

Mass Action. One of the notable illustrations of mass action is ester formation. The formation of an ethereal salt when an alcohol and an acid are directly mixed, although slow, yet proceeds until a balance between the four constituents is established (i.e., between acid, alcohol, salt, and water). This is because the reaction is a reversible one; in other words, whenever a slight excess of water comes to exist in the mixture, it decomposes the ester into the acid and alcohol, thus:

$$CH_3COOC_2H_5 + HOH \rightleftarrows CH_3COOH + C_2H_5OH.$$
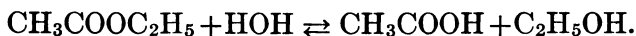
Such *reversible reactions* are often represented in equations by two arrows in place of the sign of equality.

The mixture comes to a point of equilibrium when 0.669 part of a gram molecule of ester is present, provided we started with one gram-molecule of both acid and alcohol. At the beginning of the reaction the mass action of both alcohol and acid is most marked, forcing ester production, the reverse action being very slight. As ester and water accumulate, ester formation slows up and the reverse action begins to figure in the reaction, until finally the mass action of the water to cause hydrolysis is as pronounced as that of the alcohol and acid to cause esterification. The equilibrium is not really static; for the action and the reverse

action are going on constantly to an equal degree, thus maintaining a balance.

If a gram-molecule of both the ester and water are mixed, hydrolysis occurs, but apparently ceases when the same equilibrium point as for esterification is reached. In this case also the equilibrium mixture contains about two-thirds of a gram-molecule of ester and water, and one-third of a gram-molecule of alcohol and acid.

The amount of ester thus formed depends on the relative amounts of acid and alcohol present and not on the temperature. With a given amount of alcohol an increase in the amount of acid increases the yield of ethereal salt, and, conversely, the same is true with a given amount of acid when more alcohol is used. Since the progress of the formation of the above ester can be followed by titrating the residual acid, the reaction has been extensively employed in studying the laws of mass action.

The fundamental law of mass action states that the product of the number of gram-molecules per liter of the substances on the one side of the equation, divided by the product of these on the other side, is equal to some constant. In the case of the above reaction we have therefore the equation:

$$\frac{C \text{ acid} \times C \text{ alcohol}}{C \text{ ester} \times C \text{ water}} = \text{constant},$$

where C represents gram-molecules per liter of the reacting substances.

It will be evident that if we increase C acid while C alcohol remains constant, then C ester must

increase, which leads us to the conclusion that if enough acid is added, all the alcohol will become converted into ester, or, conversely, that if more alcohol is added, the acid remaining constant, the same will be true. For example if one gram-molecule of acetic acid and eight gram-molecules of ethyl alcohol interact, they come to equilibrium when 96.6% of a gram-molecule of ethyl acetate is formed.

Temperature does not affect the constant to any marked degree, so that it does not influence the ultimate amount of ethereal salt produced. On the other hand, it greatly influences the rate of reaction, i.e., the time that it takes before the condition of chemical equilibrium is reached. Thus a rise in temperature increases the velocity of the reaction (as a rule the rate doubles for each increase of ten degrees in temperature). At 55° cane sugar is hydrolyzed by acids about five times as fast as at 25°. By studying different alcohols and acids, it has been found that if equimolecular amounts of acid and alcohol be used, the limit of esterification varies only slightly;[1] but the rate is much greater for such acids as acetic than it is for such as benzoic, and for primary than for secondary alcohols.

The amount of ester produced can be greatly

[1] For example the per cent of a gram-molecule of ester formed by some alcohols and acids is as follows:

Acetic acid + methyl alcohol 67.5, benzoic acid + methyl alcohol 64.5.

Acetic acid + ethyl alcohol 66.9, benzoic acid + ethyl alcohol 67.

Acetic acid + amyl alcohol 68.9, benzoic acid + amyl alcohol 70.

increased by removing the water formed during the reaction, and in some cases this can be accomplished. By removing the ethereal salt as it is formed (e.g., by distillation or crystallization), much higher yields can also be obtained (see exp., p. 181).

Preparation of Ethereal Salts. The more usual methods for preparing ethereal salts are the following:

1. By heating a mixture of the acid and alcohol with sulphuric acid: ethylsulphuric ·acid is first formed and then reacts with the acid, sulphuric acid being re-formed (cf. ether, p. 134), thus:

(*a*) $C_2H_5 OH + H \cdot HSO_4 = C_2H_5 \cdot HSO_4 + H_2O.$

(*b*) $C_2H_5 \cdot HSO_4 + H OOCCH_3 =$
$$C_2H_5 — OOC \cdot CH_3 + H_2SO_4.$$
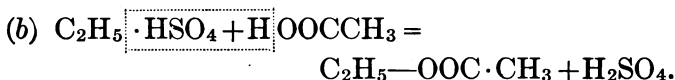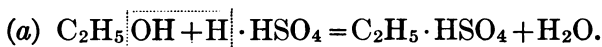
2. By heating a mixture of the acid and alcohol with hydrochloric acid gas: an acid chloride is probably first formed, which then reacts with the alcohol:

(*a*) $CH_3CO OH + H Cl = CH_3CO \cdot Cl + H_2O.$

(*b*) $CH_3CO Cl + H OC_2H_5 = CH_3COO \cdot C_2H_5 + HCl.$
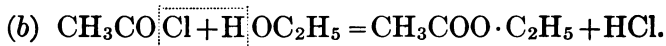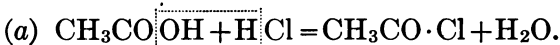
3. Or the second stage of this reaction (*b*) can be itself used for the production of ethereal salts by treating an alcohol with an acid chloride or an anhydride of an acid. In this latter manner the acetyl or benzoyl (see p. 359) derivatives of many substances can be produced, and these, being readily

purified, are extensively prepared for purposes of identification. .The addition of sodium hydroxide accelerates this reaction in the case of benzoyl compounds (see p. 359).

4. By treating a silver salt of an acid with an alkyl halide (as iodide):

$$CH_3COO\,Ag + I\,C_2H_5 = CH_3COOC_2H_5 + AgI.$$
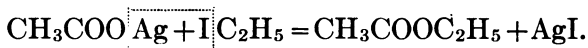
Properties. Esters in a pure state are stable; in watery solution they slowly decompose into acid and alcohol, the decomposition being greatly accelerated by boiling with water and by the action of acids or bases. Hydrolysis most readily occurs with those esters which are easily formed; thus methyl acetate is more readily formed and is more easily hydrolyzed than ethyl acetate.

Many esters have pleasant odors, often simulating those of fruits; for instance, isoamyl acetate has an odor resembling pears. On this account some of them are used as artificial fruit essences (see p. 187).

Ethereal salts include the *neutral fats* (see p. 203). The two most important ethereal salts of acetic acid are methyl and ethyl acetates. Prepared by the general methods described above, both these bodies are liquids with pleasant odors. Ethyl acetate is commonly called acetic ether.

From a biochemical standpoint the acceleration which acids induce in the hydrolysis of esters is of interest, partly because a method for the quantitative determination of the acid in gastric juice is based on it, and partly because it typifies *catalytic*

action, which is the means by which enzymes pro-
duce their actions.   Enzymes have a much more
powerful action than other catalysts.

Catalysis is defined as consisting in acceleration of
reactions, which would take place without the cata-
lyzer, but more slowly.   (Some catalytic agents
cause retardation of reactions.)   Neither the acid
molecule nor the ions enter into the chemical reac-
tion.   When a chemical agent enters into the reac-
tion and is recovered, as sulphuric acid in ether
production, it is a *pseudo-catalyst.*

If equimolecular quantities of different acids be
added to similar quantities of methyl acetate, it
will be found that the acceleration of hydrolysis
produced varies greatly with the acid employed.
HCl and HNO_3 produce about the greatest accelera-
tion, whereas the commonest organic acids have
only a feeble influence; thus the accelerating influ-
ence of oxalic acid is only 19% and of acetic only
0.4% of that of HCl (see table in Appendix, p. 452).
Now it has been found that the electrical conduc-
tivity of dilute solutions of the acids is directly
proportional to their accelerating (catalytic) power,
which leads us to the conclusion that the catalytic
power depends on the amount of dissociation which
the acids undergo; in other words, on the number of
hydrogen ions existing in the solution (see p. 172).

By this means, therefore, we have a practical
method for gauging the relative strengths of acids
(see p. 184).

Further, if we add dilute solutions of varying con-
centrations of the same mineral acid to methyl

acetate it will be found that the rate of hydrolysis is proportional to the strength of acid added. It is important to note that this law holds only for dilute solutions (less than decinormal) of strong acids and not at all for weak acids. By comparing the amount of hydrolysis of methyl acetate that occurs when a known quantity of acid is added, with the amount occurring in a similar solution of methyl acetate having an unknown quantity of the same acid, an estimate can be made of the amount of acid actually present in the latter. In this comparison the two solutions must of course be kept at the same temperature and the action allowed to proceed for the same length of time (see exp. below).

EXPERIMENTS. (1) Put into a medium-sized flask 10 c.c. of alcohol and 10 c.c. of C.P. H_2SO_4. Use a three-hole cork; by one hole suspend a dropping funnel, by another connect with a condenser, and insert a thermometer so that its bulb is in the liquid. Heat until the liquid is at 135°, then begin running in slowly by the dropping funnel a mixture of 80 c.c. of alcohol and 80 c.c. of glacial acetic acid, keeping the temperature of the mixture constant at about 135°. Regulate the inflow of acid alcohol to correspond approximately to the rate of distillation. Wash the distillate in the receiving flask with small portions of saturated sodium carbonate solution until the top layer is no longer acid to litmus. Separate with a separating funnel. Add to the acetic ether a cold solution of 20 gm.

of calcium chloride in 20 c.c. of water and shake.
(The ester is soluble in 17 parts of water).   Separate
with the funnel.   Put the ethyl acetate into a dry
flask, add solid calcium chloride, cork, and let it
stand a day or so.   Redistill on a water bath, noting
the boiling-point (77°).   Determine the specific
gravity (0.905 at 17°).

(2) Determine the rate of hydrolysis of methyl
acetate as influenced by different strengths of acid
(HCl).   Into each of two small flasks put 1 c.c. of
methyl acetate measured accurately with a pipette;
to one add with a pipette 20 c.c. of HCl solution
of known strength (say 0.4%); to the other add
20 c.c. of HCl more dilute but of unknown concen-
tration; cork each flask and shake.   As quickly
as possible titrate 5 c.c. of each mixture successively
with decinormal NaOH, using phenolphthalein as
an indicator.   This gives the acidity of each at the
beginning of the experiment.   Cork the flasks
tightly with rubber stoppers and keep them in an
incubator at about 40° for three or four hours;
then, after shaking and cooling, take 5 c.c. from each
and titrate again.   The increase in acid (due to
liberation of acetic acid by hydrolysis) is found by
deducting the initial titration from this second
titration.   The stronger solution causes the greater
amount of hydrolysis.   To calculate the exact
strength of the unknown acid solution by com-
parison with the known, we must find out the limit
of hydrolysis for the known strength; to do this
leave the flask containing this acid in the incubator
for forty-eight hours, then titrate again.   The

titration at the end of this period, less the initial titration, gives an acid value called A; this is the number of cubic centimeters of decinormal acetic acid that can be liberated by hydrolysis of the methyl acetate by 0.4% HCl. Now we can reckon the per cent of HCl in the other solution in the following manner: Find the value of the constant in the formula $C = \log \left(\dfrac{A}{A-X}\right)$ for each solution, but call the constant of the known solution C'. The observed increase in acid content during the three or four hours' incubation is X.

Take a particular experiment. A known solution (0.43435% HCl) gave $A = 24.9$ (c.c.). The increase (after four hours) in the known solution was 12.1 (c.c.); therefore $A - X = 24.9 - 12.1 = 12.8$:

$$C' = \log \left(\frac{24.9}{12.8}\right) = .2878.$$

With the unknown solution $X = 7$ (c.c.), $A - X = 17.9$:

$$C = \log \left(\frac{24.9}{17.9}\right) = .1430.$$

Now the per cent of HCl in the unknown

$$= \left(\frac{C \text{ of unknown}}{C' \text{ of known}}\right) \text{ (per cent HCl in known).}$$

Therefore per cent $= \left(\dfrac{.1430}{.2878}\right) (0.43435) = 0.21544.$

In this particular case the unknown was of exactly half the strength of the known solution.

The rate of hydrolysis bears a definite relation to the number of hydrogen ions present in the solution. Therefore with dilute solutions of easily ionizable acids an accurate estimation of the quantity of acid present can be made by this method. Most organic acids furnish so few hydrogen ions (see p. 157) that their presence has practically no effect. In consequence, the method is available for determining the per cent of HCl present in gastric juice or stomach contents.

It must not be forgotten, however, that the presence of salts (as in stomach contents) can change the rate of hydrolysis from what it would be if only pure acid were present.

EXPERIMENT 3. Determine the relative strength of several acids, repeating the procedure of experiment 2. Decinormal solutions of tartaric, oxalic, trichloracetic and hydrochloric acids give interesting results. Ethyl acetate may be used instead of methyl acetate. Make a third titration of acidity after hydrolysis has proceeded for at least a day. Compare directly the c.c. increase of decinormal acid in the various mixtures. This will give a rough idea of the relative H ion concentrations.

OTHER FATTY ACIDS

Propionic acid (propanoic acid), $CH_3 \cdot CH_2 \cdot COOH$, resembles acetic acid. It can be prepared by oxidation of propyl alcohol, by hydrolysis of ethyl cyanide, and by the action of CO_2 on sodium-ethyl.

In addition it can be made by reduction of lactic acid, thus:

$$CH_3 \cdot CHOH \cdot COOH + 2HI$$
<div align="center">(Lactic acid)</div>

$$= CH_3 \cdot CH_2 \cdot COOH + H_2O + I_2.$$
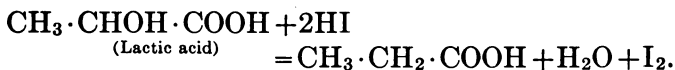
The hydriodic acid furnishes nascent hydrogen, and this brings about reduction.

Corresponding to chloracetic acids there are chlorpropionic acids. But the halogen may take the place of hydrogen either in the CH_3 group or in the CH_2 group of propionic acid. It becomes necessary, therefore, to distinguish between these two positions in the molecule. This is done by using Greek letters, α and β. In order to have a rule that will apply to all acids, no matter how many carbon atoms the acid may contain, it is necessary to count backwards from the carboxyl group: thus, the group next to the COOH is in the α position, the second group is in the β position, and so on; for example, $CH_3 \cdot CHCl \cdot COOH$ is *α-chlorpropionic acid*, $CH_2Cl \cdot CH_2 \cdot COOH$ is *β-chlorpropionic acid*.

Butyric acid $CH_3 \cdot CH_2 \cdot CH_2 \cdot COOH$, is normal butyric acid.

Isobutyric acid or methylpropanoic acid has the formula $\begin{matrix} CH_3 \\ CH_3 \end{matrix}\Big\rangle CH{-}COOH.$ Normal butyric acid is fermentation butyric acid, and occurs in Limburger cheese, rancid butter, and sweat. It may be prepared by oxidation of butyl alcohol and by hydrolysis of propyl cyanide. Butter contains

about 6% of butyrin, which is the glycerol ester of butyric acid (see p. 200); the acid can therefore be obtained by hydrolysis or saponification of butter (see exp., p. 207). Microörganisms can cause fermentation of butter, with resulting hydrolysis of the ester (butyrin) and setting free of butyric acid. Butyric acid is soluble in water and volatile. Oleomargarine contains very little butyric or other soluble volatile fatty acids. On this account it can readily be identified by making an estimation of the volatile acids in the manner to be described later in an experiment (see p. 207).

Butyric acid can also be made from cane sugar as follows: The sugar solution, acidified with tartaric acid, is inoculated with sour milk: one variety of microörganisms in the latter " inverts " the sugar into dextrose and lævulose; another variety ferments these monosaccharides, producing lactic acid; while a third variety converts the lactic acid into butyric acid:

$$C_{12}H_{22}O_{11} + H_2O = C_6H_{12}O_6 + C_6H_{12}O_6,$$
(Cane sugar)   (Dextrose)   (Lævulose)

$$C_6H_{12}O_6 = 2C_3H_6O_3,$$
(Lactic acid)

$$2C_3H_6O_3 = CH_3 \cdot CH_2 \cdot CH_2 \cdot COOH + 2CO_2 + 2H_2.$$
(Butyric acid)
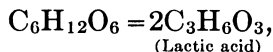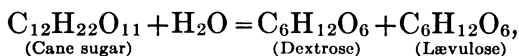
Similar fermentation, with production of lactic and butyric acids, may occur in the stomach when the hydrochloric acid of the gastric juice is deficient in amount or absent altogether. The gases formed (CO_2 and H_2) cause the flatulence present in such

cases. Butyric acid has the peculiar disagreeable odor characteristic of rancid butter.

The ethereal salt $C_3H_7 \cdot COOC_2H_5$, **ethyl butyrate**, resembles pineapple in odor. It is used as a flavoring material in place of pineapple juice.

Valeric acid (valerianic acid),
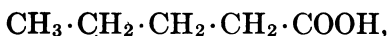
$$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot COOH,$$

is the normal acid. Ordinary valeric acid, however, is isovaleric acid, $\begin{matrix} CH_3 \\ CH_3 \end{matrix} \Big> CH \cdot CH_2 \cdot COOH.$ It occurs in valerian root.

Amyl valerate, $C_4H_9 \cdot COOC_5H_{11}$, smells like apple, and is therefore used as an apple essence. This is the ester of isoamyl alcohol with isovaleric acid. It has been used as a medicine.

Of the other acids of the formic acid series, only those containing an even number of CH_2 groups are of importance.

> *Caproic* acid is $CH_3(CH_2)_4COOH$.
> *Caprylic* acid is $CH_3(CH_2)_6COOH$.
> *Capric* acid is $CH_3(CH_2)_8COOH$.
> *Lauric* acid is $CH_3(CH_2)_{10}COOH$.
> *Myristic* acid is $CH_3(CH_2)_{12}COOH$.
> *Palmitic* acid is $CH_3(CH_2)_{14}COOH$.
> *Stearic* acid is $CH_3(CH_2)_{16}COOH$.
> *Arachidic* acid is $CH_3(CH_2)_{18}COOH$.
> *Behenic* acid is $CH_3(CH_2)_{20}COOH$.

Most of these occur in fats. The lowest acids are volatile with steam and soluble. The higher acids

are non-volatile and insoluble.   The melting-point of palmitic acid is 62.6°, and of stearic acid is 69.2°.

The calcium salt of monoiodo-behenic acid is a remedy called *sajodin;* it is used for administration of iodine.

CHAPTER XIII

SECONDARY AND CERTAIN OTHER MONACID ALCOHOLS. KETONES

SECONDARY ALCOHOLS AND THEIR OXIDATION PRODUCTS

SECONDARY alcohols contain the group CHOH, as in $CH_3 \cdot CHOH \cdot CH_3$, *secondary propyl alcohol.* None of the secondary alcohols is of any importance.

When a secondary alcohol is oxidized an aldehyde is not formed, but a *ketone:*

$$CH_3 \cdot CHOH \cdot CH_3 + O = CH_3 \cdot CO \cdot CH_3 + H_2O$$
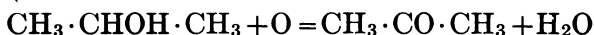
or
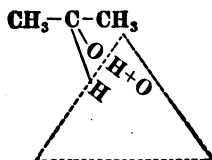
A **ketone** is in all essential points identical with an aldehyde, the only difference being that in the case of an aldehyde the oxygen atom is attached to a carbon atom at one end of the chain, while in a ketone it is attached to an inner carbon atom. Some ketones can be oxidized, but this involves splitting up the chain of carbon atoms. Some ketones give the fuchsin test (see p. 154), particularly

those that have $CH_3 \cdot CO$ in the molecule. Many ketones form addition compounds with acid sulphites and with hydrocyanic acid (cf. aldehydes). Phenylhydrazine reacts with ketones in the same manner as with aldehydes, forming hydrazones. Ketones do not polymerize, but they form condensation products.

The reaction of phosphorus pentachloride with ketones is similar to that with aldehydes:

$$CH_3 \cdot CO \cdot CH_3 + PCl_5 = CH_3 \cdot CCl_2 \cdot CH_3 + POCl_3.$$
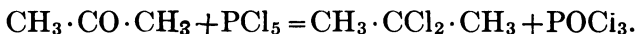
No hydrochloric acid is produced, and a dichlor derivative is formed; therefore *a ketone does not contain hydroxyl*. The most important ketone is acetone.

Acetone (dimethylketone or propanone) is the simplest ketone, its formula being $CH_3 \cdot CO \cdot CH_3$. It is produced commercially by the dry distillation of calcium acetate at about 300°:

$$\begin{array}{l} CH_3-CO-O \\ CH_3 \text{———} COO \end{array} \Big\rangle Ca = CH_3 \cdot CO \cdot CH_3 + CaCO_3.$$
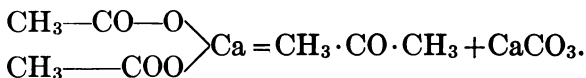
It can also be obtained by oxidation of secondary propyl alcohol. Its synthesis from zinc methyl and acetyl chloride proves the structural formula for acetone.

$$\begin{cases} CH_3 \cdot CO \cdot Cl \\ CH_3 \cdot CO \cdot Cl \end{cases} + Zn \Big\langle \begin{array}{l} CH_3 \\ CH_3 \end{array}$$
$$= 2CH_3 \cdot CO \cdot CH_3 + ZnCl_2.$$
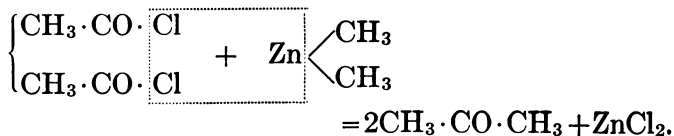
Acetone is present in the urine under certain conditions, especially in severe cases of diabetes. It is a useful solvent. It is a liquid, boiling at 56.3° (corrected), with a specific gravity of 0.812 at 0°. Nascent hydrogen converts it into secondary propyl alcohol. It does not oxidize to an acid containing the same number of carbon atoms, but to acetic and formic or carbonic acids. Acetone gives the iodoform test.

EXPERIMENTS. (1) Make iodoform, using acetone instead of alcohol (see p. 130).

The reactions involved are of the same nature as in the preparation of iodoform from alcohol; in this case the intermediate compound is triiodoacetone, $CI_3 \cdot CO \cdot CH_3$.

(2) Dissolve 2 c.c. of acetone in dilute H_2SO_4; add $KMnO_4$ solution until a pink color remains on warming. Filter, make the filtrate strongly acid with 20% H_2SO_4, and distill. Test the distillate for acetic acid (see p. 163).

(3) Shake 5 c.c. of acetone with 8 c.c. of a saturated solution of sodium bisulphite; cool; crystals of the addition compound of acetone appear. Filter and wash. Save samples.

Chloretone (chloroform acetone, trichlor-tertiary-butyl-alcohol), $CH_3 - C\overset{\diagup O-H}{\underset{\diagdown CH_3}{\underline{\hspace{1cm}}}}CCl_3$, is an addition product of acetone. It is formed by the interaction of acetone and chloroform in the presence of an excess of KOH. It is a useful hypnotic.

Brometone, the corresponding bromine preparation, produced from acetone and bromoform, is analogous to chloretone. As a remedy it is used instead of bromides.

Ketone acids. Some acids contain both the carbonyl and carboxyl groups. **Aceto-acetic acid,** $CH_3 \cdot CO \cdot CH_2 \cdot COOH$, typifies these, and is of importance, since it may occur in the urine (see p. 218).

Pyruvic acid (pyroracemic acid) is another ketone acid of importance. Its formula is $CH_3 \cdot CO \cdot COOH$. It shows a strong tendency to polymerize.

Tertiary alcohols, when oxidized, decompose into compounds containing fewer carbon atoms than the alcohol. The tertiary alcohols are of no importance.

Little need be said of other monacid alcohols, except that most **waxes** contain esters of monacid alcohols having a large number of carbon atoms; for example:

> Ceryl alcohol, $C_{26}H_{53}OH$.
> Cetyl alcohol, $CH_3(CH_2)_{14}CH_2OH$.
> Melissic alcohol, $C_{30}H_{61}OH$.

In waxes some of the alcohol is not in ester combination, but free.

Cetyl palmitate has been found in the fat of an ovarian cyst. Lanolin contains some wax esters (see p. 211).

Myricyl palmitate, $C_{30}H_{61}OOC \cdot C_{16}H_{31}$, is the chief constituent of *beeswax.*

CHAPTER XIV

DIACID ALCOHOLS AND DIBASIC ACIDS

DIACID ALCOHOLS

DIACID alcohols contain two hydroxyl groups. They are comparable to $Ca(OH)_2$. The simplest diacid alcohol, and the only one of importance, is **glycol** (ethanediol), $\begin{matrix} CH_2OH \\ | \\ CH_2OH \end{matrix}$. The method of preparation shows that both hydroxyl groups are not attached to the same carbon atom. Ethylene is produced from ethyl alcohol by heating the latter with an excess of sulphuric acid. The ethylene is saturated with bromine, forming ethylene bromide, in the manner described in the experiment (see p. 301). From ethylene bromide glycol can be obtained by the action of silver hydroxide:

$$
\begin{matrix} CH_2Br \\ | \\ CH_2Br \end{matrix} + \begin{matrix} Ag\,OH \\ \\ Ag\,OH \end{matrix} = \begin{matrix} CH_2OH \\ | \\ CH_2OH \end{matrix} + 2AgBr.
$$
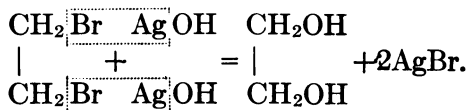
Glycol is a colorless glycerol-like liquid, of sweetish taste. It boils at 195° and has a specific gravity of 1.128 at 0°.

It forms two classes of ethereal salts, according

to whether one or both hydroxyls are replaced. Similarly there are two sodium alcoholates of glycol:

$$\begin{array}{l} CH_2ONa \\ | \\ CH_2OH \end{array}, \text{ monosodium glycolate,}[1] \text{ and}$$

$$\begin{array}{l} CH_2ONa \\ | \\ CH_2ONa \end{array}, \text{ disodium glycolate.}$$
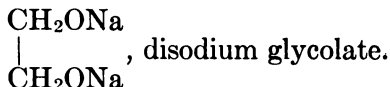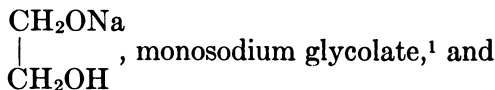
The oxidation products of glycol are numerous because of the presence of two primary alcohol groups. There are two aldehydes:

$$\begin{array}{l} CH_2OH \\ | \\ CHO \end{array}, \text{ glycolic aldehyde, and}$$

$$\begin{array}{l} CHO \\ | \\ CHO \end{array}, \text{ glyoxal.}$$
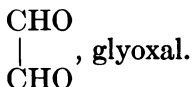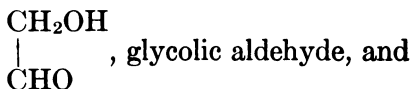
Oxidation of the first gives rise to *glycollic acid,*

$$\begin{array}{l} CH_2OH \\ | \\ COOH \end{array}; \text{ this will be considered under hydroxy-}$$
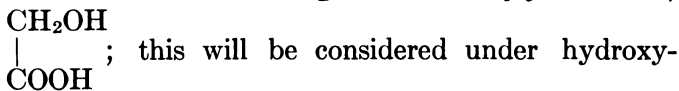
acids (see p. 212). Oxidation of glyoxal gives

$$\begin{array}{l} CHO \\ | \\ COOH \end{array}, \text{ *glyoxylic acid;* this is really a dihydroxy-}$$
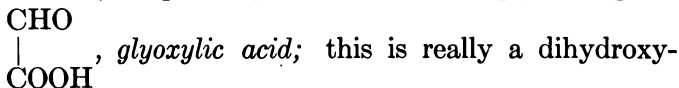
acid, as will be seen later (see p. 219). These two acids are monobasic. Complete oxidation of glycol

---

[1] Distinguish from the *glycollates* derived from glycollic acid (p. 213).

results in the formation of a dibasic acid, *oxalic acid*,

$$\begin{matrix} COOH \\ | \\ COOH \end{matrix}.$$

DIBASIC ACIDS

The simplest is *oxalic acid*. The next members of the series are *malonic acid*, $CH_2\begin{matrix} COOH \\ COOH \end{matrix}$, *succinic acid*, $\begin{matrix} CH_2\!-\!COOH \\ | \\ CH_2\!-\!COOH \end{matrix}$, and *glutaric acid*,

$$CH_2\begin{matrix} CH_2\!-\!COOH \\ CH_2\!-\!COOH \end{matrix}.$$
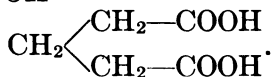
General methods for the production of dibasic acids are (1) by hydrolysis of cyan-acids, (2) by oxidation of diacid alcohols, and (3) by oxidation of an hydroxy-acid.

The acids of the oxalic acid series show the same behavior as regards melting-points as do the acids of the formic acid series (see p. 158).

Oxalic acid, $\begin{matrix} COOH \\ | \\ COOH \end{matrix}$, forms crystals containing two molecules of water for each molecule of oxalic acid. The crystals readily effloresce. It may be prepared by oxidation of cane sugar with nitric acid. It was formerly made by heating·sawdust with caustic potash and .soda. After cooling the oxalate is dis· solved out of the mass, precipitated by slaked lime as calcium oxalate, and the separated oxalate is treated with sulphuric acid, so that the oxalic acid is set free. It is now made by heating together

potassium formate and hydroxide (and a little oxalate); and treating the product with sulphuric acid. Oxalic acid is one of the strongest of all organic acids, because its solution contains more hydrogen ions than the corresponding solutions of most other organic acids (see p. 172).

As the number of C atoms interposed between the carboxyls of acids of this series is increased, acid power is decreased.

When oxalic acid is heated, it first loses its water of crystallization, then decomposes into carbon dioxide, carbon monoxide, water, and some formic acid. If heated in the presence of glycerol, formic acid and carbon dioxide are formed (see p. 159). Sulphuric acid decomposes it to carbon monoxide, carbon dioxide, and water. Potassium permanganate in warm acid solution oxidizes it to carbon dioxide and water:

$$2KMnO_4 + 5(COOH)_2 + 3H_2SO_4 = 10CO_2 + K_2SO_4$$
$$+ 2MnSO_4 + 8H_2O.$$
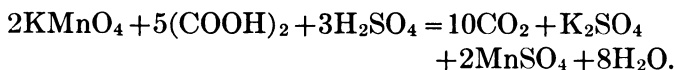
Oxalic acid forms two classes of salts, acid and neutral. *Acid potassium oxalate*, $\begin{matrix} COOH \\ | \\ COOK \end{matrix}$, occurs in plants, particularly sorrel. *Ammonium*, *potassium*, and *sodium oxalates* are soluble; all other oxalates of metals are practically insoluble. *Calcium oxalate* frequently occurs in the urine as a crystalline sediment.

Oxalic acid is poisonous and has been used for suicidal purposes.

EXPERIMENTS. (1) *Preparation of oxalic acid.* Heat 200 c.c. of HNO_3 in a large flask to 100°. Set in a fume-closet and add 50 gm. of cane sugar. When the evolution of fumes has ceased, evaporate the acid mixture in an evaporating dish to about one third its original volume. Cool and collect the crystals. Recrystallize, using as little hot water as possible.

(2) Heat some dry crystals of oxalic acid in a test-tube, loss of water of crystallization occurs, as shown by drops collecting on the cool part of the tube.

(3) Decompose some oxalic acid with H_2SO_4; test the evolved gases for CO_2 (baryta water, as on p. 3) and CO (hæmoglobin solution, as on p. 161).

(4) To 5 c.c. of oxalic acid solution add a few drops of H_2SO_4, warm, then add potassium permanganate solution, it is decolorized.

Malonic acid, $CH_2\underset{\diagdown COOH}{\overset{\diagup COOH}{}}$, is of importance mainly in bringing about certain organic syntheses.

Succinic acid, $\begin{array}{l} CH_2{-}COOH \\ | \\ CH_2{-}COOH \end{array}$, is *normal* succinic acid and may be produced by hydrolysis of β-cyan-propionic acid:

$$CH_2CN \cdot CH_2 \cdot COOH + 2H_2O = \begin{array}{l} CH_2{-}COOH \\ | \\ CH_2{-}COOH \end{array} + NH_3.$$
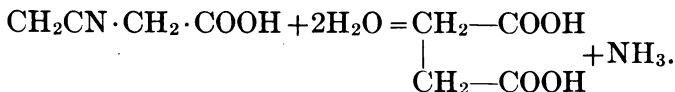
If caustic potash is used to effect hydrolysis, potassium succinate would be formed.

If α-cyanpropionic acid be hydrolyzed, *iso*succinic acid is formed:

$$CH_3 \cdot CHCN \cdot COOH + 2H_2O = CH_3 \underset{CH}{\overset{|}{\underset{}{}}} \diagup^{COOH}_{\diagdown COOH} + NH_3.$$
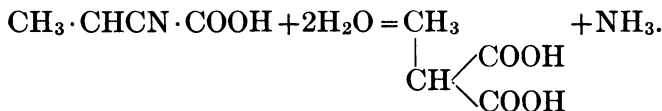
These two acids give different reactions.

Normal succinic acid when heated to 235°, yields *succinic anhydride* and water:

$$COOH \cdot CH_2 \cdot CH_2 \cdot COOH = \begin{matrix} CH_2 - CO \\ | \\ CH_2 - CO \end{matrix} \diagdown^{}_{\diagup} O + H_2O.$$
(Succinic anhydride)
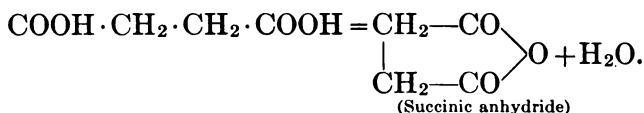
Isosuccinic acid, however, when heated above 130°, breaks up into propionic acid and carbon dioxide:

$$CH_3 \cdot CH \diagup^{COOH}_{\diagdown COOH} = CH_3 \cdot CH_2 \cdot COOH + CO_2.$$
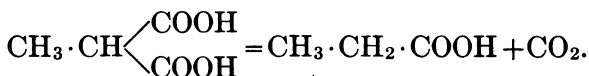
It is, indeed, a general rule in organic chemistry that two carboxyl groups cannot remain attached to the same carbon atom at high temperatures, carbon dioxide being split off from one of the carboxyls.

Alphozone (disuccinyl peroxide) is an organic peroxide (cf. acetozone p. 352):

$$HOOC(CH_2)_2CO—O—O—OC(CH_2)_2COOH.$$
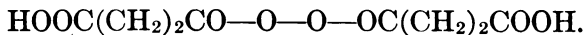
It is an oxidizing agent, and is said to be antiseptic.

TRIACID ALCOHOLS, FATS, AND SOAPS

TRIACID ALCOHOLS

Glycerol (glycerine or propanetriol),

$$CH_2OH$$
$$|$$
$$CHOH, \text{ is the}$$
$$|$$
$$CH_2OH$$

only triacid alcohol of importance.   Glycerol occurs
in fats in combination with fatty acids and oleic
acid, as glycerol esters of these acids.   By hydrolyz-
ing fats, glycerol is set free.   This is accomplished
commercially by heating fats (at 170–180°) in
a closed boiler or autoclave with water and lime.
The lime combines with fatty acids, forming insolu-
ble calcium salts, while the glycerol goes into
solution.   The calcium remaining in solution is
precipitated with sulphuric acid.   Glycerol is also
a by-product of soap manufacture.   The liquid
left after the separation of hard soap, containing
4-5% of glycerol, is purified to remove salts and
alkali.   The dilute glycerol solution is then evapor-
ated under diminished pressure, at as low a tem-
perature as possible, until its specific gravity
becomes 1.24.   The crude glycerol is purified by
combined steam and vacuum distillation.   C.P.
glycerol is prepared by treatment of distilled

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glycerol with charcoal and distillation with steam in vacuo.

Glyceryl butyrate or butyrin yields on hydrolysis glycerol and butyric acid, thus:

$$CH_2—OOC\cdot C_3H_7 \qquad CH_2OH$$
$$CH \ —OOC\cdot C_3H_7 + 3H_2O = CHOH + 3C_3H_7\cdot COOH.$$
$$CH_2—OOC\cdot C_3H_7 \qquad CH_2OH$$
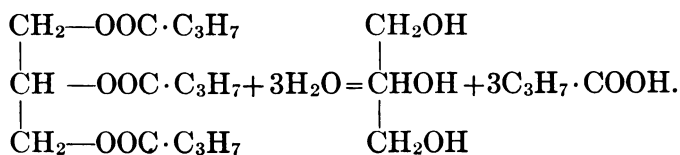
The other fats will be considered more fully presently.

Pure glycerol is a colorless, syrupy liquid, having a sweet taste. It boils at 290° and has a specific gravity of 1.265 at 15°. It is hygroscopic. Crystals of glycerol can be obtained by cooling to a low temperature (0°); these melt at 17°. It is volatile with water-vapor. It is useful as a solvent and as a preservative agent.

One, two, or three of the hydroxyl groups can be replaced by chlorine to form **mono-, di-, or trichlor-**

$$CH_2Cl \qquad CH_2Cl \qquad CH_2Cl$$

hydrin respectively: $CHOH, \qquad CHOH, \qquad CHCl$

$$CH_2OH \qquad CH_2Cl \qquad CH_2Cl.$$
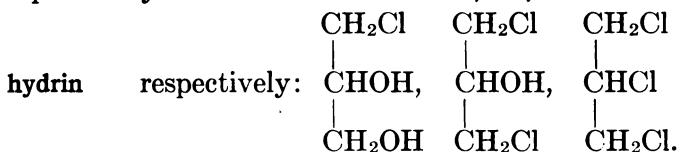
If trichlorhydrin be heated with water to 170°, it is hydrolyzed to glycerol. Glycerol can be obtained from ethyl alcohol by producing successively acetic acid, acetone, isopropyl alcohol, propylene, propylene dichloride, trichlorhydrin, and, finally, glycerol:

$$CH_3 \cdot CH_2OH \rightarrow CH_3COOH \rightarrow CH_3 \cdot CO \cdot CH_3 \rightarrow$$
(Alcohol)   (Acetic acid)   (Acetone)

$$\rightarrow CH_3 \cdot CHOH \cdot CH_3 \rightarrow CH_3 \cdot CH{=}CH_2 \rightarrow$$
(Isopropyl alcohol)   (Propylene)

$$\rightarrow CH_3 \cdot CHCl \cdot CH_2Cl \rightarrow CH_2Cl \cdot CHCl \cdot CH_2Cl \rightarrow$$
(Propylene dichloride)   (Trichlorhydrin)

$$\rightarrow CH_2OH \cdot CHOH \cdot CH_2OH.$$
(Glycerol)
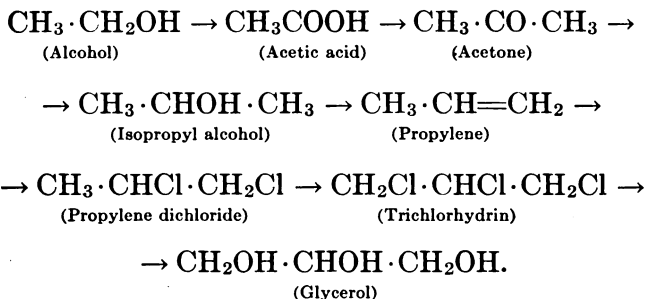
Glycerol forms salts with nitric acid. The tri-nitrate is **nitroglycerine** or nitroglycerol. It is a yellow, oily liquid, made by mixing glycerol with sulphuric and nitric acids. When the action has ceased, the mixture is poured into a large volume of cold water; the nitroglycerine separates as a heavy oil. Its formula is

$$\begin{array}{l} CH_2{-}O{-}NO_2 \\ | \\ CH\ {-}O{-}NO_2. \\ | \\ CH_2{-}O{-}NO_2 \end{array}$$
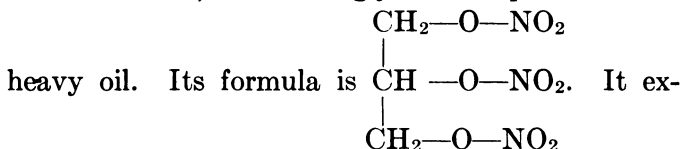
It ex-plodes when suddenly heated or percussed, with the formation of nitrogen, nitric oxide, carbon dioxide, and water. **Dynamite** consists of infusorial earth or other material impregnated with nitroglycerol, and may contain as much as 75% of the latter.

Nobel discovered that nitrocellulose (p. 247) will absorb nitroglycerine; a gelatinous mass being formed. Such explosives as cordite and ballistite are prepared in this way.

Gelatin dynamite is prepared from resin, collodion gun-cotton, a little wood pulp, and nitroglycerol.

Nitroglycerol is a strong poison, causing violent

headache and lowering of blood-pressure.   In 1%
alcoholic solution it is used as a medicine.[1]

Tetranitrol is similar to nitroglycerol, chemically and phar-
macologically.   It is the tetranitrate of the tetracid alcohol
erythrol.

Glycerol forms glyceryl acetates when treated with
acetic anhydride.   This will be considered more
fully under fats.

On oxidation glycerol yields *glyceric acid,* $\begin{array}{c} COOH \\ | \\ CHOH, \\ | \\ CH_2OH \end{array}$

and *tartronic acid,* $\begin{array}{c} COOH \\ | \\ CHOH. \\ | \\ COOH \end{array}$ These are studied with
the hydroxy-acids (see pp. 219 and 221).

Glycerophosphoric acid consists of one molecule
of orthophosphoric acid combined with glycerol,
$CH_2OH \cdot CHOH \cdot CH_2(H_2PO_4)$.

EXPERIMENTS.   (1) Heat 1 c.c. of glycerol with 5
gm. of $KHSO_4$ in an evaporating dish until it turns
brown.   Note the odor (acrolein) (see p. 302).
The fumes will blacken a strip of paper that has
been moistened with ammoniacal silver nitrate
solution.

(2) Repeat the same experiment, using lard or
some other fat.   Glycerol in combination also gives
the acrolein test.   ·

(3) To a few cubic centimeters of NaOH solution

[1] This is nitrite action (cf. amyl nitrite, p. 265).

add $CuSO_4$ until a copious precipitate of $Cu(OH)_2$ is obtained; now add some glycerol and shake, a deep-blue solution results.

Fats contain esters of glycerol with fatty acids and with the unsaturated acid, oleic acid. Only those members of the fatty acid series that contain an even number of CH_2 groups in their formulæ, occur in fats. Most fats are mixtures of *palmitin* (glyceryl tripalmitate), *stearin* (glyceryl tristearate), and *olein* (glyceryl trioleate). Olein is a liquid. Palmitin melts at 65°, while stearin has the highest melting-point (about 72°). The esters of low molecular weight, butyrin, caproin, caprylin, (these three are liquids), and caprin (melting at 31°) are peculiar to butter. Mutton-fat contains a large percentage of stearin. Lard contains esters of lauric, myristic and linoleic acids, as well as the commoner esters. The softer fats contain less stearin and palmitin and relatively more olein. Physiologically, the fats of lower melting-point are more easily digested.

$$
\begin{array}{l}
\text{CH}_2\text{—OOC} \cdot \text{C}_{15}\text{H}_{31} \\
\quad | \\
\textbf{Palmitin is } \text{CH —OOC} \cdot \text{C}_{15}\text{H}_{31}. \\
\quad | \\
\text{CH}_2\text{—OOC} \cdot \text{C}_{15}\text{H}_{31}
\end{array}
$$

$$
\begin{array}{l}
\text{CH}_2\text{—OOC} \cdot \text{C}_{17}\text{H}_{35} \\
\quad | \\
\textbf{Stearin is } \text{CH —OOC} \cdot \text{C}_{17}\text{H}_{35}. \\
\quad | \\
\text{CH}_2\text{—OOC} \cdot \text{C}_{17}\text{H}_{35}
\end{array}
$$
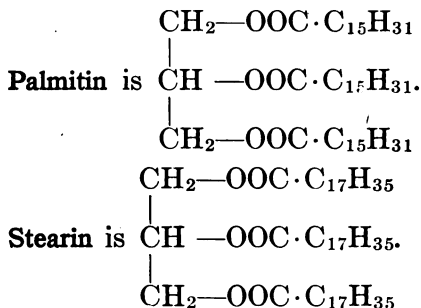
Mixed esters of glycerol can be obtained; some have been proved to occur naturally.

$$CH_2—OOC\cdot C_{15}H_{31}$$
$$|$$
$$CH\ —OOC\cdot C_{17}H_{35}$$
$$|$$
$$CH_2—OOC\cdot C_{17}H_{35}$$
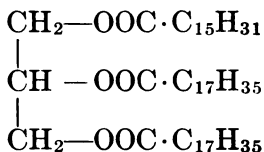
is a mixed ester.

The following mixed esters have been detected in beef and mutton fat: dipalmito-stearin, dipalmito-olein, palmito-distearin, and oleo-palmito-stearin.

Butter contains glycerol esters of fatty acids that are *volatile* and *soluble*, namely, butyric, capric, caprylic, and caproic acids. Artificial butters (as oleomargarine) contain only very small amounts of these acids.

Butter also contains esters of myristic, lauric and dihydroxystearic acids.

It will be of interest to give the composition of the oils that are used most commonly in medicine:

Cod-liver oil contains glycerides of palmitic, stearic, oleic, myristic, erucic, and two other unsaturated acids, also cholesterol.

Croton oil contains tiglic, crotonic, formic, acetic, butyric, valeric, myristic, and lauric acids, besides palmitic, stearic, and oleic acids.

Castor oil is composed chiefly of esters of ricinoleic and isoricinoleic acids, and contains also sebacic, stearic, and dihydroxystearic acids.

Olive oil has olein to the extent of 70%, and contains also esters of palmitic and arachidic acids, and some phytosterol.

Fat Values. By determining certain analytical values [1] and by finding the melting-point and specific gravity, a fat can generally be identified with the aid of the tables compiled for the purpose. The values referred to will now be briefly explained in order.

(1) The *Reichert-Meissl number* indicates the amount of volatile soluble acid present in the fat. When butter or any other fatty substance is saponified so as to free the fat acid and then distilled as described in the experiment below, the volatile acid in solution in the distillate can be readily estimated by titration. The Reichert-Meissl value is the number of cubic centimeters of decinormal acid contained in the distillate from five grams of fatty substance.

(2) The *acid number* of a fat is found by titration of a solution of the fat in alcohol ether mixture with decinormal KOH, phenolphthalein being used as an indicator. This determines the amount of free acid present. The acid value is expressed as milligrams of KOH required to neutralize the free acids in one gram of fat.

(3) The total amount of acid present, free and combined, is indicated by the *saponification number*. A weighed quantity of fat (2-4 gm.) is saponified by heating it with an accurately measured quantity of alcoholic KOH solution of known strength (half normal); the resulting soap is diluted and titrated with half normal HCl to find how much KOH

[1] A very satisfactory book on this subject is Chemical Analysis of Oils, Fats, and Waxes, by *J. Lewkowitsch.*

remains unneutralized. Then the amount in milligrams of KOH combined with fatty acid as soap for each gram of fat taken is readily calculated; this is the saponification number.

(4) The *ester number* of a fat represents the combined acid, being the saponification number less the acid number.

(5) The *iodine number* estimates the amount of unsaturated acid (e.g., oleic) present. The iodine forms an addition compound with the acid (see p. 299). This value is expressed as the grams of iodine taken up by 100 grams of fat.

(6) The *acetyl number* estimates the hydroxyl content. If glycerol is treated with acetic anhydride one molecule of acetic acid is produced for each hydroxyl group attached (see p. 169):

$$
\begin{array}{l}
CH_2OH \qquad OC\cdot CH_3 \\
| \qquad\qquad\;\; \diagup \\
CHOH + O \\
| \qquad\qquad\;\; \diagdown \\
CH_2OH \qquad OC\cdot CH_3 \\
\qquad\qquad = CH_3\cdot COOH + CH_2\cdot OOC\cdot CH_3 \\
\qquad\qquad\qquad\qquad\qquad\qquad\quad | \\
\qquad\qquad\qquad\qquad\qquad\quad CHOH \\
\qquad\qquad\qquad\qquad\qquad\qquad\quad | \\
\qquad\qquad\qquad\qquad\qquad\quad CH_2OH
\end{array}
$$

(Glyceryl monacetate)
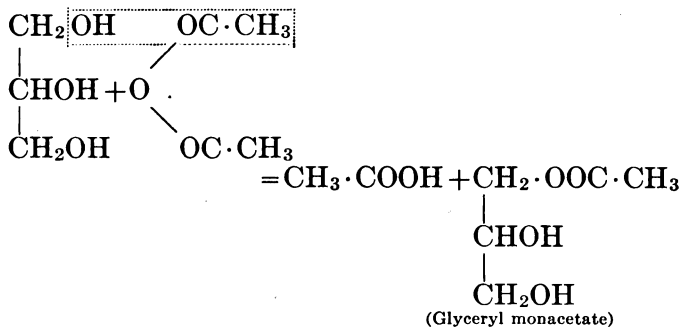
The reaction can be pushed until all of the hydroxyl groups are displaced, giving, as the products, glyceryl triacetate and acetic acid (three molecules of the latter for each molecule of glycerol). In a similar manner a fat which contains some hydroxyl groups can be " acetylated," and by estimating the acetic

acid in combination with the alcohol, or acids of the fat, the hydroxyl content can be calculated. The acetyl number is the number of milligrams of KOH required to neutralize the acetic acid after hydrolysis of one gram of the acetylated fat. Partially hydrolyzed fat esters (e.g., a diglyceride) and hydroxy-acids are mainly responsible for this number. Such an acid is ricinoleic acid (p. 304) contained in castor oil, also dihydroxy-stearic acid, $CH_3(CH_2)_7(CHOH)_2(CH_2)_7COOH$, which is present in butter and in castor oil.

The *viscosity number* (see p. 79) may be determined for the purpose of detecting adulteration of olive oil, since the cheaper vegetable oils have a lower viscosity.

EXPERIMENTS. (1) Compare the specific gravity of filtered butter with that of oleomargarine by successively putting a little of each in alcohol of specific gravity 0.926 at 15°. There must be no air bubbles adhering to the fat. The oleomargarine will float (it having a specific gravity of about 0.918 at 15°); the butter will either sink or remain suspended.

· (2) *Reichert-Meissl number.* Into a 300-c.c. flask put 5 gm. of filtered butter, 2 c.c. of 60% KOH solution, and 20 c.c. of glycerol. Heat with a small flame, shaking to prevent excessive foaming. In about five minutes the water is boiled off and saponification is almost complete. Tip the flask and rotate to bring down any fat adhering to the walls. Heat again for a few minutes, then partly cool. The soap solution should be clear. Add

90 c.c. of hot distilled water and shake until the soap is dissolved. Add 50 c.c. of 5% H_2SO_4 and some zinc powder or small pieces of pumice.[1] Distill on a sand-bath. Collect 110 c.c. of distillate in a graduated flask. The distilling should be accomplished in thirty minutes. Filter the distillate; take 100 c.c. of the filtrate with a pipette and transfer it to a beaker. Add a little phenolphthalein solution and titrate with decinormal KOH until slightly pink. Multiply the number of cubic centimeters of alkali by 1.1; this gives the Reichert-Meissl number. For butter this value should not be less than 24. The experiment may be repeated with oleomargarine.

(3) *Acid number.* Mix equal volumes of alcohol and ether; add phenolphthalein solution, then a drop or more of decinormal KOH until slightly pink. Now dissolve a weighed quantity of butter (5–10 gm.) in some of the ether-alcohol, and titrate with decinormal KOH to a faint pink, which remains after mixing. If the mixture becomes turbid during titration, warm it in a water bath (with no flame near it).

When fats are decomposed with the aid of alkali, **soap** is formed. Hence the origin of the term *saponification.* In the strictest sense, saponification means the action of an alkali on an ester, the resulting products being an alcohol and a salt of the acid. Many use the word loosely as synonymous with hydrolysis.

[1] To prevent bumping.

Soaps are metallic salts of the acids that occur in fats. Ordinary soaps are mixtures of potassium or sodium palmitate, stearate, and oleate. Potassium soap is soft soap, commonly called green soap. In many countries its yellow color is changed to green by the addition of indigo. It contains the glycerol that is freed by saponification. Sodium soap is hard soap, which has been freed of glycerol by " salting out " in the manner described in the experiment. Castile or Venetian soap, if genuine, is made from olive oil. It contains no free alkali. It is slightly yellow in color. Calcium, mercury, lead, copper, and many other metals form insoluble soaps.

Cheap soaps are made with resin, sodium resinate acting similarly to true soap.

The *cleansing action* of soap is largely due to hydrolytic dissociation of the salts in dilute soap solution. This dissociation can be demonstrated as follows: Add phenolphthalein to a concentrated soap solution, and only a slight red appears; now dilute with a large quantity of water, and a decided red develops (for effect of dilution on dissociation, see p. 68). The lather also aids mechanically in removing dirt. Sodium oleate is the most soluble of the salts of soap, and hydrolyzes the least. The hydrolyzed stearate and palmitate furnish colloidal particles. Various substances adsorb to these particles, facilitating their removal in the washing process. This explains why vaseline can be removed by first treating the vaseline with a fat, and then using soap; the vaseline is adsorbed.

The free alkali of soap solution probably acts to some extent to saponify the grease on the surface to be washed; while the sodium oleate acts to emulsify the fat. Saponification, emulsification, and adsorption are all of them factors in the cleansing process.

Experiments. (1) Put into a flask about 10 gm. of lard or tallow, add 5 c.c. of 60% KOH and 50 c.c. of alcohol; attach an upright air condenser tube, and boil moderately. After boiling half an hour test by shaking a drop of the fluid with half a test-tube of water; if no oily drops separate out, saponification is complete. Dilute with 50 c.c. of hot water. While hot add an equal volume of saturated solution of NaCl. Sodium soap will separate as a top layer and finally solidify.

(2) To same soap solution add hydrochloric acid. Free fatty acids separate and rise to the top. Collect the fatty acids on a filter, wash thoroughly with water, press between filter paper, and crystallize from hot alcohol.

(3) Make insoluble soap by treating same soap solution with calcium chloride solution (calcium soap), with lead acetate (lead soap), copper sulphate, and solutions of other metallic salts. Explain " hardness " of water.

In a soap solution at least part of the soap is in the *colloidal* state; a concentrated solution made with the aid of heat gelatinizes on cooling (hydrogel). The colloidal behavior of the solution is said to

be due in large measure to hydrolytic dissociation of the salt, the relatively insoluble product going into colloidal solution. Dried soap swells when soaked in water.

Lanolin is a fat-like substance prepared by purifying wool grease. It contains about 25% of water and will take up more water until it holds 80%. It is more closely related to waxes than to fats, since by saponification its esters yield monacid alcohols, such as ceryl alcohol. In addition to esters it contains free acids, free alcohols, cholesterol, and isocholesterol.

CHAPTER XVI

HYDROXY-ACIDS

Hydroxy-acids contain both alcohol (OH) and acid (COOH) groups. The acid properties, however, are more marked than the alcohol properties. They are not acid alcohols, but hydroxy-acids, and may therefore be defined as acids in which a hydrogen atom attached to one of the carbon atoms is replaced by hydroxyl. They are often called oxy-acids.

The simplest possible hydroxy-acid would be *hydroxy-formic acid,*

$$H \cdot COOH \rightarrow HO \cdot COOH.$$
(Formic acid)   (Hydroxy-formic acid)
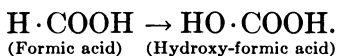
It will be observed that this is identical with the hypothetical carbonic acid, H_2CO_3.

The lowest typical hydroxy-acid is hydroxyacetic acid, $CH_2 \diagup^{OH}_{COOH}$, or glycollic acid (mentioned previously under glycol).

Glycollic acid (ethanolic acid) may be prepared in many ways, starting with either an alcohol or an acid:

(1) By oxidation of glycol or glycol aldehyde (see p. 194).

(2) By forming the cyanogen derivative of methyl

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alcohol, or, what is the same thing, the cyanhydrin of formaldehyde, then hydrolyzing:

$$H \cdot C \Big\langle {}^H_O + HCN = H \cdot CH \Big\langle {}^{CN}_{OH},$$

<div align="center">(Cyanhydrin of formaldehyde)</div>

$$CH_2 \Big\langle {}^{CN}_{OH} + 2H_2O = CH_2 \Big\langle {}^{COOH}_{OH} + NH_3.$$
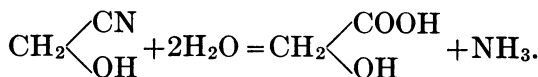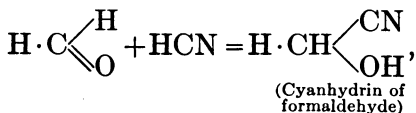
(3) By boiling monochloracetic acid with water:

$$CH_2Cl \cdot COOH + H_2O = CH_2 \Big\langle {}^{OH}_{COOH} + HCl.$$
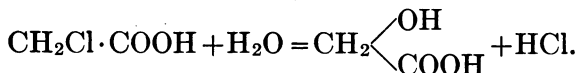
(4) By treating aminoacetic acid (glycocoll) with nitrous acid:

$$CH_2 {\overset{NH_2}{\underset{}{\diagup}} -} COOH + HNO_2 = CH_2 \Big\langle {}^{OH}_{COOH} + H_2O + N_2.$$

<div align="center">(Glycocoll)</div>
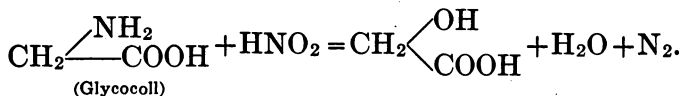
These methods are in general applicable to other hydroxy-acids.

Glycollic acid (as also other hydroxy-acids) forms esters by virtue of either the hydroxyl or the carboxyl group; for example, ethyl glycollate,[1]

$$CH_2 {\overset{OH}{\diagup} -} COO \cdot C_2H_5,$$ and glycollic acetate,

$$CH_2 {\overset{OOC.CH_3}{\diagup} -} COOH \cdot$$
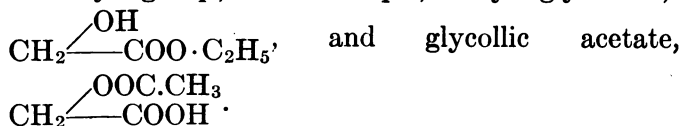
Glycollic acid is found in green grapes and elsewhere. It forms needle crystals, melting at 80°. It is a stronger acid than acetic acid. When heated

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[1] Distinguish glycollates from the glycolates derived from glycol (p. 194).

in an atmosphere of carbon dioxide at 210°, it combines with itself, losing water, and thus forms an anhydride called *glycollid:*

$$CH_2 \big\langle \begin{matrix} OH \quad HO \; OC \\ COO\;H \quad HO \end{matrix} \big\rangle CH_2$$

$$= CH_2 \big\langle \begin{matrix} OOC \\ COO \end{matrix} \big\rangle CH_2 + 2H_2O.$$
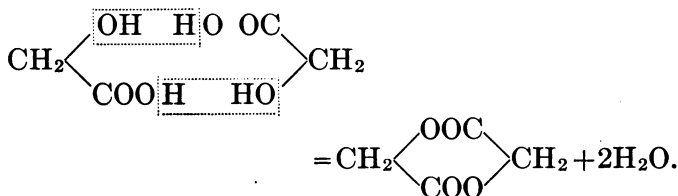
This has neither alcoholic nor acidic properties.

Hydroxypropionic acids are commonly called **lactic acids.** Just as there are two monochlorpropionic acids, α and β, so there are an α-hydroxypropionic acid and a β-hydroxypropionic acid. The β acid,

$$CH_2 \overset{OH}{\diagup} CH_2 - COOH,$$

shows by its reactions that it is related to ethylene (see p. 300). It is therefore called ethylene lactic acid. It is unimportant.

Lactic acid proper, *α-hydroxypropionic acid,*

$$CH_3 \cdot CH \overset{OH}{\diagup} COOH,$$
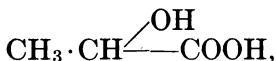
is known in three forms as isomers. As with some of the amyl alcohols (p. 144), these isomers have identical structural formulæ. Isomerism of the kind to be described now is called *stereoisomerism.*[1]

[1] Stereochemistry (*stereos* meaning solid) treats of those chemical and physical phenomena that are supposed to be caused by the relative positions in space occupied by the atoms within the molecule.

To understand this it is necessary to conceive of the atoms of the molecules as being arranged in space, and not on one plane as in ordinary formulæ. The main carbon atom is thought of as being placed in the center of a tetrahedron, at the apex of each solid angle of which is situated an atom or group. Models of wood or pasteboard will be helpful in understanding this. To represent α-lactic acid, write the groups CH₃, OH, H, and COOH at the corners of the tetrahedron, thus:
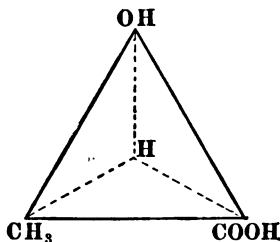
Try the effect of interchanging these groups in all possible ways. It will be found that two and only two different arrangements are possible.[1] Further, when the tetrahedron representing óne combination is held before a mirror, the image in the mirror will be seen to correspond exactly to the other possible arrangement. This is true only in the case of compounds that would be represented as having four *different* groups at the corners. If two of these

[1] The truth of this statement can be most clearly shown by writing down the various possible arrangements and then marking off those that are identical. The student will be interested in observing that his hands are mirror images of each other.

groups are the same, only one arrangement is possible and stereoisomerism cannot occur.

The tetrahedron representing lactic acid is unsymmetrical as regards the kind of groups present; its central carbon atom is therefore said to be an *asymmetric* carbon atom. It has been found that compounds containing an asymmetric carbon atom rotate the plane of polarized light.[1] Dextrolactic acid rotates it to the right, lævolactic acid rotates it to the left. As represented by models, lævolactic acid is the mirror-image of dextrolactic acid. Ordinary lactic is also an α-lactic acid, but it does not affect polarized light; it is optically inactive. It has been shown to consist of equal quantities of dextrolactic and lævolactic acid molecules; such a substance is called *racemic*.[2] The two constituent acids of racemic acid neutralize each other in their action on polarized light. Optically active substances that have a physiological action may show a different degree of action on the animal organism

[1] A few optically active organic compounds have been prepared which contain asymmetric atoms other than carbon. Certain quaternary bases have an asymmetric N atom, as

$$C_6H_5 \diagdown$$
$$C_6H_5 \cdot CH_2 {\Rightarrow} N {\diagup}{\diagdown} {\overset{CH_3}{\underset{Br}{}}} \;.$$
$$C_3H_5 \diagup$$
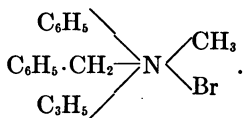
The pentavalent N atom has been conceived of as at the center of a pyramid.

[2] Racemic substances are not always mixtures; the *d, l*-mixtures might better be called *conglomerates*. The racemic, properly speaking, contain the two active molecules in some sort of molecular combination (cf. tartaric acid).

according to whether it is the *d* or *l* isomer that is acting (see nicotine, p. 430, atropine, p. 432, and cocaine, p. 433).

Dextrolactic acid (*d*-lactic acid) is also called *sarcolactic acid*, because it occurs in flesh. It is present in beef extract. It is also the product of fermentation of dextrose by the *Micrococcus acidi paralactici*. Its salts are lævorotatory.

Lævolactic acid (*l*-lactic acid) is obtainable by fermentation of dextrose by the *Micrococcus acidi lævolactici*.

Racemic lactic acid (*d*-, *l*-lactic acid) is a syrupy liquid having a specific gravity of 1.2485 at $\frac{15°}{4°}$. It is stronger than most organic acids, and much stronger than propionic and ethylene lactic acids, to which it is related. It is the product of ordinary lactic acid fermentation. When milk sours, milk-sugar becomes converted into lactic acid by microorganisms:

$$\underset{\text{(Lactose)}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{(Lactic acid)}}{4C_3H_6O_3}.$$
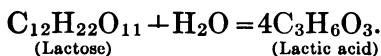
No matter in what way lactic acid is artificially produced by synthesis, the synthetic acid is always racemic. The law of probability as applied to chemical synthesis calls for the formation of just as many molecules having the dextro-arrangement as the lævo. It can be shown that *d*, *l*-lactic acid contains dextrolactic acid by growing the mold *Penicillium glaucum* in a solution of *d*, *l*-ammonium lactate, because the mold destroys the lævolactic

acid. On the other hand it may be shown to contain lævolactic acid by fractional crystallization of a solution of strychnine lactate, since the lævolactate crystals are formed first.

When heated to 150° in dry air, lactic acid changes to an anhydride called lactid (cf. glycollic acid, p. 214). Hydriodic acid reduces lactic acid to propionic acid (see p. 185).

EXPERIMENT. In a retort mix 5 c.c. of lactic acid, 10 c.c. of water, and 5 c.c. of concentrated H_2SO_4. Connect with a condenser. Heat with a smoky flame. Test the distillate for aldehyde (see p. 153) and for formic acid (see p. 160):

$$CH_3 \cdot CHOH \cdot COOH = CH_3 \cdot CHO + H \cdot COOH.$$

β-Hydroxybutyric acid (β-oxybutyric acid),

$$CH_3 \cdot CH(OH) \cdot CH_2 \cdot COOH,$$
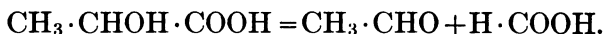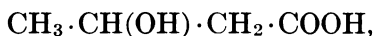
is pathologically of importance, since it may occur in the blood or urine, especially in diabetes. It is lævorotatory, its specific rotation (p. 245) being $-24.12°$.

It will be noticed that the ketone acid *acetoacetic acid* (β-ketobutyric acid) corresponds to the above alcohol acids, just as ketones correspond to secondary alcohols (see also p. 192):

$$CH_3 \cdot CHOH \cdot CH_2 \cdot COOH \ (cf. \ CH_3 \cdot CHOH \cdot CH_3)$$
$$CH_3 \cdot CO \cdot CH_2 \cdot COOH \ (cf. \ CH_3 \cdot CO \cdot CH_3).$$
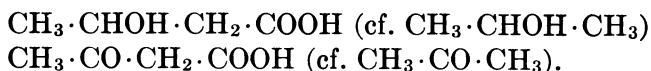
β-Hydroxybutyric acid can be readily oxidized to acetoacetic acid by hydrogen peroxide.

γ-**Hydroxy-acids** are very unstable. They readily split off water to form anhydrides called *lactones*, thus:

$CH_2(OH) \cdot CH_2 \cdot CH_2 \cdot COOH$
(γ-Hydroxybutyric acid)

$$= CH_2 \cdot CH_2 \cdot CH_2 \cdot CO + H_2O.$$
$$\underline{\qquad\qquad O \qquad\qquad}$$
(Butyrolactone)
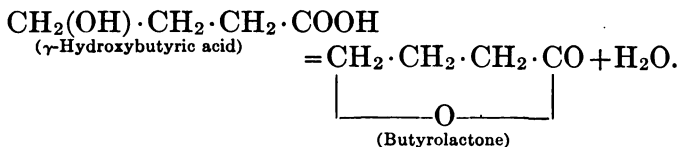
The carbon chain is closed by a linking through oxygen. It is, however, not a typical closed chain. The presence of hydrogen ions acts catalytically to hasten the formation of the lactone, and it is supposed that the H ions of the γ-hydroxy acid itself have this action, causing *autocatalysis*. When boiled with caustic alkalies, the lactones form salts of the corresponding hydroxy-acids; thus lactones give a " saponification value." This fact must be borne in mind in examining unknown substances supposed to be fats or waxes.

Dihydroxymonobasic acids are illustrated by **glyceric acid,**

CH_2OH
|
$CHOH.$
|
$COOH.$
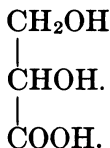
Glyoxylic acid, which has been previously mentioned (p. 194), while classed as an aldehydic acid, is according to some chemists a dihydroxy-acid, because it holds a molecule of water inseparable from it (cf. chloral hydrate):

$$COOH \cdot C\!\!<^{H}_{O} + HOH = COOH \cdot C\!\!<^{H}_{OH}\ _{OH}$$

or

$$CH(OH)_2 \cdot COOH.$$
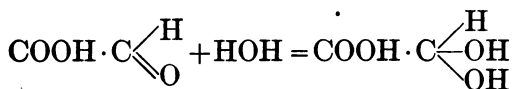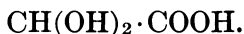
It is a reducing agent like aldehydes (as chloral hydrate).

EXPERIMENTS. (1) To 20 c.c. of a strong solution of oxalic acid add 1 gm. sodium amalgam; when evolution of gas has ceased, filter. The filtrate is a dilute solution of glyoxylic acid:

$$\begin{array}{ccc} COOH & & COOH \\ | & + \begin{Bmatrix} H \\ H \end{Bmatrix} = & | & + H_2O. \\ COOH & & CHO \end{array}$$

(Oxalic acid)   (Nascent hydrogen)   (Glyoxylic acid)
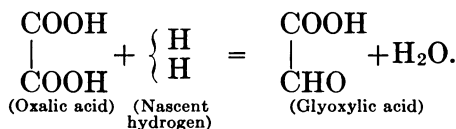
(2) To 5 c.c. of albumin solution (egg-white solution) add 5 c.c. of the glyoxylic acid solution, then 5 c.c. of concentrated H_2SO_4; mix and heat gradually; a bluish-violet color is obtained, due to trytophan contained in the protein molecule. Most proteins give this test.

An example of a **trihydroxy-acid** is **cholic** or cholalic acid, $(CH_2OH)_2\ [C_{20}H_{31}(CHOH)]$ COOH. The constitution of the $C_{20}H_{31}$ portion of the formula is unknown. This acid is important physiologically, since its combinations with glycin and with taurin, glycocholic and taurocholic acids, are the most valuable constituents of bile.

Glycocholic acid has the formula:

$$C_{20}H_{31}(CHOH)\ (CH_2OH)_2 \cdot CO-HN \cdot CH_2COOH.$$

Taurocholic acid is

$$C_{20}H_{31}(CHOH) (CH_2OH)_2CO—NH \cdot (CH_2)_2SO_3H.$$
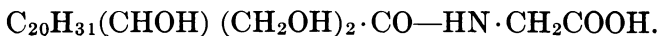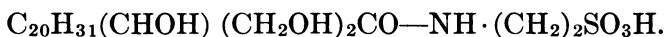
Glycuronic acid is an **aldehydic tetrahydroxy-acid**, $CHO \cdot (CHOH)_4 \cdot COOH$, the arrangement of the secondary alcohol groups being the same as in dextrose. It is formed by the animal body from dextrose when it is needed to combine with abnormal substances, such as drugs or indol. It is excreted in the urine as *paired glycuronates;* these are lævorotatory. By heating with dilute acid, glycuronic acid is set free; this is dextrorotatory. It is closely related to monosaccharides, differing only in the change of the CH_2OH group to $COOH$. The free acid and some of its combinations reduce alkaline copper solutions (like other aldehydes), more particularly after prolonged heating of the mixture; so that occasionally a mistake may be made in concluding that a reducing urine contains sugar. It is not fermentable. It gives the pentose reactions (see p. 230).

Monohydroxydibasic Acids.

Tartronic acid,
$$\begin{array}{c} COOH \\ | \\ CHOH \\ | \\ COOH \end{array}$$
has been supposed to take
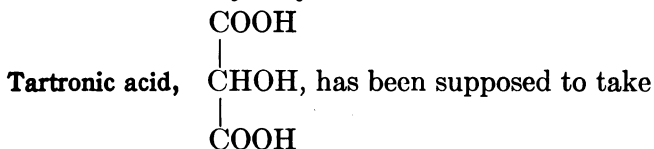
part in the physiological synthesis of uric acid, particularly in birds (see p. 290).

Malic acid is hydroxysuccinic acid,
$$\begin{array}{c} CH(OH)—COOH \\ | \\ CH_2———COOH \end{array}$$
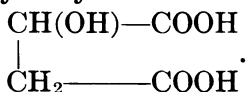
It is contained in sour fruits, e.g., apples and cherries.

Agaric Acid is used as a remedy.   Its formula is $C_{14}H_{27}(OH)(COOH)_2$.

Dihydroxydibasic Acids.

Mesoxalic acid, $C\underset{\overset{|}{COOH}}{\overset{\overset{|}{COOH}}{\underset{OH}{\overset{OH}{<}}}}$, is the third exception to

the rule that two hydroxyls cannot be attached to the same carbon atom, chloral hydrate and glyoxylic acid being the two other exceptions.

Tartaric acid is dihydroxysuccinic acid,

$$\begin{array}{l} CH(OH){-}COOH \\ | \\ CH(OH){-}COOH \end{array}.$$
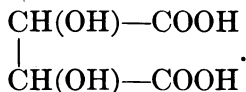
Here there are *two* asymmetric carbon atoms (see p. 216) in the molecule.   This fact causes a species of stereoisomerism, that is more difficult to understand than that of lactic acid.   With the aid of models it can be clearly understood.   Arrange pairs of tetrahedra as shown in the diagram.

It will be noticed in the case of *dextro-* and *lævo-tartaric acids* that the groups, OH and OH, H and H, are connected by straight lines and are on opposite sides of a line connecting the centers of the tetrahedra; they are diagonally opposite, while the COOH groups are vertically opposite each other, both being at an angle of the tetrahedron that points for-

ward. As with the models for lactic acid, these models for active tartaric acids cannot be made identical by turning the model about.

Place the lævotartaric model before a mirror; the image corresponds to dextrotartaric acid.

Racemic tartaric acid when in solution is a mixture of equal quantities of dextro- and lævo-tartaric acids (cf. racemic lactic acid).[1] There is, however, another inactive tartaric acid which cannot be sepa-

| Dextro-tartaric acid. | Lævo-tartaric acid. | Meso-tartaric acid |
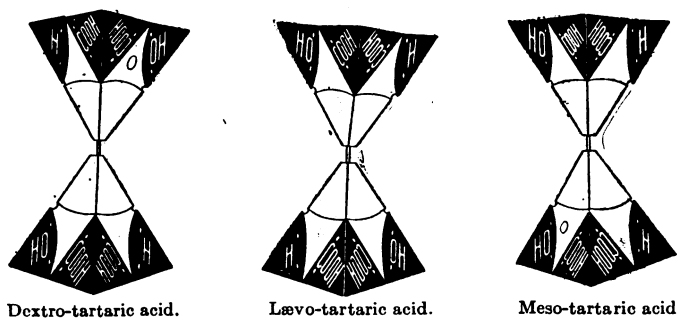
FIG. 22.

rated into optically active acids. This is *mesotartaric acid*. By studying the diagram above, or a model, it will be seen that the neutralization of optical properties is an inner molecular one, since the arrangement of the groups on the top corresponds to that of lævotartaric acid, while the arrangement at the base corresponds to that of dextrotartaric.[2]

[1] The racemic tartaric acid *crystals*, however, are represented by the formula $4C_4H_6O_6 + 2H_2O$.

[2] It will further be noted that an acid of this variety is not possible in the case of lactic acid.

Racemic and mesotartaric acids differ widely in melting-point and solubility.

Ordinary tartaric acid is dextrorotatory. It is contained in grape-juice as potassium bitartrate or acid tartrate, $HOOC(CHOH)_2COOK$. When wine is produced this salt separates out because of its relative insolubility in dilute alcohol. This crude tartar, or argol, is called cream of tartar when purified. It is used in the manufacture of the best baking-powders. Baking-powder is a mixture of sodium bicarbonate and some acid salt, which on
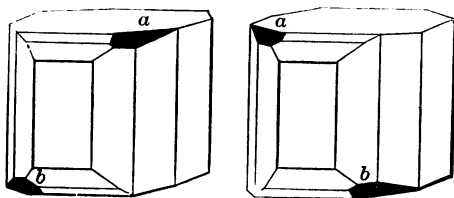
FIG. 23.

being dissolved liberates carbon dioxide from the bicarbonate. Tartaric acid is obtained from potassium bitartrate by precipitation as calcium tartrate, from which the acid is liberated by using the proper amount of dilute sulphuric acid. It forms large crystals, melting at 170°. On heating further it turns brown and gives off an odor like caramel. It is easy soluble.

Dextrotartaric acid can be converted into racemic acid by boiling with an excess of strong sodium hydroxide solution. The two methods given for separating racemic lactic acid into the active acids

are applicable also to racemic tartaric acid. Pasteur discovered a third method which is very interesting. By slow evaporation (below 28°) of a solution of sodium ammonium racemate, two classes of crystals can be obtained, which from their appearance might be called right-handed and left-handed crystals (see Fig. 23).

The crystals are mirror-images of one another. These can be picked out mechanically; one set furnishes dextrotartaric acid, the other lævotartaric acid.

Rochelle salt is sodium potassium tartrate,

$$CH(OH)-COONa$$
$$|\qquad\qquad\qquad +4H_2O.$$
$$CH(OH)-COOK$$
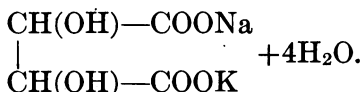
This has the power of holding $Cu(OH)_2$ in solution, as in Fehling's solution. It is used as a cathartic.

Tartar emetic is potassium antimonyl tartrate,

$$CH(OH)-COOK$$
$$|$$
$$CH(OH)-COO(SbO).$$
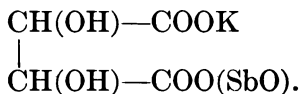
It is used as a medicine.

EXPERIMENTS. (1) Heat some tartaric acid in a test-tube, stirring it with a thermometer. Note the melting-point. Remove the thermometer and continue heating. The acid turns brown and emits an odor like scorched sugar.[1]

[1] Certain other acids act in the same way, particularly citric, malic, tannic, and gallic.

(2) Prepare tartar emetic. Dissolve 5 gm. of potassium acid tartrate in 50 c.c. of water, add 4 gm. Sb_2O_3 and boil. Filter and test some of the filtrate for antimony with H_2S. Set aside the rest of the filtrate to secure crystals by slow evaporation.

(3) After reading a description of the polariscope [1] and its manipulation, determine the rotary power of a strong solution of tartaric acid.

Monohydroxytribasic Acids.

Citric Acid,
$$
\begin{array}{l}
CH_2\text{—}COOH \\
| \\
C(OH)\text{—}COOH, \text{ is present in currants,} \\
| \\
CH_2\text{—}COOH
\end{array}
$$
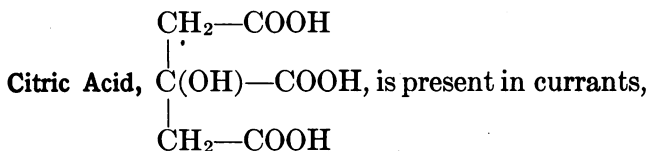
gooseberries, and lemons. It forms large crystals (having one molecule of water of crystallization) and is easily soluble. Citrates are valuable medicines. Citrates redissolve $Cu(OH)_2$ which has been precipitated by NaOH (cf. Rochelle salt in Fehling's solution).

Other hydroxyacids that are mentioned elsewhere are dihydroxystearic acid (p. 207) and ricinoleic acid (p. 304).

[1] A good description can be found in *Cohen's* Practical Organic Chemistry, also in *Mathews'* Physiological Chemistry.

CHAPTER XVII

CARBOHYDRATES AND GLUCOSIDES

CARBOHYDRATES

THIS class of compounds is of very great importance, since it includes sugars and starches. The name *carbo(n)hydrates* calls attention to the fact that the hydrogen and oxygen in their formulæ have the same ratio as in the formula for water;[1] therefore a general formula often given for carbohydrates is $C_n(H_2O)_m$.

This, however, is misleading, for there are a number of non-carbohydrate substances that conform to this formula, such as acetic acid, $C_2H_4O_2$, and lactic acid, $C_3H_6O_3$.

Carbohydrates may be defined as including monosaccharides and those more complex substances that yield by hydrolysis simply monosaccharides.

All monosaccharides contain in their formulæ a CO group, either in an aldehyde group or as the ketone group, and have also an alcoholic hydroxyl attached to each of the other carbon atoms. This may be condensed to the statement: monosaccharides are aldehyde or ketone derivatives of polyhydroxylic alcohols.

There are four classes of carbohydrates, namely,

[1] It should be pointed out in this connection that the term hydrate as applied to alkalies is inaccurate, e.g., NaOH is sodium hydroxide, not a hydrate.

monosaccharides, disaccharides, trisaccharides and *polysaccharides.*[1]   Monosaccharides are the simplest carbohydrates.   From the linking of two monosaccharide molecules, disaccharides result.   A trisaccharide contains in its molecule three monosaccharide molecules.   Polysaccharides have complex molecules that can be resolved into many monosaccharide molecules.   Monosaccharides and disaccharides act as very weak acids, but their H ion concentrations are extremely low.

MONOSACCHARIDES

According to the number of carbon atoms present, monosaccharides are called dioses, trioses, tetroses, pentoses, hexoses, heptoses, octoses, and nonoses.

Aldoses are those containing an aldehyde group, while *ketoses* are those having a ketone group.

Glycol aldehyde, $\begin{array}{c} CH_2OH \\ | \\ CHO \end{array}$, may be considered a **diose**.

Glycerose can be obtained by mild oxidation of glycerol (or lead glycerate); it is a mixture of an aldehyde and a ketone, and since each contains three carbon atoms, they are **trioses**:

$$\begin{array}{ccccc} CH_2OH & & CH_2OH & & CH_2OH \\ | & & | & & | \\ CHOH & \rightarrow & CHOH & + & CO \\ | & & | & & | \\ CH_2OH & & CHO & & CH_2OH \\ \text{(Glycerol)} & & \text{(Glyceric aldehyde)} & & \text{(Dihydroxyacetone)} \end{array}$$

(Glycerose)
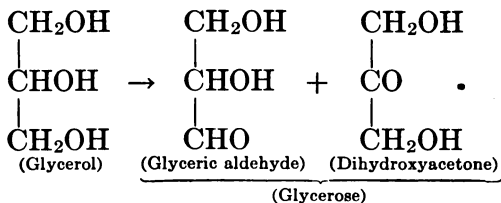
[1] These are also called monosaccharoses, disaccharoses, trisaccharoses, and polysaccharoses.

$$
\text{Tetrose,} \quad
\begin{array}{c}
\text{CH}_2\text{OH} \\
| \\
\text{CHOH} \\
| \\
\text{CHOH} \\
| \\
\text{CHO}
\end{array}
\quad \text{, can be obtained by polymeriza-}
$$
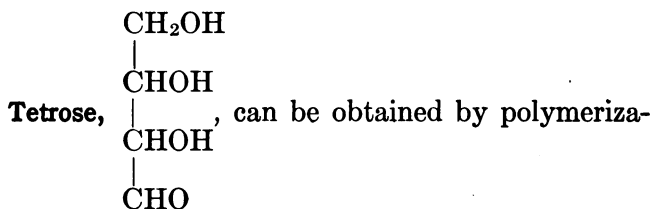
tion of glycol aldehyde. A ketose tetrose also occurs.

The chief **pentoses** are *d*-arabinose and *l*-xylose. The following formulæ represent their isomeric relation:

$$
\begin{array}{cc}
\text{CH}_2\text{OH} & \text{CH}_2\text{OH} \\
| & | \\
\text{HO—C—H} & \text{HO—C—H} \\
| & | \\
\text{HO—C—H} & \text{H—C—OH} \\
| & | \\
\text{H—C—OH} & \text{HO—C—H} \\
| & | \\
\text{CHO} & \text{CHO} \\
(\textit{d-arabinose}) & (\textit{l-xylose})
\end{array}
$$
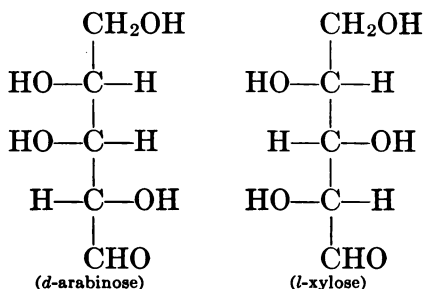
Arabinose is obtainable by boiling gum-arabic with dilute acid. **Xylose** can be obtained by similar means from bran or wood. Racemic arabinose is sometimes present in the urine as an abnormal constituent. Several ketose pentoses are known.

On account of having three asymmetric C atoms, four main arrangements and the mirror images of these are possible, so that eight aldose pentoses are obtainable. Seven of these are known at present.

Both arabinose and xylose reduce Fehling's solution and form osazones with phenylhydrazine (the

nature of the osazone reaction will be explained presently). Neither is fermented by pure yeast. They give certain color reactions, which will be illustrated in the experiment below.

If a pentose is boiled with strong HCl, an aldehyde having a closed chain (furfurol) is produced:

$$
\underset{\text{(Pentose)}}{\left.\begin{array}{l} \text{HOCH—CHOH} \\ \Big| \quad \Big| \quad \Big| \quad \Big| \\ \text{HCH} \quad \text{C}\!\!\big\langle\!\!\begin{array}{l}\text{H}\\\text{OH}\end{array} \\ \diagdown\ \diagup \\ \text{O}\ \text{H} \end{array}\right.}\cdot\text{CHO} =
\underset{\text{(Furfurol)}}{\left.\begin{array}{l}\text{CH—CH}\\ \|\quad\ \ \| \\ \text{CH} \quad \text{C}\cdot\text{CHO} \\ \diagdown\diagup \\ \text{O} \end{array}\right.} + 3\text{H}_2\text{O}
$$
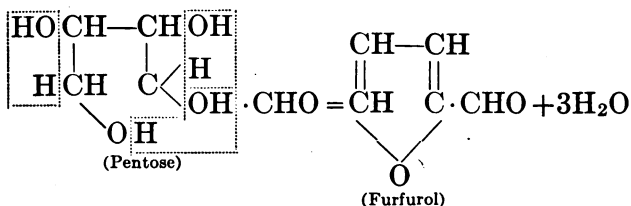
Most of the monosaccharides thus far considered have not been found in natural products.

Several methyl derivatives of monosaccharides occur in glucosides, as *digitoxose*, $C_6H_{12}O_4$, a dimethyltetrose, *digitalose*, $C_7H_{14}O_5$, a dimethylpentose, and *rhamnose*, $C_6H_{12}O_5$, a methyl pentose.

EXPERIMENT. *Pentose test.* To 2 c.c. of water in a test-tube add 2 c.c. of HCl and warm. Add phloroglucin, a little at a time, as long as it dissolves. Now add 1 c.c. of arabinose solution, and heat until a red color is obtained; examine at once with a small spectroscope, when an absorption band between the *d* and *e* lines will be seen. Heat until a precipitate forms, add some amyl alcohol, and shake; the alcohol becomes colored and gives the same spectroscopic appearance as above.

The **hexoses** are the sugars of prime impor-
tance. The chief ones are *dextrose, galactose,* and
laevulose; the first two are *aldoses,* while the last
is a *ketose*:

$$
\begin{array}{ccc}
CH_2OH & CH_2OH & CH_2OH \\
| & | & | \\
HO-C-H & HO-C-H & HO-C-H \\
| & | & | \\
HO-C-H & H-C-OH & HO-C-H \\
| & | & | \\
H-C-OH & H-C-OH & H-C-OH \\
| & | & | \\
HO-C-H & HO-C-H & C=O \\
| & | & | \\
CHO & CHO & CH_2OH
\end{array}
$$

Dextrose (*d*-glucose))   (*d*-galactose)   (Lævulose (*d*-fructose))
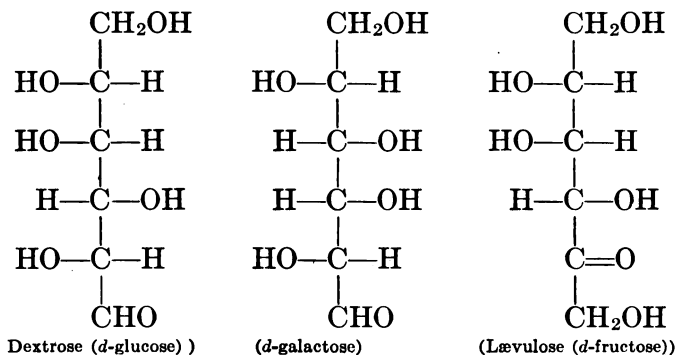
The aldoses have four asymmetric C atoms, there-
fore eight main arrangements of the secondary alco-
hol groups together with their mirror images make
sixteen aldose hexoses possible. Twelve of these
have been studied.

d-Mannose differs from *d*-glucose only in the
arrangement of the fourth secondary alcohol group.
The mirror image aldoses are the *l*-hexoses and are
lævorotatory. The chemical name for lævulose
is fructose, and it is called *d*-fructose because the
arrangement of its secondary alcohol groups is the
same as in *d*-glucose.

Six ketose hexoses are known, the only one of
importance being lævulose. Two methyl hexoses
have been prepared.

Condensation of the aldehyde and ketone trioses

in glycerose results in the production of a ketose, d, l fructose, thus:

$$
\begin{array}{ccc}
\mathrm{CH_2OH} & & \mathrm{CH_2OH} \\
| & & | \\
\mathrm{CHOH} & & \mathrm{CHOH} \\
| & & | \\
\mathrm{CHO} + \mathrm{HCHOH} & = & \mathrm{CHOH} \\
& | & | \\
& \mathrm{CO} & \mathrm{CHOH} \\
& | & | \\
& \mathrm{CH_2OH} & \mathrm{CO} \\
& & | \\
& & \mathrm{CH_2OH}
\end{array}
$$

(Glyceric aldehyde)   (Dihydroxyacetone)

(Glycerose)

(Ketohexose)
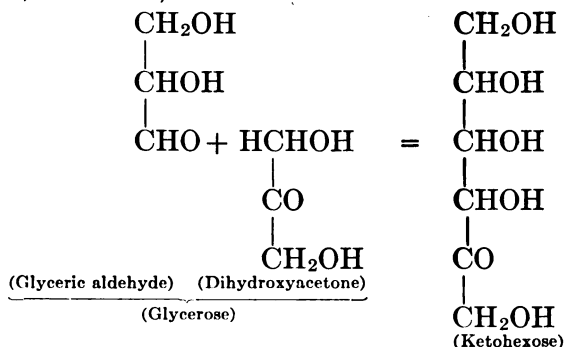
The condensation of formaldehyde induced by weak alkali yields the same product.

All the synthetic sugars are optically inactive when produced by purely chemical means.

Physiologists believe that in the animal body glycerol (from fat) may be converted into a hexose, at least under certain circumstances.

Dextrose is the aldehyde of the hexacid alcohol *sor-*

$$\mathrm{CH_2OH}$$
$$|$$

bitol, $(\mathrm{CHOH})_4$, and can be converted into the latter

$$|$$
$$\mathrm{CH_2OH}$$

by reduction. Dextrose can be oxidized to the

$$\mathrm{COOH}$$
$$|$$

dibasic acid *saccharic acid*, $(\mathrm{CHOH})_4$. The alcohol

$$|$$
$$\mathrm{COOH}$$

dulcitol, a stereoisomer of sorbitol, can be oxidized to galactose, and this aldehyde monosaccharide can

be oxidized further to *mucic acid*,
$$\begin{array}{c} COOH \\ | \\ (CHOH)_4 \\ | \\ COOH \end{array}$$
Similarly there are alcohols and acids corresponding to the other hexoses.

These alcohols and acids have the same arrangement of the secondary alcohol groups as the monosaccharides to which they are related.

Glycuronic acid (p. 221) is a monobasic acid, having the same arrangement of the CHOH groups as *d*-glucose, the aldehyde group also being present.

There are certain proteins that contain a carbohydrate derivative combined with the protein molecule proper; such are called **glucoproteins**. This combined sugar has been found in most cases to be an aminohexose, generally *glucosamine*,
$$\begin{array}{c} CH_2OH \\ | \\ (CHOH)_3 \\ | \\ CHNH_2 \\ | \\ CHO \end{array}$$
,
sometimes galactosamine. *l*-Xylose is found in combination in nucleoproteins. The sugar group in protein may be detected by certain color reactions (see exp. below).

The question of the possibility of the formation of dextrose from proteins other than glucoproteins is of very great physiological importance. The chemistry of the problem will now be briefly considered. Proteins readily split up into aminoacids (see p. 267). When we reason on purely chemical grounds,

we see that it is possible that amino-acids containing three or six carbon atoms can be converted into dextrose.

Alanin can be changed to lactic acid, the latter to glyceric acid, which can be reduced to glyceric aldehyde, and finally this can be converted into a dextrose-like sugar by aldol condensation. Such a synthesis when carried out in the animal organism would undoubtedly result in production of dextrose, i.e., dextrorotatory glucose. It is quite likely that serin is also convertible into lactic acid and therefore into dextrose:

$CH_2OH \cdot CHNH_2 \cdot COOH$, serin.

$CH_3 \quad \cdot CHNH_2 \cdot COOH$, alanin.

$CH_3 \quad \cdot CH\overset{\downarrow}{O}H \quad \cdot COOH$, lactic acid.

$CH_2OH \cdot CH\overset{\downarrow}{O}H \quad \cdot COOH$, glyceric acid.

$CH_2OH \cdot CH\overset{\downarrow}{O}H \quad \cdot CHO$, glyceric aldehyde.

$CH_2OH \cdot (CH\overset{\downarrow}{O}H)_4 \cdot CHO$, dextrose-like aldose.
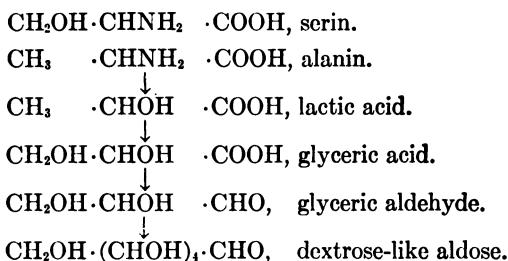
The production of dextrose from alanin, glycocoll, aspartic acid and glutaminic acid in the animal body has been experimentally demonstrated, lactic acid being noted as an intermediate product.

EXPERIMENT. To 1 c.c. of a strong solution of egg protein add a drop of saturated solution of α-naphthol in alcohol (acetone-free); then with a pipette add 1 c.c. of C.P. H_2SO_4, so that the acid does not mix, but forms a bottom layer. The greenish color at the zone of contact is due to the reagents; let the tube stand until a violet ring forms. If the violet color does not appear, tap the tube so as to cause a slight mixing of the two layers. This is *Molisch's test* and is given by all carbohydrate-containing substances.

Instead of the alcoholic solution a 10% solution of α-naphthol in chloroform may be used.

General Reactions of Monosaccharides. They all reduce alkaline silver, copper, and bismuth solutions, as do other aldehydes and some ketones (see p. 153). All form osazone crystals when treated with phenylhydrazine acetate (see exp. below). The reaction occurs in two stages; first the O of CO is substituted (as in hydrazones), then secondly the excess of phenylhydrazine removes two H atoms of the neighboring CHOH group, converting it to CO, and the latter reacts with phenylhydrazine. The osazone from lævulose is identical chemically with that from dextrose, because lævulose has the same arrangement of CHOH groups as dextrose, and the end CH₂OH is changed to CO in this case. In similar manner *d*-mannose gives an osazone that is the same as glucosazone.

Methylphenylhydrazine gives osazones with ketoses only, and can therefore be used to detect the presence of lævulose. Glucosazone has the formula,

$$
\begin{array}{l}
CH_2OH \\
\quad | \\
(CHOH)_3 \\
\quad | \\
C{=}N \cdot NH \cdot C_6H_5. \\
\quad | \\
C{=}N \cdot NH \cdot C_6H_5 \\
\quad | \\
H
\end{array}
$$
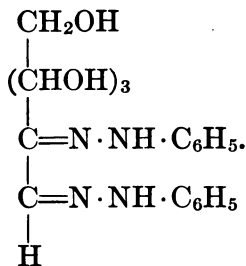
This can be converted by treatment with warm hydrochloric acid into glucosone,

$$\begin{array}{c} CH_2OH \\ | \\ (CHOH)_3 \\ | \\ CO \\ | \\ CHO \end{array}$$
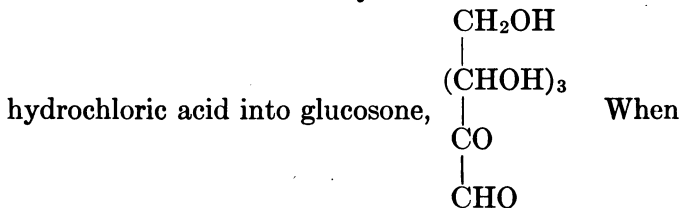
When glucosone is treated with nascent hydrogen (as by using zinc dust), fructose is formed. Thus we can convert an aldose into a ketose.

Dextrose and galactose are dextrorotatory; lævulose is lævorotatory. They all have a different rotary power when freshly dissolved from that which they show after allowing the solution to stand. This phenomenon is called *mutarotation* or *multirotation*.

This has been explained by supposing a lactone-like linking in the sugar molecule so that the C of the aldehyde group comes to hold H and OH. This C atom is now asymmetric and two stereoisomers become possible, designated as α and β. This has been investigated in the case of *l*-arabinose, *d*-galactose, lactose and *d*-glucose. This will be illustrated by *d*-glucose:

α-*d*-glucose   β-*d*-glucose
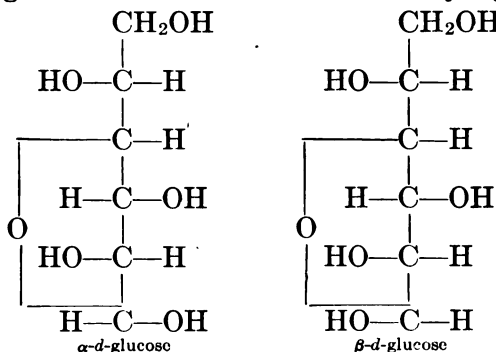
The α variety, immediately after preparing a solution, has a specific rotation (p. 245) of 110°, the β variety 19°. On standing each solution changes and both finally come to a specific rotation of 52.5°; in the one solution α partly changes to β, and in the other solution β partly changes to α. The two come into equilibrium when 40% of the glucose is α and 60% β in the case of concentrated solutions. The change from the one form of glucose to the other is believed to take place through an intermediate fcrm, this being not a lactone but the hydrated aldehyde, $CH_2OH(CHOH)_4CH(OH)_2$. There is supposed to be a trace of this present in the equilibrium mixture, thus explaining the response of the sugar solution to aldehyde tests. Maltose is believed to be made up of two α-d-glucose molecules, and isomaltose of two β-d-glucose molecules.

These hexoses are fermented by yeast, the main products being alcohol and carbon dioxide. l-Glucose does not ferment, possibly because the optically active enzyme *fits* only the d-form.

In making a test for reducing sugar (dextrose, lævulose, pentose, or lactose) in the urine, reduction of Fehling's solution is not sufficient, for the urine may reduce this reagent slightly after the administration of chloral hydrate, camphor, menthol, thymol or antipyrin because these bodies are excrcted in glycuronic acid combination (see p. 221). While the bismuth test excludes many non-saccharine substances (uric acid and creatinin) that reduce Fehling's solution, it may yet be positive with urine after the administration of antipyrin, salol, turpentine, kairin, senna, rhubarb, benzosol, sulphonal, or trional. The phenylhydrazine test is the most delicate and the most positive. The fermentation test, if positive, is generally con-

clusive. If lactose or a pentose alone be present, fermentation will not occur. These can be distinguished by a special pentose test, and in the case of lactose by increase in dextrotation after boiling with dilute HCl (hydrolysis).

Lævulose can be differentiated from dextrose by the special ketose test and by lævorotation. Chloroform added to urine as a preservative gives reduction because heating it with alkali produces formic acid.

Normal urine has a reducing power equivalent to 0.2% dextrose, but less than one-fifth of this is due to dextrose.

Dextrose (glucose, grape sugar) is present in many fruits and plants, in honey, and in the urine of diabetic patients. Commercial glucose is made by boiling starch with dilute acid; it is used for making candies, cheap syrup, etc. This crude glucose contains dextrin. Pure glucose is crystalline; if crystallized from water it contains a molecule of water of crystallization, but if crystallized from methyl alcohol it is anhydrous. It is not so sweet as cane sugar.

Galactose is obtained from lactose, by hydrolysis of the latter. It ferments slowly.

Lævulose (fructose, fruit sugar) is contained in many sweet fruits, in honey, and rarely in urine. It is difficult to crystallize. Its rotary power is greatly dependent on temperature and concentration. Calcium forms a compound with lævulose that is only slightly soluble. The corresponding glucose compound is easily soluble.

EXPERIMENTS. (1) Prepare *osazone* crystals from dextrose and lævulose as follows: To 10 c.c. of a strong solution of the sugar add 0.25 gm. of phenyl-

hydrazine hydrochloride and 0.5 gm. of sodium acetate, heat in a boiling water bath for an hour, and cool. Examine the yellow crystals under the microscope. Collect the crystals on a filter, wash thoroughly with cold acetone or water acidulated with acetic acid, press between filter-paper, recrystallize from a little 80% alcohol, dry the crystals in a desiccator, and later make melting-point determinations.[1]

The osazones of the important sugars have the following melting-points:

Dextrose Lævulose	}	204°–205°
Lactose..................		200°
Maltose..................		206°

(2) *Ketose test.* To 5 c.c. of lævulose solution add 5 c.c. of 25% HCl. Add a little resorcin and heat the mixture. A deep red color develops, and later a brown precipitate, which is soluble in alcohol. The alcoholic solution is red.

(3) (*a*) Try the aldehyde tests (see p. 153) with dextrose solution. (*b*) To some dextrose solution add one-fifth its volume of alkaline bismuth reagent (4 gm. Rochelle salt and 2 gm. of bismuth subnitrate dissolved in 100 c.c. of 10% NaOH), and boil five minutes. On cooling a black precipitate separates out.

[1] A quicker and more satisfactory way of securing osazone crystals is as follows: To 0.5 c.c. phenylhydrazine (base) add 0.5 c.c. glacial acetic acid; after mixing add 10 c.c. of the sugar solution, and heat in a boiling water-bath; glucosazone crystals appear in 5–10 minutes. For lact- and maltosazone, heat 20–30 minutes, then cool before examining.

Several *heptoses* and *octoses* and two *nonoses* are known, but they are unimportant.

DISACCHARIDES

These are the result theoretically of the union of two monosaccharide molecules, with the elimination of a molecule of water, cane sugar being a combination of dextrose and lævulose, lactose of dextrose and galactose, and maltose of two α-d-glucose molecules:

$$C_6H_{12}O_6 + C_6H_{12}O_6 = C_{12}H_{22}O_{11} + H_2O.$$
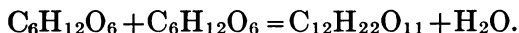
By hydrolysis the constituent monosaccharides are easily obtained:

$$C_{12}H_{22}O_{11} + H_2O = C_6H_{12}O_6 + C_6H_{12}O_6.$$
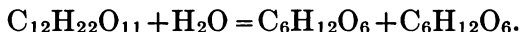
Dilute mineral acids and ferments (invertases) bring about this hydrolysis, which is called *inversion*. Yeast produces an invertase that hydrolyzes maltose quickly and another that hydrolyzes cane sugar slowly, but none that has an effect on lactose. Therefore lactose does not ferment with yeast, while cane sugar and maltose do.

Inversion by the action of dilute mineral acids is due to catalytic action of hydrogen ions, just as in the case of hydrolysis of esters (p. 180) (see appendix, p. 452).

Maltose and lactose reduce alkaline copper and bismuth solutions; pure cane sugar does not. After inversion, however, cane sugar reduces these reagents. Therefore Fehling's solution can be used for quantitative estimation of all the sugars treated

of in this chapter.   10 c.c. of Fehling's solution is reduced by

0.048   gram dextrose.
0.051   "   lævulose.
0.0676   "   lactose ($+H_2O$).
0.074   "   maltose.
0.0475   "   cane sugar (after conversion into
                  invert-sugar).

A solution of copper acetate acidified with acetic acid (Barfoed's reagent) is not reduced quickly to cuprous oxide by disaccharides, but is so reduced by monosaccharides.

Maltose and lactose form osazones with phenyl-hydrazine, each of these having a characteristic crystalline form and melting-point (see p. 239), while cane sugar forms no such combination provided hydrolysis is guarded against.

In order to explain the non-aldehydic action of cane sugar as shown by its behavior in these two re-actions, the following formula has been suggested for it:
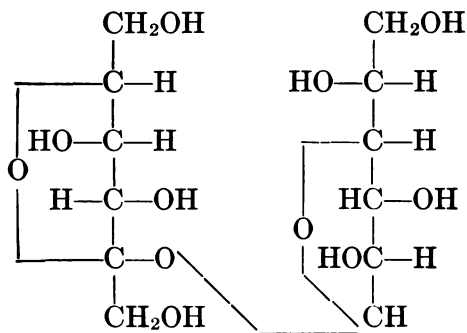
Both the aldehyde and ketone groups are tied up by the linking together of their C atoms.

The other disaccharides have the following formulæ:

Maltose.

$$\text{CH}_2\text{OH} \qquad\qquad \text{CH}_2$$
$$\text{HO—C—H} \qquad\qquad \text{HO—C—H}$$
$$\text{C—H} \qquad\qquad \text{C—H}$$
$$\text{H—C—OH} \qquad\qquad \text{H—C—OH}$$
$$\text{O} \qquad\qquad \text{O}$$
$$\text{HO—C—H} \qquad\qquad \text{HO—C—H}$$
$$\text{H—C———O} \qquad \text{H—C—OH}$$

(α-d-glucose   +   α-d-glucose)

α Lactose.

$$\text{CH}_2\text{OH} \qquad\qquad \text{CH}_2$$
$$\text{HO—C—H} \qquad\qquad \text{HO—C—H}$$
$$\text{H—C} \qquad\qquad \text{C—H}$$
$$\text{H—C—OH} \qquad\qquad \text{H—C—OH}$$
$$\text{O} \qquad\qquad \text{O}$$
$$\text{HO—C—H} \qquad\qquad \text{HO—C—H}$$
$$\text{H—C———O} \qquad \text{H—C—OH}$$
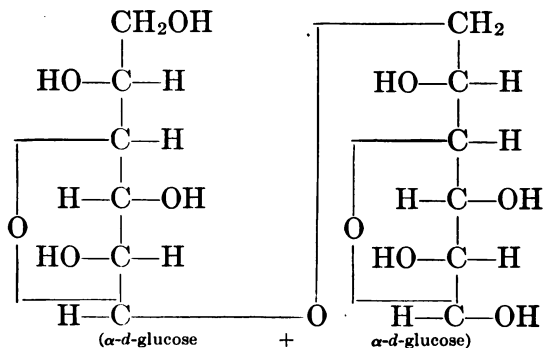
(d-galactose   +   d-glucose)
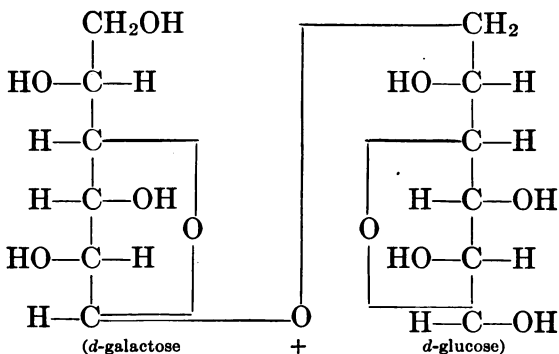
These disaccharides are all dextrorotatory. Maltose shows the greatest rotary power, lactose the least; maltose and lactose manifest multirotation. Lactose solution contains α and β lactose in equilib-

rium; β lactose has the formula above but with the end group arranged as in β-d-glucose. Invert-sugar is distinctly lævorotatory, while the cane sugar from which it is produced is dextrorotatory; this is due to the fact that the lævulose produced (invert-sugar is a mixture of equal parts of lævulose and dex-trose) rotates polarized light more to the left than does dextrose to the right.

The rotary power of maltose is decreased by in-version, while that of lactose is increased.

Saccharose (cane sugar, beet sugar, sucrose), $C_{12}H_{22}O_{11}$, is the most important of the sugars because of its use as food. It is contained in sugar cane, beets, the sap of certain maple trees, and in many other vegetables and plants.

The method of commercial preparation of cane sugar is, in brief, as follows: The juice is obtained from the sugar cane by shredding and then crush-ing the cane between rollers. The sugar beet, how-ever, is cut into slices and these are soaked with successive portions of hot water, the sugar diffusing out of the beet pulp. The sugar extract is treated with lime (which removes acids and many im-purities), then with carbon dioxide (which removes the excess of lime), and is then evaporated in vacuum pans. On cooling, sugar crystallizes out. This crude sugar is dissolved, filtered through bone-black (animal charcoal), evaporated, and recrystal-lized. The syrup that is left is *molasses*. Cane sugar as sold is commonly called granulated sugar.

Cane sugar forms large crystals when slowly crystallized; they are monoclinic prisms. It melts

at 160°; at 210°–220° it is converted into caramel with loss of water. It is extremely soluble, 100 gm. of water at 15° dissolving 197 gm. of sugar; this saturated solution has a specific gravity of 1.329. It forms saccharates with bases.

Its rotary power is influenced somewhat by concentration; it is lessened by presence of acids, alkalies or salts, but it is practically uninfluenced by temperature.

Lactose (milk sugar), $C_{12}H_{22}O_{11}+H_2O$, is the sugar contained in milk. It occasionally occurs in the urine of pregnant and nursing women. Certain microörganisms convert lactose into lactic acid. When heated it forms lactocaramel, $C_6H_{10}O_5$. Lactose is crystalline and contains a molecule of water of crystallization. It can be obtained as amorphous lactose, which is anhydrous. Lactose forms compounds with bases. Its specific rotation is not influenced much by concentration or temperature.

Maltose, $C_{12}H_{22}O_{11}+H_2O$, is the product of the action of the ferments diastase (in malt), ptyalin (in saliva), or amylopsin (in pancreatic juice) upon starch. It can also be obtained from starch by treatment with dilute mineral acids, the action of the acid being stopped at a stage before glucose is formed. It crystallizes in fine needles. Its specific rotation varies with concentration and temperature.

Isomaltose (gallisin) is distinguished from maltose in that it does not ferment with yeast, and that its osazone has a lower melting-point (150°).

EXPERIMENTS. (1) Produce osazone crystals from lactose and from maltose (footnote, p. 239). When the solutions have cooled, examine microscopically. Make melting-point determinations.

(2) (*a*) Examine a 10% solution (10 gm. dissolved in enough water to make 100 c.c. of solution) of pure cane sugar with the polariscope (see p. 226). (*b*) To 50 c.c. of a 20% cane sugar solution in a 100 c.c. graduated flask add 1 gm. of citric acid, and heat in a boiling water-bath for 30 minutes. Cool, almost neutralize, and fill up to the mark. Examine this invert-sugar solution (corresponding in concentration to the solution in (*a*) with the polariscope.[1] The specific rotation $[\alpha]D$ of the important sugars in 10% solution (at 20°) when sodium light is used is as follows:

Dextrose (anhydrous).....	+ 52.5°
Lævulose...............	− 93.0°
Maltose (anhydrous)......	+137.04°
Lactose ($+H_2O$).........	+ 52.5°
Cane sugar.............	+ 66.54°
Invert sugar.............	− 20.2°
Galactose...............	+ 81.0°

(− means rotation to the left.)

(3) Test cane sugar before and after inversion (solutions of experiment 2, *a* and *b*) with Fehling's solution.

(4) Try the ketose test (see p. 239) on cane sugar.

[1] For calculation, % sugar $= \dfrac{100 \times \text{rotation observed}}{[\alpha]D \times \text{decimeters tube length}}$.

(5) *Galactose test.* To 10 c.c. of a strong solution of lactose add 3 c.c. of HNO_3 and boil for a few minutes. Now evaporate on a water-bath to about 3 c.c. while stirring. Add 2 c.c. of water and cool. If no crystals of mucic acid separate out, let the material stand and examine after twenty-four hours.

The **trisaccharide** *raffinose*, consists of *d*-fructose, *d*-glucose and *d*-galactose linked together as in saccharose, none of the CO groups being free. It therefore does not reduce nor give an osazone. Emulsin hydrolyzes it to cane sugar and galactose. Invertase of yeast hydrolyzes it, therefore it ferments. It gives the ketose test. Its specific rotation is $+104°$.

POLYSACCHARIDES

These have complex molecules, the empirical formula of each being an unknown multiple of $C_6H_{10}O_5$.

Cellulose, $(C_6H_{10}O_5)x$ or $(C_6H_7O_2(OH)_3)x$, of high molecular weight, is essential to all plants, being the basis of the woody fiber. Cotton-fiber, hemp, flax, and the best filter-paper are almost entirely cellulose. Ordinary paper is composed mainly of cellulose. Cellulose is affected by only a few chemical agents; concentrated acids and alkalies and an ammoniacal solution of copper oxide (Schweitzer's reagent) are able to dissolve it. If unsized paper be treated momentarily with sulphuric acid, its surfaces become changed to *amyloid*, which renders the paper tough when dried. Parchment paper is made in this way. If a solution of cellulose

in sulphuric acid be diluted and boiled, dextrin and glucose are produced by hydrolysis of the cellulose.

EXPERIMENTS. (1) Dissolve some scraps of filter-paper in a little cold concentrated H_2SO_4, dilute with 200 c.c. of water, and boil for an hour. Neutralize some of this hydrolyzed cellulose solution and test with Fehling's solution.

(2) Immerse a piece of blotting-paper in 80% H_2SO_4 for a moment only, transfer to a large beaker of water, and wash out the acid thoroughly. Allow the paper to dry out; it will be found to be tough.

(3) Detection of lignin [1] in paper made from wood. Coat a sheet of cheap white paper with a solution of aniline in HCl; if it turns yellow, lignin is present.

Esters of cellulose can be formed by the action of reagents that attack alcoholic hydroxyl groups (as acetic anhydride).

When cellulose is treated with nitric acid in the presence of sulphuric acid, **nitro-celluloses** are formed, just as nitroglycerol is produced from glycerol. These range from mononitro- to trinitrocellulose.

Guncotton (nitrocellulose, pyroxylin) is trinitrocellulose. It is explosive. By dissolving guncotton in acetone a gelatinous mass is obtained; then on removing the solvent, the guncotton is left in such a physical condition that it burns and explodes more slowly. This substance is used in

[1] A substance present with cellulose in wood; it is supposed to contain pentosans and aromatic bodies.

smokeless powders. The products of the explosion are nitrogen, hydrogen, carbon monoxide and dioxide, and water-vapor.

The two lower nitrates are contained in *celloidin*. *Collodion* is a solution of these nitrates in a mixture of ether and alcohol. *Celluloid* is made by dissolving them in camphor with the aid of a little alcohol.

An artificial silk can be produced by means of trinitrocellulose, fine filaments being made and spun into thread. After being woven the nitrocellulose fabric is treated with a solution of calcium sulphide, which removes the NO_2 groups. Almost pure cellulose, resembling silk, is left. Artificial silk is produced by two other methods, one of these, called the viscose method, is supplanting the others. Viscose silk is made from as pure cellulose as can be obtained from wood pulp. The latter is treated with NaOH solution and CS_2, and is macerated for a considerable time. The cellulose solution is squirted through very fine openings into an acid bath which precipitates the cellulose as fibers. Large quantities of artificial silk are now produced.

EXPERIMENT. Mix 5 c.c. of C.P. HNO_3 and 10 c.c. of C.P. H_2SO_4. When it is cool, immerse some absorbent cotton in the mixture for half a minute, then wash out the acid from the cotton with a large quantity of water, press out the water, and dry at room temperature. When dry, shake part of it with a mixture of ether and alcohol, pour the liquid into an evaporating dish and allow to evaporate. A syrupy liquid (collodion) is obtained, and later a glassy skin. Test the inflammability of another piece of the dry cotton, and compare with untreated cotton.

Starch (amylum), $(C_6H_{10}O_5)x$, comprises a large part of all vegetable food. It exists in the plant as granules, having different forms and sizes in different plants. Starch grains are spherocrystals, covered with a layer of specially modified starch substance which is more resistant to the action of water, ferments and chemical agents than the substance within the grains.

Starch and cellulose are probably synthesized by plants from formaldehyde by processes of condensation and polymerization.

Ordinary starch is made from corn or potatoes. Starch is insoluble in cold water. When boiled, it apparently goes into solution or forms a gelatinous mass, according to the amount of water present. It is a colloidal solution containing also tiny masses in suspension.

It is precipitated from solution by low concentration of alcohol, and by saturation with certain salts (as Na_2SO_4 and $NaCl$). A dilute solution of boiled starch is readily hydrolyzed by ferments (diastase, ptyalin, etc.) and by platinum black (catalytic action) at a temperature of about 40°. Dextrin is first formed, then maltose, while hydrolysis by boiling with dilute mineral acid carries the process further, the end product being glucose. Heat alone converts starch into dextrin; the crust on bread is mainly dextrin. Starch takes up iodine, probably by adsorption, thus forming a blue substance; heat drives the iodine from this substance, so that the color is lost until the mixture becomes cool again. Natural starch contains two dif-

ferent materials, a soluble substance *amylose* (60–80% of the weight of the starch) and an insoluble substance, *amylopectin*, which gelatinizes with hot water. Amylopectin gives little color with iodine, while amylose gives a deep blue. Both are hydrolyzed by ferments. It is probable that there is a very large number of amyloses (stereoisomers).

Dextrins are less complex bodies than starch. The intermediate substances between starch and maltose formed during digestion are, in the order of complexity, amylodextrins, erythrodextrins, achroödextrins, and maltodextrins. The first gives a blue color with iodine, the second a red or reddish brown (a mixture of erythro- and amylo-dextrins gives a bluish red color), while the simpler dextrins give no color test. Commercial dextrin is prepared from starch by means of heat. It forms a gummy solution, which is used for making labels. It is insoluble in alcohol. Most dextrins are precipitated by saturating their solutions with salts, such as ammonium sulphate and sodium sulphate. Most dextrins are precipitated by alcohol when the concentration reaches 75%; the lower dextrins require as much as 90% for precipitation.

The dextrins are dextrorotatory, the $(\alpha)D$ being 192–196° for the higher dextrins. Acid hydrolyzes them to glucose. Diastatic ferments change them to maltose.

Glycogen, $(C_6H_{10}O_5)x$, resembles dextrin. It is present in animal tissues, mainly in the liver. The liver acts as a storehouse for carbohydrates, storing up in the form of glycogen the sugar that comes to

it from the digestive organs, and then reconverting the latter into sugar as needed by the tissues. A substance has been found in certain vegetables resembling glycogen. Glycogen forms a colloidal solution, which is characteristically opalescent. With iodine it gives a reddish brown color. Its $(\alpha)D$ is $+196.5°$. It hydrolyzes to dextrose. Diastatic ferments form from it dextrins, and finally maltose. It is precipitated by 55% alcohol and by basic lead acetate.

EXPERIMENTS. (1) Test solutions of starch, dextrin, and glycogen with iodine solution.

(2) Test them with lead subacetate solution.

(3) Test them with Fehling's solution before and after hydrolyzing by boiling with dilute HCl.

Gums contain polysaccharides similar to dextrin. *Gum arabic* (acacia) contains a pentosan, araban, $(C_5H_8O_4)_n$ which hydrolyzes to *l*-arabinose. *Gum tragacanth* contains bassorin.

Agar-agar is a pectin-like substance containing at least seven different carbohydrates, including some starch and cellulose. The most important constituent is gelose, a galactan, which can be hydrolyzed to galactose.

GLUCOSIDES

Natural glucosides are vegetable substances which can be split up by hydrolysis into a sugar (or sugars) and some other characteristic organic compound or compounds. Many of them are important medi-

cines. A large number of glucosides have been studied. The sugar derived from them is generally glucose.

Phloridzin, $C_{21}H_{24}O_{10}$, is used to produce experimental diabetes in animals. It splits up into glucose and phloretin, $C_{15}H_{14}O_5$ (see also phloroglucin, p. 348).

Arbutin, $C_{12}H_{16}O_7$, is a comparatively simple glucoside, hydrolyzing to dextrose and hydroquinone.

Gaultherin, $C_{14}H_{18}O_8$, is a glucoside contained in the wintergreen plant; an accompanying ferment hydrolyzes it to dextrose and methyl salicylate.

Salicin, $C_{13}H_{18}O_7$, is used in medicine; it hydrolyzes to dextrose and saligenin (p. 354). Its structural formula is $C_6H_4 \Big\langle \begin{array}{l} O \cdot C_6H_{11}O_5 \\ CH_2OH \end{array}$.

Amygdalin, $C_{20}H_{27}NO_{11}$, is found in bitter almonds, peach-pits, etc. The ferment emulsin, as well as acids, hydrolyzes it to glucose, hydrocyanic acid, and benzaldehyde (see p. 351).

Its structural formula is said to be:

$$
\begin{array}{l}
\overline{O} \\
CH(CHOH)_2CH \cdot CHOH \cdot CH_2 \\
| \\
O \quad\quad OCH\ (CHOH)_2CH \cdot CHOH \cdot CH_2OH. \\
\overline{O} \\
| \\
C_6H_5 - CH - CN
\end{array}
$$
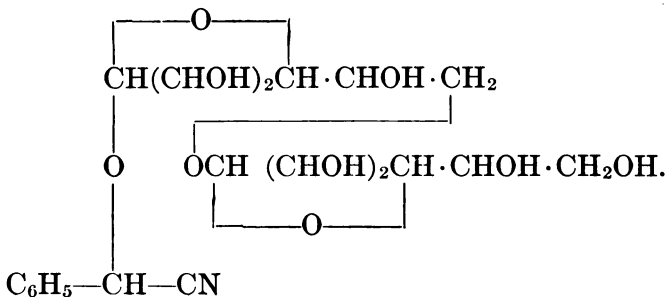
Digitalin, $C_{35}H_{56}O_{14}$, an active principle of digitalis, hydrolyzes to dextrose, digitaligenin, $C_{22}H_{30}O_3$, and digitalose, $C_7H_{14}O_5$.

Digitoxin, $C_{34}H_{54}O_{11}$, the chief active glucoside of digitalis, yields by hydrolysis digitoxigenin, $C_{22}H_{32}O_4$, and digitoxose, $C_6H_{12}O_4$.

Strophanthin, $C_{40}H_{66}O_{19}$, from strophanthus, hydrolyzes to strophanthidin, $C_{27}H_{38}O_7$, methyl alcohol, mannose. and rhamnose.

Sinigrin, $C_{10}H_{18}NS_2KO_{10}$, the glucoside of black mustard, by the action of a ferment present in the mustard splits up into mustard oil, dextrose, and $KHSO_4$. In similar manner **sinalbin,** $C_{30}H_{44}N_2S_2O_{16}$, of white mustard yields dextrose, parahydroxytolyl mustard oil and, sinapin bisulphate.

Indican, $C_{14}H_{17}O_6N$, is the glucoside which is contained in those plants from which indigo is produced. It is a combination of glucose and indoxyl. The indican present in urine (p. 417) is a different compound.

Saponins. A large number of glucosides are grouped together into this sub-class. They are non-nitrogenous and form solutions that foam on shaking (cf. soaps).

Digitonin is a saponin contained in digitalis, $C_{54}H_{92}O_{28}$; it splits up into digitogenin, $C_{30}H_{48}O_6$, and two molecules each of glucose and galactose.

Artificial glucosides are simpler compounds; for example, a methyl glucoside of *d*-glucose has the CH_3 group attached to O of the aldehyde group of glucose.

EXPERIMENTS. (1) Try Molisch's test (see p. 234) on a solution of a glucoside.

(2) Hydrolyze some glucoside solution by boiling with dilute H_2SO_4, neutralize, and examine for sugar with Fehling's solution.

CHAPTER XVIII

NITROGEN DERIVATIVES. (ALSO PHOSPHORUS AND ARSENIC COMPOUNDS)

NITROGEN DERIVATIVES

THESE fall into four classes: (1) cyanogen derivatives, (2) substituted ammonias, (3) nitro compounds, and (4) nitrites.

Cyanogen Derivatives. Organic cyanides can be prepared by treatment of alkyl halides with potassium cyanide, as

$$\underset{\text{(Ethyl chloride)}}{C_2H_5\,Cl} + \underset{}{K\,CN} = \underset{\text{(Ethyl cyanide)}}{C_2H_5CN} + KCl,$$
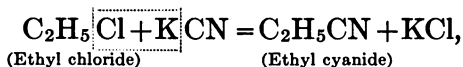
also by anhydrolysis (removal of water) of an acid amide (see p. 273), thus (see exp.):

$$\underset{\text{(Acetamide)}}{CH_3\cdot CONH_2} = \underset{\text{(Methyl cyanide)}}{CH_3\cdot CN} + H_2O.$$
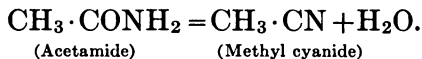
EXPERIMENT. Into a dry 250-c.c. wide-mouth Jena flask (extraction flask) put 10 gm. of dry acetamide and add quickly about 15 gm. of phosphorus pentoxide. Mix quickly with a dry rod. As soon as possible add 10 gm. more of the oxide as a top layer. Cork and connect with a condenser immediately. Heat with a small smoky flame.

Collect the distillate in a large clean test-tube. Shake the distillate with half its volume of water, then add small pieces of solid KOH until no more dissolves, keeping the solution cool with running water; the cyanide now separates as a top layer. Transfer to a narrow test-tube, and remove the cyanide carefully with a clean dry pipette. Use the product for synthesis of acetic acid (p. 171).

The CN group of organic cyanides can be hydrolyzed to COOH; in consequence the alkyl cyanides are called acid *nitriles;* for example, $CH_3 \cdot CN$ is acetonitrile because acetic acid can be obtained from it (see exp., p. 171):

$$CH_3CN + 2H_2O = CH_3 \cdot COOH + NH_3 (\text{i.e.,}$$
$$CH_3COONH_4.)$$
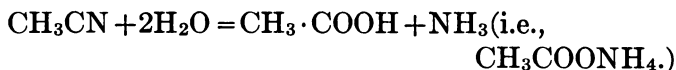
HCN, *hydrocyanic acid,* may be called formonitrile because it can be hydrolyzed to formic acid. As regards acid power it is extremely weak; its dissociation constant is less than one ten-thousandth of that of acetic acid. It is very poisonous, but is used in 2% solution as a remedy.

This reaction also shows that the carbon atom of CN is linked directly to the carbon chain. There are cyanides, however, in which it is the nitrogen atom of the CN group that is linked to the carbon chain. These are **isocyanides** or **isonitriles.** $CH_3 - N \equiv C$ is *methyl isocyanide.*

Some chemists think that hydrocyanic acid may be a mixture of HCN and HNC, and that the metallic cyanides are mainly isocyanides.

Chloroform when heated with alkali and a primary

amine gives rise to the disagreeable vapor of iso-cyanide:

$$CHCl_3 + R—NH_2 = R—NC + 3HCl.$$
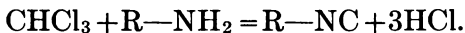
When an isocyanide is hydrolyzed, an amide and formic acid are formed:

$$CH_3 \cdot NC + 2H_2O = CH_3NH_2 + HCOOH.$$
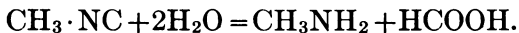
EXPERIMENT. *Isocyanide reaction.* Mix to-gether in a test-tube a few drops of chloroform, 1 c.c. of aniline, and 2 c.c. of alcoholic KOH. Warm gently. Note the peculiar disagreeable odor of the isocyanide. As soon as this odor is detected, dilute the mixture with much water in the sink, since the fumes are poisonous.

Other Cyan-compounds.

Cyanic acid may be $HO—C{\equiv}N$ or $HN{=}C{=}O$, or a mixture of both.

Sulphocyanic (thiocyanic) acid has sulphur re-placing O in the cyanic acid molecule.

Cyan-acids, e.g., cyan-acetic acid, $CH_2CN \cdot COOH$, are analogous to monochloracetic acid. Such an acid is much stronger than the simple acid and even stronger than the corresponding monochlor acid.

Substituted Ammonias. These may be considered as ammonia in which one or more hydrogen atoms are replaced by organic groups. *Primary substituted ammonias,* $N{\langle}^{\text{H}}_{\text{R}}{-}\text{H}$, contain the group NH_2, called

the amido or amino group. *Secondary substituted ammonias,* $N\underset{R}{\overset{H}{\diagup}}R$, contain the imido group, NH.

Tertiary substituted ammonias, $N\underset{R}{\overset{R}{\diagup}}R$, have all the hydrogen of ammonia displaced.

These are all called **amines.** They are prepared by the action of ammonia on alkyl halides:

$$C_2H_5Br + NH_3 = C_2H_5NH_2 \cdot HBr,$$
(Ethylamine hydrobromide)

$$C_2H_5NH_2 + C_2H_5Br = (C_2H_5)_2NH \cdot HBr,$$
(Diethylamine hydrobromide)

$$(C_2H_5)_2NH + C_2H_5Br = (C_2H_5)_3N \cdot HBr.$$
(Triethylamine hydrobromide)
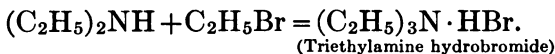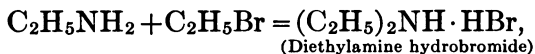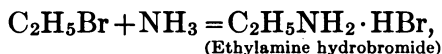
The HBr is removed by treating the above compounds with KOH.

Amines form salts with acids by adding on the entire acid molecule, N changing its valence from three to five. The salts of alkaloids are of similar nature.

Some amines have two NH_2 groups, as ethylene diamine, $NH_2-CH_2 \cdot CH_2-NH_2$.

The amines may also be prepared by treating an acid amide with sodium hypobromite (see exp.):

$$CH_3 \cdot CONH_2 + Br_2 + 4NaOH = CH_3 \cdot NH_2 + 2NaBr$$
(Acetamide)   (Methylamine)
$$+ Na_2CO_3 + 2H_2O.$$
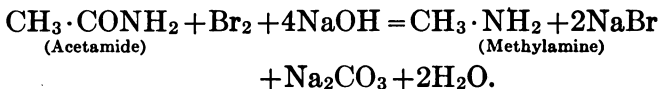
(Br forms hypobromite with NaOH.)

EXPERIMENT. Treat 12.5 gm. of dry acetamide in a half-liter flask with 11.5 c.c. of bromine; add a cooled solution of 20 gm. of KOH in 175 c.c. of water until the mixture turns a bright yellow, meanwhile keeping the flask cooled with running water. Run this hypobromite mixture by means of a dropping funnel rapidly into a solution of 40 gm. of KOH in 75 c.c. of water. Keep the temperature of the liquid at 70–75°. Cool the flask if the temperature gets above 75°. Keep at 75° for thirty minutes. Add some powdered pumice and distill on a sand-bath. Attach an adapter (see Fig. 19, p. 126) to the condenser; dip this slightly below the surface of strong hydrochloric acid in the receiving flask (50 c.c. C.P. HCl +50 c.c. of water). Distill until the distillate, tested by detaching the adapter momentarily, is no longer strongly alkaline to litmus. Evaporate the acidulated distillate in an evaporating dish heated over wire gauze. When down to small bulk complete the drying in an oven at 110°. Pulverize the residue; treat with several portions of 10 c.c. of hot alcohol, filtering the decanted alcohol into a dry beaker. Crystals of methylamine hydrochloride separate out by cooling. Filter off the crystals; press between filter-paper; keep part as a specimen. Put the rest into a small test-tube, and add strong KOH solution; methylamine is evolved. Note the odor and the reaction of the gas to litmus. Test its inflammability by corking the test-tube with a cork fitted with a glass tube that has a finely drawn tip, and applying a flame to this tip. Heat the

mixture if necessary to secure free evolution of gas.

Nascent hydrogen converts an alkyl cyanide into an amine,

$$\underset{\text{(Methyl cyanide)}}{CH_3CN} + 4H = \underset{\text{(Ethylamine)}}{CH_3 \cdot CH_2NH_2}.$$
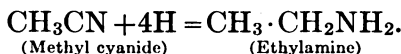
Many amines, particularly the primary ammonia bases, are decomposed by nitrous acid. This is a reaction of considerable importance. An ammonium nitrite derivative is formed first, but this is so unstable that it breaks down, liberating nitrogen:

$$\underset{\text{(Ethylamine)}}{NH_2 \cdot C_2H_5} + HNO_2 = \underset{\text{(Ethyl ammonium nitrite)}}{NH_3(C_2H_5) \cdot NO_2},$$

$$NH_3(C_2H_5) \cdot NO_2 = N_2 + H_2O + C_2H_5OH.$$
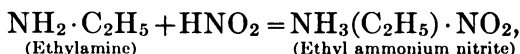
Many amines result from decomposition of protein material. Amines resemble ammonia in odor, and their vapors are alkaline to litmus. When dissolved in water they form bases, i.e., they give rise to hydroxyl ions. Many of the amines are more strongly basic than ammonium hydroxide.

There are **quaternary bases** in which four organic groups are linked to nitrogen; these are really substituted ammonium compounds. *Tetraethyl ammonium hydroxide* is $(C_2H_5)_4NOH$ (cf. NH_4OH). This is a very strong base; its saponifying power is almost equal to that of sodium hydroxide. If the saponifying power (*affinity constant*) of LiOH be taken as 100,

$$KOH \text{ and } NaOH = 98$$

$$(C_2H_5)_4NOH = 79$$

$$NH_4OH = 2$$

Methylamine, **dimethylamine,** and **trimethyla-mine** are gases. They are contained in herring-brine. They are also obtained by destructive distillation of the residue that is left after preparing alcohol from the molasses of beet sugar. HCl is used to hold the amines as salts. This amine distillate is used commercially to produce methyl chloride, because the latter can be obtained from trimethylamine by treatment with hydrochloric acid:

$$(CH_3)_3N—HCl + 3HCl = 3CH_3Cl + NH_4Cl.$$

Choline is a substituted ammonium hydroxide, trimethylhydroxyethyl ammonium hydroxide:

$$(CH_3)_3N \begin{cases} CH_2 \cdot CH_2OH \\ O\overline{H} \end{cases} .$$
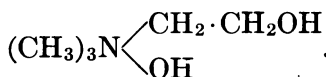
It will be noticed that it is also related to primary alcohols. It is of physiological importance.

Choline is oxidized to *betaine* by removal of the H atoms of both the alcohol and the basic hydroxyl groups,

$$(CH_3)_3N \begin{cases} CH_2 \cdot CO \\ | \\ O— \end{cases} .$$
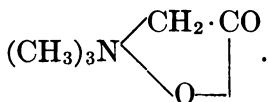
Analogous to choline and betaine is *carnitine* (*novaine*),

$$(CN_3)_3N\begin{cases}CH_2 \cdot CH_2 \cdot CH(OH) \cdot CO \\ O\end{cases}.$$
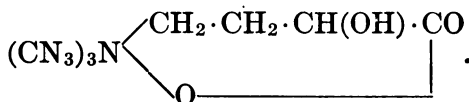
The **lecithins** are salts of choline. The chief one (distearyl lecithin) contains stearic and glycerophosphoric acids in combination with choline, having the formula:

$$CH_2—OOC_{18}H_{35} \text{ (Stearic acid)}$$
$$CH—OOC_{18}H_{35}$$
$$CH_2—O—PO\begin{cases}OH\\O—C_2H_4N(CH_3)_3OH\end{cases}$$
(Glycerol)   (Phosphoric acid)   (Choline)
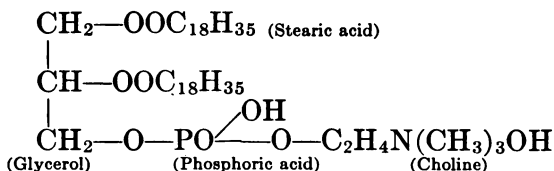
Lecithin is an important constituent of yolk of egg, of nerve-tissue, of bile, and of the envelope of red blood-corpuscles.

Phosphatides. The lecithins belong to this class of compounds. Phosphatides contain phosphoric acid in ester combination with an alcohol, generally glycerol, and one or more fatty acid radicles, and also one or more radicles containing nitrogen, generally choline. They are of importance in biochemistry. One of these is *cephalin*, which has been obtained from brain tissue. It contains the radicle of stearic acid and of an unsaturated acid of the linoleic acid series, $C_{17}H_{30}COOH$, while the nitrogenous part differs from choline in having one methyl group instead of three.

Muscarine is closely related to choline. It has

been suggested that it is the aldehyde corresponding to choline considered as an alcohol:

$$(CH_3)_3N\begin{cases} CH_2{-}CHO(+H_2O) \\ OH \end{cases}.$$
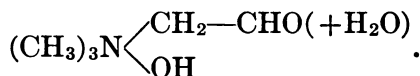
Some chemists believe that the CHO group is combined with water, so that it is really $-CH(OH)_2$ as in chloral hydrate.

Muscarine is a basic substance classed as an alkaloid (see p. 425). It is very poisonous and is contained in toadstools (*Agaricus muscarius*) and some other plants.

Many **ptomaines** [1] are amine bases. Methylamine, dimethylamine, trimethylamine, ethylamine, diethylamine, triethylamine, propylamine, butylamine, amylamine, muscarine, and choline occur as ptomaines.

Cadaverine and **putrescine** are diamine ptomaines. Cadaverine is

$$CH_2\begin{cases} CH_2{-}CH_2 \cdot NH_2 \\ CH_2{-}CH_2 \cdot NH_2 \end{cases}.$$
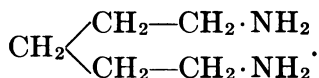
Putrescine has the formula,

$$\begin{array}{l} CH_2{-}CH_2{-}NH_2 \\ | \\ CH_2{-}CH_2{-}NH_2 \end{array}$$
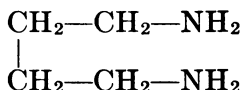
[1] Ptomaines are organic bases formed by the action of bacteria on nitrogenous matter. Decomposing animal tissue is very apt to contain ptomaines. Many of them are highly toxic and are the cause of death in certain cases of poisoning by canned meats, etc.

Neurine, like choline, is a ptomaine-containing oxygen,

$$(CH_3)_3N\diagup\begin{matrix}CH=CH_2\\OH\end{matrix}$$.
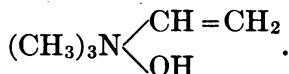
Urotropine is hexamethylentetramine, $(CH_2)_6N_4$, and is obtained by the action of ammonia on formaldehyde.

Acid solutions, even those of very low H ion concentration, act on urotropine, liberating formaldehyde.

Piperazine (spermine) is diethylendiamine,

$$NH\diagup\begin{matrix}CH_2-CH_2\\CH_2-CH_2\end{matrix}\diagdown NH.$$
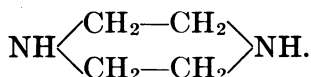
Piperazine acts as a solvent for uric acid, provided the former is present in sufficient concentration. *Sidonal, lycetol,* and *lysidin* are piperazine derivatives and are used for the same purpose.

Analogous to the substituted ammonias are the substitution derivatives of phosphine (PH_3) and arsine (AsH_3)   Since they will be mentioned in no other place, it may be well in this connection to state that there are organic acids containing phosphorus or arsenic, as, for example, *cacodylic acid,* which is dimethylarsenic acid,

$$O=As\diagup\begin{matrix}CH_3\\CH_3.\\OH\end{matrix}$$
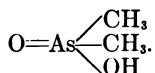
Nitro Compounds.—Nitroparaffins have N of the nitro group linked directly to C of the chain, e.g., nitroethane, $CH_3 \cdot CH_2—NO_2$. The nitro compounds of the benzenes are much more important

than are those of the paraffins, and will be considered later.

The Nitrites. Ethyl Nitrite, C_2H_5—O—NO, and **amyl nitrite,** C_5H_{11}—O—NO, are of importance. Both are used as medicines. Amyl nitrite is a very valuable remedy; its physiological action is similar to that of nitroglycerol (see p. 202), but comes on quickly and is very evanescent. It consists chiefly of isoamyl nitrite. These organic nitrites are often called nitrous esters, being formed by the action of nitrous acid on alcohols.

EXPERIMENT. Prepare amyl nitrite as follows: Mix in a small flask 20 c.c. of fermentation amyl alcohol and 15 gm. of finely powdered sodium nitrite. Set the flask in ice-water; add to the alcohol, drop by drop, 5 c.c. of C.P. H_2SO_4 from a dropping funnel. Amyl nitrite forms a top layer; decant it off into a separating funnel. Add some water to the mixture in the flask and shake; when more amyl nitrite separates out, decant again. Separate the nitrite from the aqueous liquid. Dry with calcium chloride and distill. Note the color, odor, and the effect of cautious inhalation (flushing of the face and vascular throbbing).

AMINO ACIDS AND ACID AMIDES

AMINO ACIDS

Amino or **amido acids** are acids containing an NH_2 or amido group. Corresponding to mono-chloracetic acid, $CH_2Cl \cdot COOH$, is aminoacetic acid, $CH_2NH_2 \cdot COOH$.

The simplest amino acid is aminoformic acid, $NH_2 \cdot COOH$, called **carbamic acid.** The free acid is unknown. The salts are unstable, showing a decided tendency to become converted into carbonates. Ammonium carbamate is of considerable importance in physiology, because it is believed to be one of the forerunners of urea. It can be changed into urea by heating it in a sealed tube at a temperature of 135–140°:

$$NH_2 \cdot COONH_4 = NH_2 \cdot CO \cdot NH_2 + H_2O.$$
<div style="text-align:center">(Ammonium carbamate)   (Urea)</div>

EXPERIMENT. Prepare ammonium carbamate by bubbling dry CO_2[1] and dry NH_3 simultaneously into alcohol contained in a cylinder or graduate. Secure the dry NH_3 as previously described (see p. 153). Dry the CO_2 by bubbling it through H_2SO_4. When

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[1] CO_2 is obtained by putting marble chips into a bottle or generator and adding HCl by a dropping funnel.

a considerable quantity of crystals has been pro-
duced, stop the process. Filter off the alcohol;
press the crystals between filter-paper. To test
the carbamate, dissolve some of the crystals in 5 c.c.
of distilled water that has been cooled to 0°; and
immediately add some cold $CaCl_2$ solution. No
reaction is apparent because calcium carbamate
in solution is stable at very low temperatures.
Now warm the solution; the carbamate decom-
poses and a heavy precipitate of calcium carbonate
appears. Leave the rest of the crystals exposed
to the air several days; a small amount of a white
powder (NH_4HCO_3) is obtained:

$$2NH_3 + CO_2 = CO{\overset{\displaystyle NH_2}{\underset{\displaystyle ONH_4}{\Big\langle}}}.$$
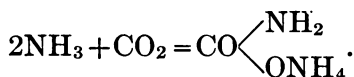
Ethyl carbamate, or **urethane,** $NH_2 \cdot COOC_2H_5$, is
an ester having a hypnotic action.

Amino acids may be obtained by treating a halo-
gen fatty acid with ammonia, thus:

$$H_2N|H + Cl|H_2C \cdot COOH = NH_2 \cdot CH_2 \cdot COOH + HCl.$$
<div align="center">(Monochloracetic acid)   (Aminoacetic acid)</div>
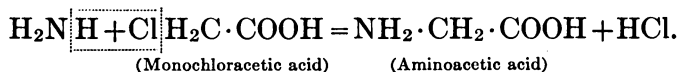
Ammonium salts are, of course, formed. They
can also be obtained by decomposing proteins by
means of acids, alkalies, or hydrolytic ferments.

All the amino-acids that are considered in this
chapter are of great importance in physiology.
They are very weak acids. In fact they are am-
photeric electrolytes, their solutions behaving as
if they contained both hydrogen and hydroxyl ions.

The amino group gives the basic character to the molecule. Proteins and some other organic compounds act in the same manner.

Glycocoll (glycin) is aminoacetic acid,

$$CH_2 \underset{}{\overset{NH_2}{\diagdown}} COOH.$$
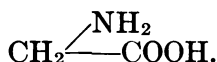
It can be produced from glue (or gelatin) by boiling with dilute sulphuric acid or baryta water. It can be prepared by allowing an excess of strong ammonium hydroxide to act on monochloracetic acid for twenty-four hours. In the animal body it combines with benzoic acid to form hippuric acid (see p. 360), and with cholic acid to form one of the bile acids, glycocholic acid.

Methyl glycocoll, $CH_2 \diagdown \overset{NH \cdot CH_3}{\underset{COOH}{}}$, is called *sarcosin*. It can be synthesized from monobromacetic acid and methylamine:

$$CH_2Br \cdot COOH + 2CH_3 \cdot NH_2 = CH_2 \diagdown \overset{NH-CH_3}{\underset{COOH}{}}$$

$$+ NH_3 \diagdown \overset{CH_3}{\underset{Br}{}}.$$
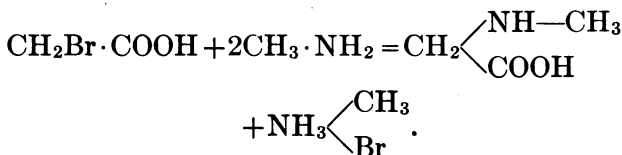
It is a product of decomposition of creatin and of caffeine.

Alanin, $CH_3 \cdot CH \cdot NH_2 \cdot COOH$, is α-aminopropionic acid. It can be made from α-chlorpropionic acid by treatment with ammonia. It is isomeric with sarcosin.

Serin is hydroxyalanin, $\cdot CH_2OH \cdot CHNH_2 \cdot COOH$.

Valin is α-aminoisovaleric acid,

$$\begin{matrix} CH_3\diagdown \\ CH_3\diagup \end{matrix} CH \cdot CHNH_2 \cdot COOH.$$

Leucin is α-aminoisobutylacetic acid, or α-amino-isocaproic acid,

$$\begin{matrix} CH_3\diagdown \\ CH_3\diagup \end{matrix} \underset{\text{(Isobutyl)}}{CH-CH_2} \underset{\text{(Aminoacetic acid)}}{\overset{\diagup NH_2}{CH-COOH.}}$$
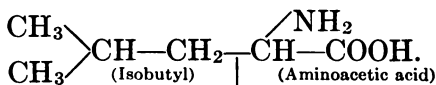
This may occur in the urine in certain diseases. It is a decomposition product of protein, being an important end product of tryptic digestion.

Isoleucin, $\begin{matrix} C_2H_5\diagdown \\ CH_3\diagup \end{matrix} CH-CH\begin{matrix} \diagup NH_2 \\ \diagdown COOH \end{matrix}$, is contained in certain proteins.

Aspartic acid (asparaginic acid) is aminosuccinic acid,

$$\begin{matrix} CH\overset{\diagup NH_2}{\underline{\quad\quad}}COOH \\ | \\ CH_2\underline{\quad\quad}COOH \end{matrix}$$
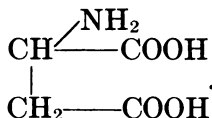
It is obtainable from asparagin and from protein.

Glutaminic acid (glutamic acid) is α-aminoglutaric acid,

$$CH_2\begin{matrix} \diagup CH\overset{\diagup NH_2}{\underline{\quad}}COOH \\ \diagdown CH_2-COOH \end{matrix} \cdot$$
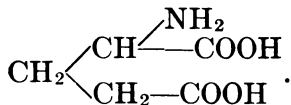
Gelatin and caseinogen can be split up so as to furnish a considerable proportion of this acid.

Phenylalanin and **tyrosin** are aromatic mono-amino-acids derived from proteins (see p. 371). The amino

acids considered thus far have the amino group in the α-position.

Lysin is $\alpha\epsilon$-diaminocaproic acid,

$$NH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH \underset{\displaystyle COOH}{\overset{\displaystyle NH_2}{<}}.$$
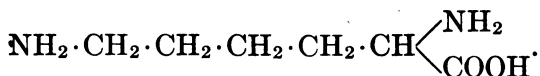
It is one of the products of protein when boiled with mineral acid.

Ornithin is $\alpha\delta$-diaminovaleric acid,

$$NH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH \underset{\displaystyle COOH}{\overset{\displaystyle NH_2}{<}}.$$
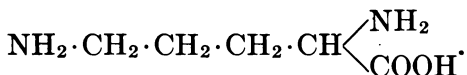
Arginin is related to ornithin, being δ-guanidin-α-aminovaleric acid,

$$NH = C \underset{\displaystyle \underset{\text{(Guanidin)}}{NH}}{\overset{\displaystyle NH_2}{<}} - CH_2 \cdot CH_2 \cdot CH_2 \cdot CH \underset{\displaystyle \underset{\text{(α-Aminovaleric acid)}}{COOH}}{\overset{\displaystyle NH_2}{<}}.$$
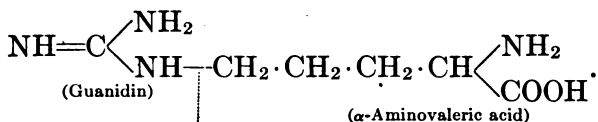
It can be hydrolyzed to urea and ornithin, thus:

$$NH = C \underset{\displaystyle NH}{\overset{\displaystyle NH_2}{<}} - CH_2 \cdot CH_2 \cdot CH_2 \cdot CH \underset{\displaystyle COOH}{\overset{\displaystyle NH_2}{<}} + H_2O$$

$$= \underset{\displaystyle \underset{\displaystyle \underset{\text{(Urea)}}{O}}{\overset{\displaystyle \|}{C}}}{\overset{\displaystyle NH_2 \quad NH_2}{\diagdown \diagup}} + NH_2 \cdot CH_2 \cdot CH_2 \cdot \underset{\text{(Ornithin)}}{CH_2} \cdot CH \underset{\displaystyle COOH}{\overset{\displaystyle NH_2}{<}}.$$
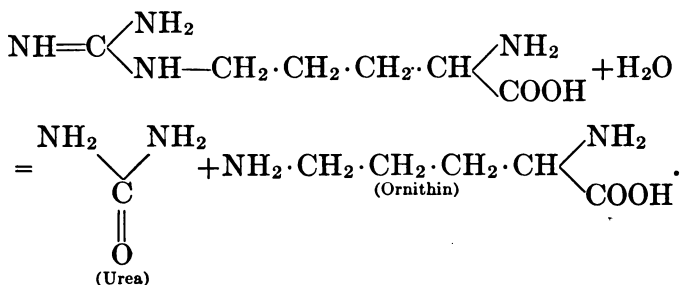
A ferment, arginase, found mainly in the liver, can also bring about this hydrolysis.

Lysin and arginin are called **hexone bases** (hexone

refers to their possessing six carbon atoms in the molecule). Another hexone base is **histidin,** $C_6H_9N_3O_2$, probably β-imidazol α-aminopropionic acid,

$$
\begin{array}{c}
\text{CH} \\
\diagup \diagdown \\
\text{HN} \quad \text{N} \qquad\qquad \text{NH}_2 \\
| \qquad | \qquad\qquad\qquad | \\
\text{CH}=\text{C}-\text{CH}_2-\text{CH}-\text{COOH.}
\end{array}
$$
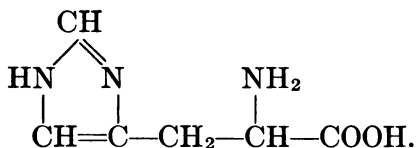
It is a heterocyclic compound (see p. 414). It is now believed that these hexone bases are present in combination in all protein molecules. The simplest proteins, *protamines*, seem to contain practically nothing besides hexone bases.

Another heterocyclic compound derived from proteins is **tryptophan** (see p. 418), also an α-amino acid.

It seems advisable to mention in this place two derivatives of pyrrolidine (a heterocyclic compound, p. 415) because they are obtained, together with the above amino acids, as decomposition products of proteins. They are *prolin* or α-pyrrolidine-carboxylic acid,

$$
\begin{array}{c}
\text{H}_2\text{C}\text{---}\text{CH}_2 \\
| \qquad\qquad | \\
\text{H}_2\text{C} \diagdown \diagup \text{CH}-\text{COOH,} \\
\text{NH}
\end{array}
$$
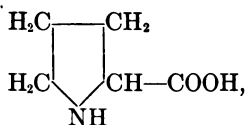
and γ-hydroxy-α-pyrrolidine-carboxylic acid or *hydroxyprolin.*

Optical activity of the decomposition products of proteins: Alanin, valin, isoleucin, glutaminic acid, ornithin, arginin, and lysin are dextrorotatory. Serin, leucin, cystin, aspartic acid, histidin, phenylalanin, tyrosin, tryptophan, prolin, and hydroxyprolin are lævorotatory.

SULPHUR DERIVATIVES OF AMINO ACIDS

Cystein is α-amino-β-thiolactic acid:

$$CH_2\diagup\overset{SH}{\underset{}{}}\!\!-CH\diagup\overset{NH_2}{\underset{}{}}\!\!-COOH.$$
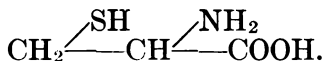
Two molecules combine to form one molecule of cystin.

Cystin has the formula

$$\begin{array}{l} S-CH_2-CH\diagdown\overset{NH_2}{\underset{COOH}{}} \\ | \\ S-CH_2-CH\diagdown\overset{NH_2}{\underset{COOH}{}}. \end{array}$$
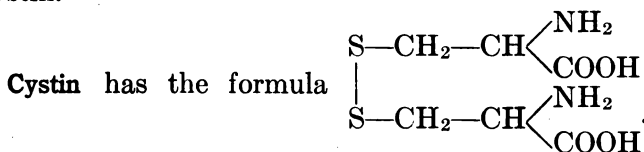
Cystein and cystin occur as decomposition products of proteins.

Cystin crystals may occur in pathological urine. Reduction of cystin gives cystein as its product.

Taurin is β-aminoethylsulphonic acid,

$$CH_2\diagup\overset{NH_2}{\underset{}{}}\!\!-CH_2-SO_3H.$$
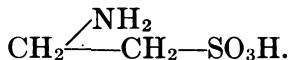
It is found in bile combined with cholic acid as taurocholic acid. It has been synthesized from β-hydroxyethylsulphonic acid (see p. 306), as indicated by the following equations:

$$CH_2(OH)\cdot CH_2\cdot SO_3H + 2PCl_5 =$$
$$= CH_2Cl\cdot CH_2SO_2Cl + 2POCl_3 + 2HCl.$$
<div align="center">(Chlorethylsulphon chloride)</div>

$$CH_2Cl\cdot CH_2\cdot SO_2Cl + H_2O = CH_2Cl\cdot CH_2SO_3H + HCl.$$
<div align="center">(Chlorethylsulphonic acid)</div>

$$CH_2Cl\cdot CH_2\cdot SO_3H + 2NH_3 =$$
$$= CH_2NH_2\cdot CH_2\cdot SO_3H + NH_4Cl.$$
<div align="center">(Taurin)</div>
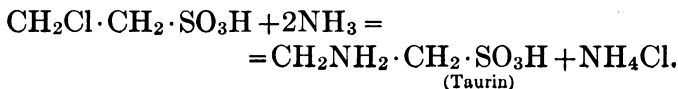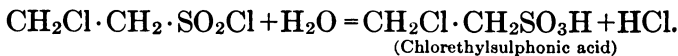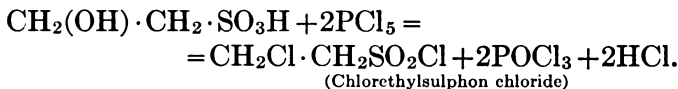
ACID AMIDES

The next group of amido compounds to be considered is that of the acid amides. Just as there are acid chlorides, e.g., acetyl chloride, $CH_3 \cdot COCl$, so there are acid amides, NH_2 occupying the position of Cl, as acetamide, $CH_3 \cdot CONH_2$.

Acid amides may be made in several ways:

(1) By treating an acid chloride with ammonia:

$$CH_3 \cdot CO\,Cl + H\,NH_2 = CH_3 \cdot CONH_2 + HCl.$$
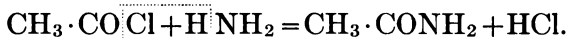
(2) By heating an acid in an atmosphere of ammonia while constantly bubbling dry ammonia gas into the acid:

$$CH_3 \cdot CO\,OH + H\,NH_2 = CH_3 \cdot CONH_2 + H_2O.$$
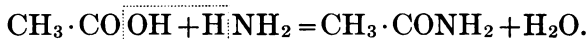
(3) By treating an ester with ammonia:

$$\begin{array}{l} COO \cdot C_2H_5 \\ | \qquad\quad + 2NH_4OH = \\ COO \cdot C_2H_5 \\ \text{(Diethyloxalate)} \end{array} \quad \begin{array}{l} CO \cdot NH_2 \\ | \qquad\quad + 2C_2H_5OH + 2H_2O. \\ CO \cdot NH_2 \\ \text{(Oxamide)} \end{array}$$
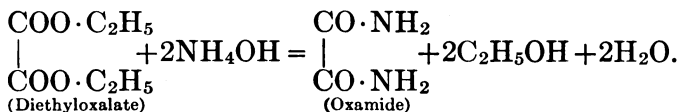
(4) By heating the ammonium salt of the acid, generally in a sealed tube (the process being anhydrolysis).

$$CH_3 \cdot COONH_4 = CH_3 \cdot CONH_2 + H_2O.$$
$$\text{(Ammonium acetate)} \qquad\quad \text{(Acetamide)}$$
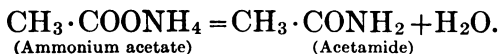
Acid amides are decomposed by the action of nitrous acid, nitrogen being liberated. Amides are hydrolyzed by water, the action being greatly accelerated by hydrogen ions. This can be taken

advantage of to determine hydrion concentration of solutions of different acids (p. 172). The simpler amides, as formamide, conduct electricity. Salts dissolved in these ionize somewhat.

Formamide, $H \cdot CONH_2$, is a liquid. The other acid amides are solid crystalline substances.

Acetamide, $CH_3 \cdot CONH_2$, is prepared by the fourth method given above (see exp.). It can also be prepared by the action of ammonium hydroxide on ethyl acetate. It forms colorless crystals, which melt at 82° and distill at 223°. It generally has a mouse-like odor, due to slight admixture of impurities. It can be purified by crystallization from chloroform. Heating with phosphorus pentoxide converts it into methyl cyanide (see p. 255).

EXPERIMENT. To 40 gm. of glacial acetic acid heated in an evaporating dish to 40–50° on a water bath, add powdered ammonium carbonate (about 55 gm.) while stirring, until a drop diluted with a few cubic centimeters of water shows a weak alkaline reaction to litmus. Now heat to 80–90° on a boiling water-bath until a drop diluted with water shows a slightly acid reaction. Pour the mass while hot into a Volhard tube or bomb-tube through a hot funnel (so as not to smear the walls of the tube). With a strip of filter-paper remove any of the substance that may be adhering to the upper eight inches of the tube.

Seal the tube carefully. The sealing of bomb-tubes requires practice. Experiment first with waste pieces of tubing. First cover the tube with soot in a smoky flame at the point

where it is to be sealed. Increase the heat gradually, then begin with a large blast flame. When the soot is burned off, decrease the size of the flame, increasing the force of the blast. Keep rotating the tube, and when it softens do not draw it out, but make the tube sink in by the force of the blast. In this way the thickness of the wall is preserved. When the caliber of the tube has become very small, the tube can be quickly drawn out and sealed off. A tapering tip is the best. Heat the tip in the flame until rounded. Keep the hot end of the tube in a cold smoky flame until a deposit of soot is obtained. Let it cool slowly.

Heat the tube in a bomb-furnace for five hours at 220–230°. Open the tube by making a scratch-mark with a file on the tip; wrap the tube in a heavy towel; put the tip into the blast-flame, when it will snap off. Sometimes there is a high pressure of gases in a bomb-tube, so that it may fly to pieces as soon as the pressure is suddenly relieved. Break off the end of the tube; remove the acetamide and transfer it to a distilling flask. Distill, reject the distillate coming over below 130°, then change to a wide tube (air-condenser) in the place of the Liebig condenser. Collect the fraction distilling between 180° and 230° in a beaker. Cool it with ice-water until crystals form; if necessary, scratch the wall of the beaker with the sharp end of a glass rod (see p. 8). Dry the crystals by pressing them on a porous plate.

An easier method of preparation of acetamide is as follows: Let a mixture of 50 gm. of ethyl acetate and 100 c.c. of concentrated ammonium hydroxide stand for one week. Distill as above.

Glycinamide, $NH_2 \cdot CH_2 \cdot CONH_2$, the acid amide

of glycocoll, is of interest in connection with the biuret test (p. 280).

Oxamide, $\begin{matrix} CONH_2 \\ | \\ CONH_2 \end{matrix}$ is prepared by the third method.

EXPERIMENT. Connect two flasks with a glass tube bent at a right angle at each end. In the second flask the tube is long enough to reach almost to the bottom. Into each flask put 50 c.c. of alcohol. Into the second flask put also 50 gm. of oxalic acid from which the water of crystallization has been driven off by heating in a oven at 100°. The first flask is supported on wire gauze, while the second is placed in an oil-bath. Place a thermometer in the oil. Connect the second flask with a condenser. Heat the oil-bath to 100°, then begin heating the flask containing only alcohol. While the alcohol-vapor is passing over, allow the temperature of the oil-bath to rise slowly to 125–130°. When most of the alcohol has disappeared from the first flask, disconnect this flask and remove the flame. Cool the second flask; the residue and the distillate both contain diethyl oxalate. Treat each with strong ammonium hydroxide. A white precipitate of oxamide is obtained. Filter and wash the precipitate thoroughly. Save a sample. Put some oxamide into a test-tube, add strong alkali, and boil, noting the evolution of ammonia. Take another portion in a test-tube, treat with cold NaOH, and add very dilute copper sulphate solution a drop at a time until a reddish or violet color appears (biuret reaction, see p. 282):

$$\begin{array}{c} COOH \\ | \\ COOH \end{array} +2C_2H_5OH = \begin{array}{c} COOC_2H_5 \\ | \\ COOC_2H_5 \end{array} +2H_2O,$$

$$\begin{array}{c} COOC_2H_5 \\ | \\ COOC_2H_5 \end{array} +2NH_4OH = \begin{array}{c} CONH_2 \\ | \\ CONH_2 \end{array} +2C_2H_5OH +2H_2O.$$
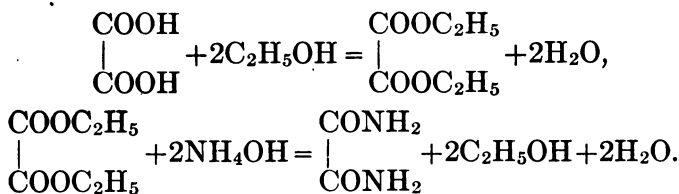
Asparagin is the mono-amide of aspartic acid, its
formula being $\begin{array}{c} CH_2—CONH_2 \\ | \\ CH(NH_2)—COOH \end{array}$. It occurs as both
the dextro and the lævo variety; the commoner kind
(lævo) is tasteless while the dextro tastes sweet. It
is found in many vegetables, particularly asparagus,
peas, beans, beets, and wheat.

Glutamin is the mono-amide of glutaminic acid,
having the formula

$$CH_2 \Big\langle \begin{array}{c} CH \diagdown \begin{array}{c} NH_2 \\ \diagup \\ \diagdown COOH \end{array} \\ CH_2——CONH_2 \end{array}.$$
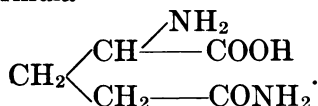
The most important acid amide of all is *carbamide*.
Urea (carbamide), $NH_2 \cdot CONH_2$, is the acid amide
of carbamic acid. It is also the diamide of carbonic
acid:

$$O{=}C \Big\langle \begin{array}{c} OH \\ OH \end{array} \quad \rightarrow \quad O{=}C \Big\langle \begin{array}{c} NH_2 \\ NH_2 \end{array}.$$
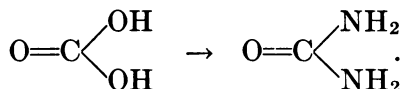
The relationship of urea to carbamic acid is shown by
its preparation from ammonium carbamate by heat-
ing in a sealed tube at a temperature of 135°:

$$O{=}C \Big\langle \begin{array}{c} NH_2 \\ ONH_4 \end{array} = O{=}C \Big\langle \begin{array}{c} NH_2 \\ NH_2 \end{array} +H_2O.$$

(Ammonium carbamate)   (Urea)
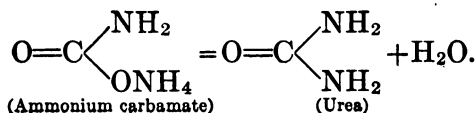
Its relationship to carbonic acid is evidenced by its production from carbonyl chloride and ammonia:

$$O{=}C\underset{\underset{\text{(Carbonyl chloride)}}{}}{\overset{Cl}{\diagdown_{Cl}}} + 2NH_3 = O{=}C\overset{NH_2}{\diagdown_{NH_2}} + 2HCl,$$
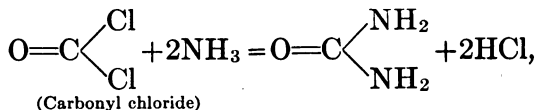
also from ethyl carbonate and ammonia:

$$O{=}C\underset{\underset{\text{(Ethyl carbonate)}}{}}{\overset{OC_2H_5}{\diagdown_{OC_2H_5}}} + 2NH_3 = O{=}C\overset{NH_2}{\diagdown_{NH_2}} + 2C_2H_5OH.$$
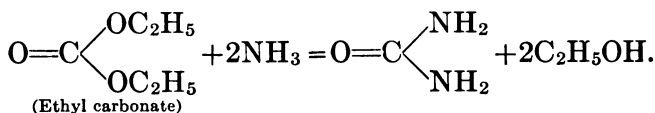
That it bears a relationship to cyanic acid, HCNO, and its amide cyanamide, $N{\equiv}C{-}NH_2$, is proved by its preparation from both of these. By hydrolysis cyanamide is converted into urea.

$$CN \cdot NH_2 + H_2O = O{=}C\overset{NH_2}{\diagdown_{NH_2}}.$$
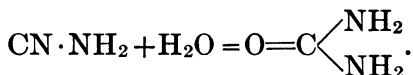
Mere evaporation of a solution of ammonium iso-cyanate is sufficient to convert the salt into urea (see exp.); this involves intramolecular change:

$$C\underset{\underset{\text{(Ammonium iso-cyanate)}}{}}{\overset{N{-}NH_4}{\diagup^{\diagup}}}{\diagdown_O} \rightleftarrows O{=}C\overset{NH_2}{\diagdown_{NH_2}}.$$
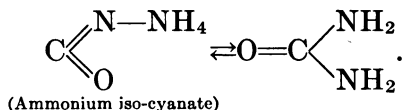
The change of cyanate to urea is a reversible reaction. A decinormal solution of ammonium isocyanate changes on standing until it reaches an equilibrium point, at which 95% of the cyanate has become urea. On the other hand a urea solution changes until it reaches the same equilibrium point, i.e., when 5% has been changed to cyanate.

Physiologists have advocated three main hypotheses as to the origin of urea in the animal body, corresponding to the above methods of synthesis, namely, that it is derived from (1) ammonium carbonate, (2) from ammonium carbamate, or (3) from ammonium cyanate. It seems most likely that the derivation of urea is as follows: Ammonia enters the blood of the portal venous system mainly as the result of fermentative and bacterial hydrolysis of the proteins of the food. In the presence of the large amount of carbonic acid in the blood, ammonium carbonate and carbamate are formed in accordance with the laws of mass action; both of these are then converted in the liver into urea by a process of anhydrolysis:

$$O{=}C\underset{\text{ONH}_4}{\overset{\text{ONH}_4}{{<}}}\ ({-}H_2O) \rightarrow O{=}C\underset{\text{ONH}_4}{\overset{\text{NH}_2}{{<}}}\ ({-}H_2O) \rightarrow O{=}C\underset{\text{NH}_2}{\overset{\text{NH}_2}{{<}}}.$$

(Ammonium carbonate)　　　(Ammonium carbamate)　　　(Urea)
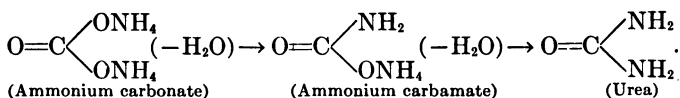
A certain portion of the amino acids which are not used by the tissues for synthesis of proteins probably become a source of urea in the following manner: The monoamino-acids may be acted on by ferments (deamidization) so that ammonia is split off (the presence of ferments possessing that power has been demonstrated in many organs), and then the ammonia becomes ammonium carbonate and carbamate, and is changed to urea. Arginin may be hydrolyzed by a ferment, arginase, which is present in many organs, urea being one of the products (see p. 270).

Urine contains a large quantity of urea, 20 to 30 gm. of urea being excreted in the urine of man in twenty-four hours on a mixed diet. It crystallizes in colorless needles or rhombic prisms. It melts at 132° (corrected melting-point is 132.6°). It is very soluble in water and hot alcohol, less soluble in cold alcohol.

Bacterial fermentation of urine converts urea into

ammonium carbonate, hence the ammoniacal odor
of decomposed urine.   An enzyme urease, also boil-
ing with alkalies or acids or superheating with water,
can accomplish a similar hydrolysis:

$$CO{\Large\diagup}^{NH_2}_{\diagdown NH_2} + \left\{{H_2O \atop H_2O}\ {NH_4 \atop NH_4}\right\} = {\diagup \atop \diagdown}CO_3.$$
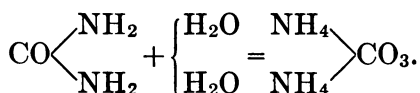
Of course by the action of alkali NH_3 is liberated
from the $(NH_4)_2CO_3$, while by the action of acid
CO_2 is liberated.   This reaction is the ·basis of
Bunsen's and Folin's methods of quantitative
estimation of urea.   The most satisfactory method
of estimation is that in which urease is used.   Sodium
hypochlorite and hypobromite decompose urea,
liberating nitrogen:

$$CO(NH_2)_2 + 3NaBrO = N_2 + 3NaBr + CO_2 + 2H_2O.$$

This reaction is made use of in the usual clinical
method for urea estimation.   Nitrous acid also
liberates free nitrogen (see p. 260):

$$CO(NH_2)_2 + 2HNO_2 = 2N_2 + CO_2 + 3H_2O.$$
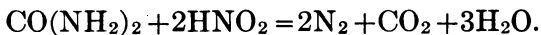
When heated strongly, urea yields, among other
substances, *biuret*, $NH_2 \cdot CO \cdot NH \cdot CO \cdot NH_2$, which
gives a reddish-violet color reaction with caustic
soda or potash containing a trace of copper sulphate
(*biuret reaction*).   This reaction is given by oxam-
ide, in fact by all substances containing two groups
of $CO \cdot NH_2$ linked together either directly (as in
oxamide) or through a single nitrogen (as in biuret)

or carbon atom $\left(\text{as in } CH_2, \begin{array}{c} \diagup CONH_2 \\ \diagdown CONH_2 \end{array}\right)$ or through one

or more CO·NH groups $\left(\text{as in } \begin{array}{c} CO·CONH_2 \\ | \\ NH·CONH_2 \end{array}\right)$.

$CH_2·NH_2$ may take the place of one of the $CONH_2$ groups, as in glycinamide (p. 275). All proteins give the biuret reaction (p. 296).

Urea acts as a weak monacid base toward certain acids, the nitrate and oxalate being particularly characteristic salts. In the common method for extraction of urea from urine, it is precipitated from the urine (previously concentrated by evaporation) by treatment with nitric acid. The urea is liberated from the nitrate by treating the latter with barium carbonate.

EXPERIMENT. (1) Synthesize urea as follows: Heat 25 gm. of powdered potassium cyanide in an iron dish until it begins to fuse (do this under a hood), then add gradually 70 gm. of red oxide of lead a little at a time, stirring in well. When the frothing ceases pour on an iron plate. When it is cool powder the mass, separating out the metallic lead. Digest this crude cyanate for an hour with 100 c.c. of cool water. Filter through a plaited filter into an evaporating dish. Add to the filtrate 25 gm. of ammonium sulphate that has been dissolved in a small quantity of water. Evaporate to dryness on a water-bath, stirring frequently to prevent crusting over. Cool the residue and powder it in a mortar. Transfer it to a small flask, add 100 c.c. of

alcohol, attach to a reflux condenser, and boil for fifteen minutes. Filter off the hot alcohol into an evaporating dish. Use 25 c.c. more of alcohol in a similar manner. Evaporate the alcohol on a water-bath to very small bulk. When it is cool, urea crystals should form. Test a few crystals or some of the solution as below.

(2) *Urea tests.* (a) Put one drop of concentrated urea solution on a glass slide; mix with it one drop of colorless concentrated nitric acid. Place a cover-glass over the crystals and examine under a micro-scope.

(b) In a test-tube melt some dry urea, then heat gently for a minute while gas (NH_3) is being evolved. Cool; add 1 c.c. of water, then an equal amount of 20% NaOH solution, and finally a small drop of very dilute copper sulphate solution. A violet or pinkish color is obtained. This is called the biuret reaction (see above):

$$OC \Big\langle \begin{matrix} NH_2 \\ + \\ NH_2 \end{matrix} \quad \begin{matrix} NH_2 \\ \\ H\,NH \end{matrix} \Big\rangle CO =$$
$$\text{(Urea)} \qquad \text{(Urea)}$$

$$= NH_2-CO-NH-CO-NH_2 + NH_3.$$
$$\text{(Biuret)}$$
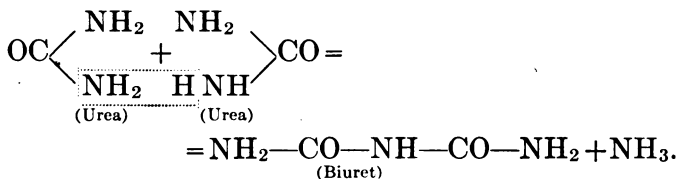
If the heating has been continued beyond a certain point, an insoluble compound, *cyanuric acid*, $(HCNO)_3$, is formed; this results from the combination of one molecule of biuret with one of urea, $2NH_3$ being eliminated.

Veronal is a urea derivative, being diethylmalonyl-urea or diethylbarbituric acid,

$$C_2H_5 \diagdown \atop C_2H_5 \diagup C \diagup{CO-NH} \atop \diagdown{CO-NH} \diagdown CO.$$
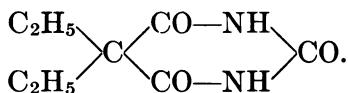
This is used as a hypnotic. The sodium salt of veronal is also used for the same purpose.

Another hypnotic related to urea is hedonal, which is really a carbamate similar to urethane. **Hedonal** is methylpropylcarbinolurethane:

$$CO \diagup{NH_2} \atop \diagdown{O-CH} \diagup{CH_3} \atop \diagdown{C_3H_7} .$$
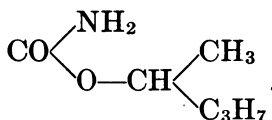
Bromural is another hypnotic, derived from urea. It is monobrom-iso-valeryl-urea,

$$CH_3 \cdot CH \cdot CHBr \cdot CO-NH \cdot CO \cdot NH_2.$$
$$| \atop CH_3$$
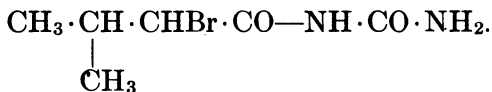
Neuronal is a hypnotic, having a somewhat similar structure, $CBr(C_2H_5)_2CONH_2$.

ACID IMIDES. COMPLEX AMINO AND IMIDO COMPOUNDS, INCLUDING POLYPEPTIDES

ACID IMIDES

THESE contain the group NH, illustrated by succinimide, $\begin{array}{c} CH_2-CO \\ | \qquad\qquad >NH. \\ CH_2-CO \end{array}$ They are formed from acid amides by loss of ammonia, the amide of a dibasic acid being necessary:

$$\begin{array}{ccc} CH_2 \cdot CONH_2 & CH_2 \cdot CO \\ | & = | \qquad\qquad >NH + NH_3. \\ CH_2 \cdot CONH_2 & CH_2 \cdot CO \\ \text{(Succinamide)} & \text{(Succinimide)} \end{array}$$
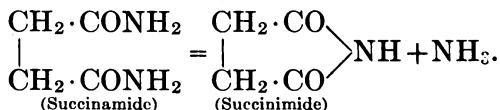
OTHER AMINO AND IMIDO COMPOUNDS

Guanidin, $NH = C \begin{array}{c} NH_2 \\ NH_2 \end{array}$, may be considered as an imido derivative of urea, and might be called imido-carbamide. It can be synthesized from cyanamide and ammonia:

$$\underset{\text{(Cyanamide)}}{CN \cdot NH_2} + NH_3 = \underset{\text{(Guanidin)}}{NH = C \begin{array}{c} NH_2 \\ NH_2 \end{array}}.$$
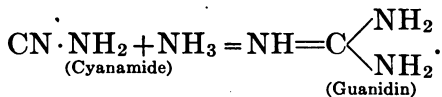
It is more strongly basic than urea, undoubtedly because of the changing of the carbonyl linking of

urea for the naturally basic NH group. *Methyl-guanidin*, $HN{=}C\diagup^{NH_2}_{\diagdown NH(CH_3)}$, occurs as a ptomaine (p. 263). Of more importance are the derivatives of guanidin, namely, *creatin* and *creatinin*.

Creatin is methylguanidinacetic acid,

$$NH{=}C\diagup^{NH_2}{-}{-}N\diagup^{CH_3}_{CH_2\cdot COOH.}$$
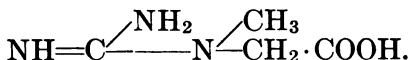
Creatin can be synthesized from cyanamide and sarcosin:

$$CN\cdot NH_2 + CH_2\diagup^{NH{-}CH_3}_{{-}{-}COOH} =$$
(Cyanamide)   (Sarcosin)

$$= NH{=}C\diagdown^{NH_2}_{N\diagup^{CH_3}_{\diagdown CH_2{-}COOH.}}$$
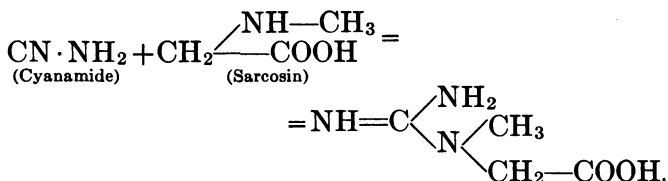
Creatin is present in considerable quantity in muscular tissue. It can be obtained from meat extract. Heating with baryta water converts it into urea, sarcosin, and some other substances. Heating with dilute acid changes it to creatinin. As a rule the appearance of creatin in the urine is pathological, though it is reported as occurring normally in the urine of children.

Creatinin is creatin less a molecule of water:

$$NH{=}C\diagdown^{NH{-}{-}CO}_{N\diagup^{CH_3\,|}_{\diagdown {-}{-}CH_2}} .$$
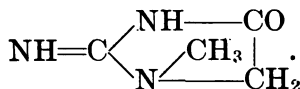
This is always present in normal human urine, about 1.5 gm. being excreted in twenty-four hours. The

amount excreted when creatinin-containing food (flesh) is debarred from the diet seems to be a fixed quantity for each individual, no matter how much the total nitrogen content of the urine may vary.

Creatinin crystallizes in monoclinic prisms. It is readily soluble. In alkaline solution it becomes converted, at least in part, into creatin. It reduces Fehling's and other alkaline copper solutions, but it holds cuprous oxide in solution; on account of these properties it may mislead in testing for sugar if the urine is concentrated. An alkaline bismuth solution, however, is not reduced by creatinin. Creatinin is precipitated by mercuric chloride and by zinc chloride, these reagents entering into chemical union with the creatinin.

Uric acid is a derivative of urea. In uric acid two molecules of urea unite by linking to an intermediate carbon chain, each NH_2 group losing one hydrogen atom and becoming NH in order to effect the union:

$$O = C \Big\langle \begin{matrix} NH- \\ NH- \end{matrix} \left\{ \begin{matrix} C \\ | \\ C \\ | \\ C \end{matrix} \right\} \begin{matrix} -HN \\ -HN \end{matrix} \Big\rangle C = O.$$
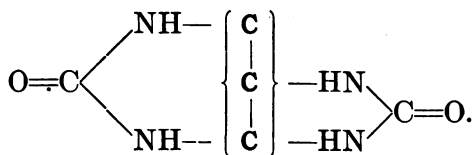
This is the skeleton of the uric acid formula. The presence of two urea molecules and of a carbon chain is shown by the nature of the decomposition products of uric acid resulting from oxidation and hydrolysis:

$$
\begin{array}{l}
\text{NH—CO} \\
\text{I. CO} \quad \text{C—NH} \\
\qquad \qquad \qquad \text{>CO} + H_2O + O = \\
\text{NH—C—NH} \\
\end{array}
$$

(Uric acid) [treated with cold HNO₃]

$$
\begin{array}{l}
\text{NH—CO} \\
= \text{CO} \quad \text{CO} + \quad \text{NH}_2 \\
\qquad \qquad \qquad \qquad \text{>CO.} \\
\text{NH—CO} \qquad \text{NH}_2 \\
\end{array}
$$

(Alloxan)   (Urea)

$$
\begin{array}{lll}
\text{NH—CO} & & \text{NH—CO} \\
\text{II.} \quad \text{CO} \quad \text{CO} + O & = & \text{CO} \quad | \quad + CO_2. \\
\text{NH—CO} & & \text{NH—CO} \\
\end{array}
$$

(Alloxan) [treated with   (Parabanic acid)
warm HNO₃]

$$
\begin{array}{lll}
\text{NH—CO} & & \text{NH—CO} \\
\text{III.} \quad \text{CO} \quad | \quad + H_2O & = & \text{CO} \quad | \\
\text{NH—CO} & & \text{NH}_2 \quad \text{COOH.} \\
\end{array}
$$

(Parabanic acid) [treated with alkali]   (Oxaluric acid)

$$
\begin{array}{lll}
\text{NH—CO} & & \\
\text{IV. CO} \quad | \quad + H_2O & = & \text{CO} < \begin{array}{l} \text{NH}_2 \\ \text{NH}_2 \end{array} + \begin{array}{l} \text{COOH} \\ | \\ \text{COOH.} \end{array} \\
\text{NH}_2 \quad \text{COOH} & & \\
\end{array}
$$

(Oxaluric acid) [boiled with water]   (Urea)   (Oxalic acid)

The presence of the pyrimidin ring, $\begin{array}{l} \text{N—C} \\ | \quad | \\ \text{C} \quad \text{C} \\ | \quad | \\ \text{N—C} \end{array}$, in uric

acid is shown by *Traube's synthesis*, which is as follows: Cyanacetic acid and urea are treated with

$POCl_3$; the latter removes hydroxyl from the acid, and urea takes its place to form cyanacetyl urea:

(1) $\underset{\text{(Cyanacetic acid)}}{CH_2 \cdot COOH} + \underset{\text{(Urea)}}{NH_2 \cdot CO \cdot NH_2} =$

$$\begin{array}{c} CH_2 - CN \\ | \\ = CO \qquad\qquad + H_2O. \\ | \\ NH - C - NH_2 \\ \parallel \\ O \end{array}$$
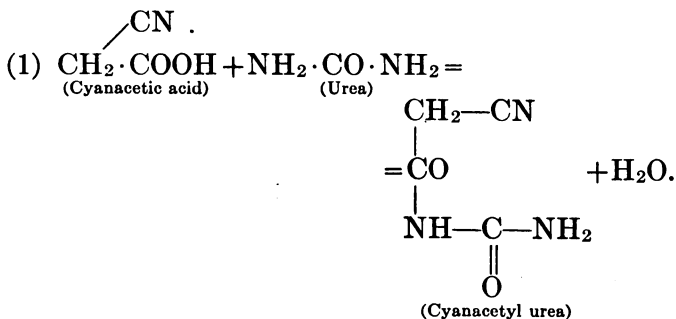
(Cyanacetyl urea)

Treating cyanacetyl urea with alkali causes a shifting within the molecule, resulting in the formation of monoamino-dioxy-pyrimidin,

$$\begin{array}{c} HN - C = O \\ | \qquad | \\ (2)\quad O = C \quad CH_2 \quad . \\ | \qquad | \\ HN - C = NH \end{array}$$
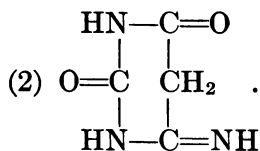
This is treated with HNO_2, giving

$$\begin{array}{c} HN - C = O \\ | \qquad | \\ (3)\quad O = C \quad C = NOH. \\ | \qquad | \\ HN - C = NH \end{array}$$
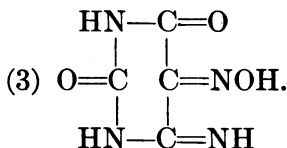
By reduction this becomes

$$\begin{array}{c} HN - C = O \\ | \qquad | \\ O = C \quad C - NH_2, \\ | \qquad \parallel \\ HN - C - NH_2. \end{array}$$
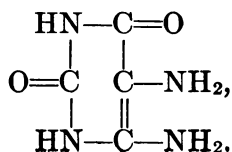
which when acted on by $CClOOC_2H_5 + KOH$ gives
<div align="center">(Ethyl chlorcarbonate)</div>

$$(4) \quad \begin{array}{ccc} HN & - & C=O \\ | & & | \\ O=C & & C-NK-COOC_2H_5, \\ | & & \| \\ HN & - & C-NH_2 \end{array}$$
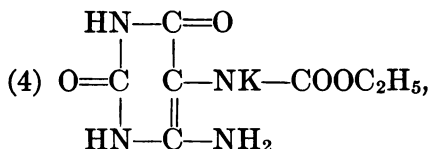
a pyrimidin derivative of urethane. By heating this potassium salt (dry) to 150°, then later to 180°– 190°, alcohol is split off, leaving uric acid (as potassium urate):

$$(5) \quad \begin{array}{ccc} HN & - & CO \\ | & & | \\ O=C & & C-NK \\ | & & \| \quad \diagdown \\ HN & - & C-NH \quad \diagup \end{array} C=O + C_2H_5OH.$$
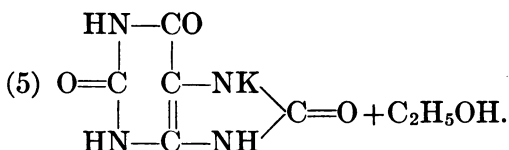
This synthesis conclusively proves the structure of uric acid.

Another interesting synthesis, because it is analogous to one which may occur in the animal body, (at least in birds), is effected by heating together urea and trichlorlactamide:

$$\begin{array}{ccc} (H)-NH & CO-(NH_2) & NH \diagdown (H) \\ \diagup & | & \diagdown CO \\ CO & C-(HOH) & NH \diagup (H) \\ \diagdown & | & \\ (H)-NH & C-(Cl_3) & \\ \text{(Urea)} & \text{(Trichlorlactamide)} & \text{(Urea)} \end{array}$$
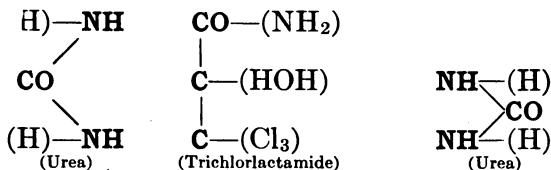
The groups in parenthesis do not enter into the uric acid molecule, but unite to form NH_4Cl, HCl, and H_2O.

Dialuric acid, $CO\underset{NH-CO}{\overset{NH-CO}{<}}>CHOH$, appears in
the case of birds to be an intermediate body in the
synthesis of uric acid by the liver. It is formed by
the combination of urea with tartronic acid (p. 221).
By the addition of another urea molecule to this,
u.ic acid is produced:

$$CO\underset{NH-C(O)}{\overset{NH-CO}{<}}\quad\begin{array}{c}|\\ C-(HOH)\\ |\end{array}+\underset{NH-(H)}{\overset{NH-(H)}{>}}CO=$$

(Dialuric acid)   (Urea)

$$\begin{array}{c}NH-CO\\ |\qquad|\\ =CO\quad C-NH\\ |\qquad\|\\ NH-C-NH\end{array}>CO+2H_2O.$$
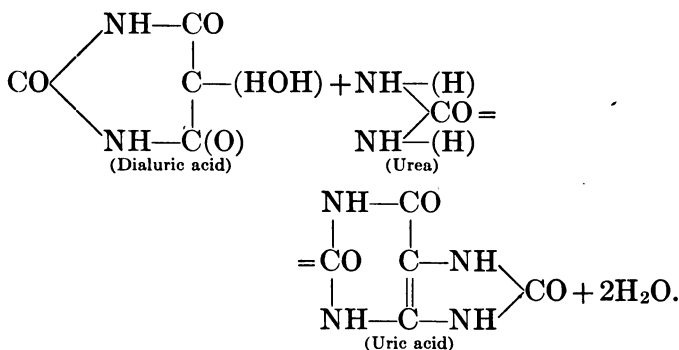
(Uric acid)

Analogous synthesis in the case of mammals
has not been proved.

Uric acid has been synthesized by heating together
glycocoll and urea. On the other hand, uric acid when
heated in a sealed tube with HCl yields glycocoll.

Tautomerism of uric acid. Uric acid exists not
only in the form corresponding to the above formula
(the *lactam* state) but also in another form (the *lactim*
state), in which the three O atoms are in hydroxyls:

$$\begin{array}{c}N=C-OH\\ |\qquad|\\ HO-C\quad C-NH\\ \|\qquad\|\\ N-C-N\end{array}>C-OH.$$
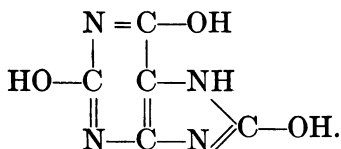
The lactam form is less stable. It is stated that in the urine uric acid is in the lactim form.

. Uric acid acts as a weak dibasic acid, forming urates. It does not, however, play any part in the acid reaction of urine. It is believed to exist mainly in the form of monosodium urate in both the blood and the urine. In very acid urine there is some free uric acid. It often crystallizes out as a reddish deposit from strongly acid urine. About 0.7 gm. is excreted daily by man. Pure uric acid is a color-less crystalline powder. It is almost insoluble in cold water and alcohol. Uric acid reduces Fehling's solu-tion, but does not reduce an alkaline bismuth solution.

EXPERIMENT. (1) Add 5 c.c. of 20% HNO_3 to a little uric acid in an evaporating-dish; evaporate to dryness on a water-bath. Alloxantin is formed. To the residue add baryta water; a blue color appears.

(2) Repeat the above, but instead of using baryta expose the residue to fumes of ammonia. A red color is obtained, due to murexide. This test is called the murexide test. If much ammonia is present in the air, the residue will be reddish because of the ammonia taken up. Ammonia converts alloxantin into purpuric acid,

$$
\begin{array}{ccccccc}
\text{HN--CO} & \text{NH} & \text{OC--NH} \\
| \quad | & \diagup\diagdown & | \quad | \\
\text{OC} \quad \text{C} & \diagup \quad \diagdown & \text{C} \quad \text{CO.} \\
| \quad | & & | \quad | \\
\text{HN--CO} & & \text{OC--NH}
\end{array}
$$
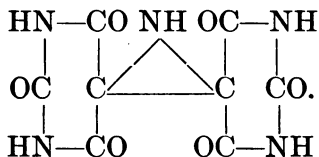
Murexide is the ammonium salt of this acid.

Allantoin, $CO \underset{\diagdown NH-CO\ NH_2}{\overset{\diagup NH-CH-NH}{|}} CO$, results from
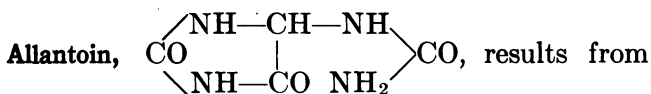
careful oxidation of uric acid by potassium permanganate. It occurs in the urine of calves and dogs, and at times in human urine.

Purin bodies. Uric acid and all the *purin bodies* contain the double-ring nucleus

$$
\begin{array}{ccc}
N-C & & \\
| \quad | & & \\
C \quad C-N & & \\
| \quad | & & \diagdown C. \\
N-C-N & &
\end{array}
$$
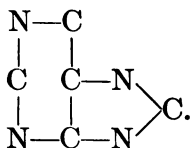
The main ring is the pyrimidin ring; the purin nucleus, therefore, is pyrimidin with urea attached as a secondary ring.[1] The relationship of the purin bodies is shown below:

Purin itself has an H atom at each of the positions numbered 2, 6, 7, and 8. It can be prepared from uric acid.

$$
\begin{array}{lll}
(1)\ N-C\ (6) & \\
(2)\ \ C\ \ \ \ C\ (5)-N(7) & \\
(3)\ \ N-C\ (4)-N(9) & \diagdown C(8) \\
\qquad\text{(Purin nucleus)}
\end{array}
\qquad
\begin{array}{ll}
NH-CO & \\
CH\ \ \ C-NH & \\
N\ \ \ \ \ C\ \ \ \ N & \diagdown CH \\
\text{(Hypoxanthin)} \\
\text{(6-oxypurin)}
\end{array}
$$
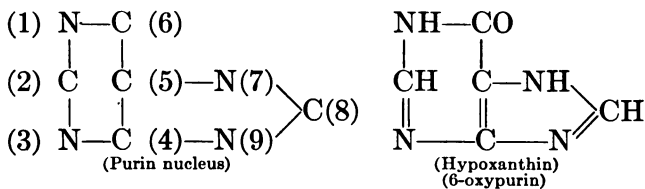
[1] The purins and pyrimidins are heterocyclic. We prefer to discuss the chemistry of them at this point because of their relationship to urea and proteins. They show no similarity to the typical heterocyclic compounds.

NH—CO
| |
CO C—NH
| >CH
NH—C——N
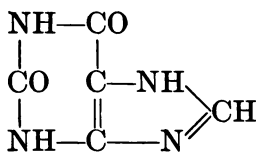
(Xanthin
(2, 6-dioxypurin)

NH—CO
| |
CO C—N(CH₃)
| || >CH
(CH₃)N——C—N
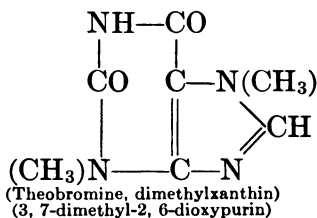
(Theobromine, dimethylxanthin)
(3, 7-dimethyl-2, 6-dioxypurin)

(CH₃)N—CO
| |
CO C—N<(CH₃)
| || >CH
(CH₃)N—C—N
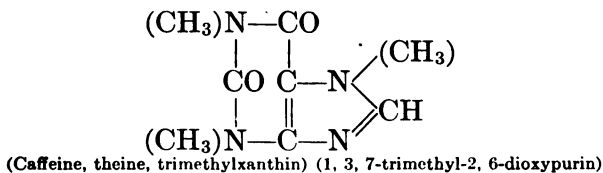
(Caffeine, theine, trimethylxanthin) (1, 3, 7-trimethyl-2, 6-dioxypurin)

NH—CO
| |
CO C—NH
| || >CO
NH—C—NH
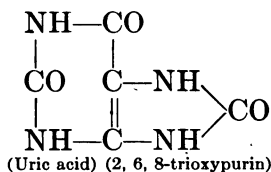
(Uric acid) (2, 6, 8-trioxypurin)

N══C—NH₂
| |
CH C—NH
|| || >CH
N——C—N
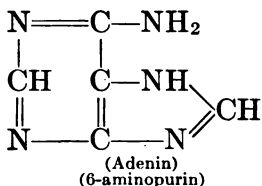
(Adenin)
(6-aminopurin)

NH—CO
| |
H₂N—C C—NH
|| || >CH
N——C——N
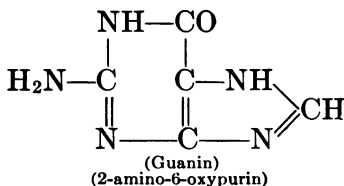
(Guanin)
(2-amino-6-oxypurin)

There are a number of methyl purins besides caffeine and theobromine, as, 1 methyl xanthin, 7 methyl xanthin (heteroxanthin), 1, 7 dimethyl xanthin (paraxanthin), and 7 methyl guanin.

The purins are also called *alloxuric, xanthin,* or *nuclein* bodies.

Caffeine and theobromine when taken as food are excreted in the urine partly unchanged and partly

as monomethyl and dimethyl xanthins. Only 35–40% of caffeine and theobromine appear in the urine as purine bodies. A number of investigators agree in the assertion that tea and coffee do not increase uric acid excretion. The other purins are excreted mainly as uric acid. It is believed by some that on a diet that is free of purin bodies, the amount of purins excreted daily is a fixed quantity for each individual (cf. creatinin). In the case of mammals the purin bodies have their origin in the nucleic acids of nucleoproteins, both those of the tissues and those of the food.

Some of the purins, mainly xanthin and hypoxanthin, are found in muscle, and therefore in meat extract. *Beef tea* or a solution o *meat extract* contains as its organic constituents chiefly creatin, purin bodies, and sarcolactic acid.

Theobromine (dimethylxanthin) is found in chocolate and cocoa. It is called an alkaloid (see p. 425).

Caffeine or **theine** (trimethylxanthin) is the alkaloidal principle in tea and coffee   Both theobromine and caffeine are used as medicines.

EXPERIMENT. Try the murexide test (see p. 291) on a little caffeine. Repeat, substituting bromine water for HNO_3.

Pyrimidin derivatives. These are derived from nucleic acid by hydrolysis whether by the action of acids or by post-mortem autolysis of animal tissue.

The most important are uracil, thymin and cytosin.

Uracil is 2, 6 dioxypyrimidin,

$$
\begin{array}{ccc}
NH & - & C = O \\
| & & | \\
O = C & & CH. \\
| & & \| \\
NH & - & CH
\end{array}
$$
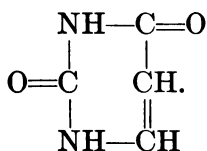
Thymin is 5 methyl 2, 6 dioxypyrimidin,

$$
\begin{array}{ccc}
NH & - & C = O \\
| & & | \\
O = C & & C - CH_3. \\
| & & \| \\
NH & - & CH
\end{array}
$$
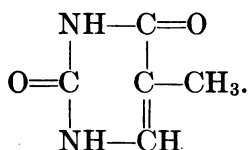
Cytosin is 6 amino 2 oxypyrimidin,

$$
\begin{array}{ccc}
N & = & C - NH_2 \\
| & & | \\
O = C & & CH \\
| & & \| \\
NH & - & CH
\end{array}
$$
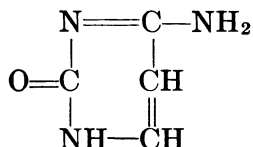
As an illustration of a **nucleic acid** might be mentioned one which has been obtained from a nucleoprotein of the thymus gland. It is believed to consist of the linking together of four hexose (p. 231) and four phosphoric acid molecules with one molecule each of guanin, adenin, thymin and cytosin. To it has been assigned the formula:

$$C_{43}H_{57}N_{15}O_{30}P_4.$$

Leucomaine is a term applied to basic substances found in living animal tissues. The purin bodies and the creatinin group of compounds are the chief leucomaines.

DIPEPTIDES AND POLYPEPTIDES

Because of the fact that the decomposition products of proteins include amino-acids (as alanin, glycocoll, leucin, tyrosin, aspartic acid, etc.) and the hexone bases, it has been proposed to explain the structure of the protein molecule as a chaining together of these amino bodies by means of the removal of OH of a carboxyl group of the one amino body and an H of the amino group of another (cf. formation of acid amides), thus:

$$NH_2 \cdot CH_2 \cdot CO \overset{\displaystyle /\overline{OH \quad H}}{\underline{\hspace{3em}}} NH \cdot CH_2 \cdot COOH;$$
(Glycylglycin)

or a more complicated chain, as:

$$-NH \cdot CH \cdot CO - NH \cdot CH \cdot CO - NH \cdot CH \cdot CO - NH -$$
$$\underset{\text{(Leucin)}}{C_4H_9} \qquad \underset{\text{(Aspartic acid)}}{CH_2 \cdot COOH} \quad \underset{\text{(Lysin)}}{C_3H_6 \cdot CH_2 \cdot NH_2}$$
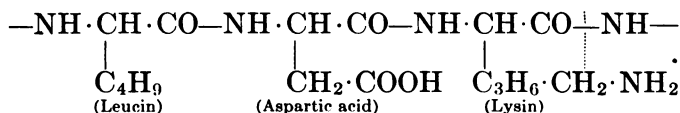
Of course the above is supposed to be only a part of the formula.

This theory of the constitution of protein molecules gives the best explanation of the universality of the biuret test as applied to proteins (see p. 281) the test being due to the many CONH groups.

On the basis of this hypothesis the problem of the synthesis of protein is now being vigorously attacked. Compounds have been synthesized in which two, three, and even up to eighteen molecules have been made to combine in this manner; these synthetic bodies are called peptides.

If two molecules have united, the compound is a dipeptide; for example, glycylglycin,

$$NH_2 \cdot CH_2 \cdot CO—NH \cdot CH_2 \cdot COOH.$$

Polypeptides are built up from more than two molecules; they include tripeptides (as diglycylglycin,

$$NH_2 \cdot CH_2 \cdot CO—NH \cdot CH_2CO—NH \cdot CH_2 \cdot COOH),$$
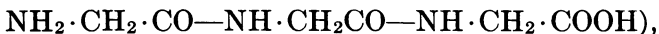
tetrapeptides, pentapeptides, hexapeptides, etc.

A polypeptide composed of three leucin and fifteen glycocoll molecules has been synthesized, the formula being $C_{48}H_{80}O_{19}N_{18}$ and the molecular weight 1213.

Certain polypeptides, identical with those produced synthetically, have been obtained by partial hydrolysis of proteins. The more complex polypeptides show certain resemblances to peptones in their actions. They taste bitter. They are precipitated by the same reagents, and give the biuret test. Those that are composed of amino acids of the same optical activity as those occurring in proteins are hydrolyzed by trypsin. Their solutions are colloidal.

E. Fischer, who is doing such brilliant work in this line of synthesis, is inclined to doubt whether this comparatively simple method of linking is the only kind of linking existing in protein molecules.

PROTEINS

Proteins are complex nitrogenous compounds that yield on complete hydrolysis mainly amino acids, hexone bases (p. 270), and ammonia. They vary

widely in the proportion of the different amino acids
and bases contained in their molecules; e.g., hæmo-
globin has not less than 20% of leucin, but gelatin
only about 2%; on the other hand there is 16.5 per
cent of glycocoll in gelatin and none in hæmoglobin.
Gelatin has very little of aromatic amino acids.
Tryptophan seems to be the amino acid of proteins
which is most essential to proper nourishment.
Most proteins contain S (cystin), some P. Since
they form colloidal solutions, molecular weight
determination has not been successful. The lowest
possible molecular weight of hæmoglobin is over
16,000, calculating on the basis of the percentage
composition, and supposing that there is one atom
of iron in the molecule; this corresponds to the
formula:

$$C_{758}H_{1203}O_{218}N_{195}FeS_3$$
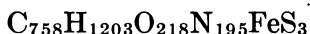
The most important classes of proteins are pro-
tamines, histones, albumins, globulins, phospho-
proteins, scleroproteins, compound proteins (chro-
moproteins, glucoproteins and nucleoproteins),
derived proteins (coagulated proteins, acid and
alkali metaproteins, proteoses and peptones), and
certain classes of vegetable proteins called glutelins
and prolamines (or gliadins).

Iodothyrin (thyroiodin) is the iodin-containing
portion of the compound protein, thyreoglobulin,
present in thyroid tissue.

Oxyproteic acid, $C_{43}H_{82}N_{14}O_{31}S$, is a derivative of
protein. It is found in the urine, and may be greatly
increased in some pathological conditions.

CHAPTER XXI

UNSATURATED HYDROCARBONS AND THEIR DERIVATIVES

THE most important unsaturated hydrocarbons are the *ethylenes and acetylenes*. Their unsaturation consists in having two or three bonds or linkings between one or more pairs of carbon atoms, thus:

$$C{=}C, \ C{\equiv}C, \ C{=}C{-}C{=}C, \ C{=}C{=}C, \text{ etc.}$$
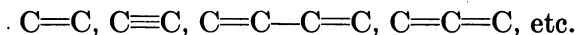
The unsaturation is undoubtedly not of so simple a nature as is indicated by the double and triple bond. Unsaturated substances of this nature readily form addition compounds, as with iodine and bromine. This fact is taken advantage of in analysis of fats and oils, the estimation of the oleic and other unsaturated acids being made by the use of an iodine solution (see p. 206).

Another illustration of the formation of addition compounds is the production of ethylene bromide, $C_2H_4 + Br_2 = C_2H_4Br_2$. Halogen acids (HBr, HI) are added to these hydrocarbons in similar manner: $C_2H_4 + HBr = C_2H_5Br$. The addition compound is, of course, saturated.

That the place of double linking is a weak point in the chain is shown by the fact that vigorous oxidation results in rupture of the C chain at this point.

ETHYLENES

Ethylenes or olefins, C_nH_{2n}, form an homologous series.

Ethylene (ethene, olefiant gas), $CH_2{=}CH_2$, is the only member of importance, and is contained in coal gas (about 2%). It is colorless and burns with a yellow flame. Ethylene forms an explosive mixture with oxygen. It is obtained by decomposition of ethyl sulphuric acid by heat, $C_2H_5HSO_4$
$= C_2H_4 + H_2SO_4$.

EXPERIMENTS. (1) In a liter flask heat a mixture of 30 c.c. of alcohol and 83 c.c. of C.P. H_2SO_4 (it is stated that H_3PO_4 can be used instead of H_2SO_4, avoiding the carbonizing), using a sand-bath. Put a little sand in the flask. Use a three-holed cork. It is best to use rubber stoppers for the entire apparatus because of the pressure of gas that is obtained. Insert a dropping funnel, also a thermometer placed so that the bulb is immersed in the liquid. Connect with a series of wash-bottles as shown in the diagram; the first bottle having H_2SO_4, the Woulff bottle (having a safety-tube) containing dilute NaOH solution, and each of the last bottles having a mixture of 10 c.c. of bromine and 10 c.c. of water. A *loosely* corked flask partly filled with dilute alkali catches any bromine vapor that may pass over. Begin heating the flask, and when the temperature reaches 170–175° this is maintained thereafter. At the start raise the safety-tube of the Woulff bottle out of the liquid, and attach a piece

of tubing. By means of this tube bubble the evolved ethylene through a mixture of solutions of potassium permanganate and sodium carbonate in a test-tube (Von Baeyer's reagent [1]) until the pink color is lost and a brownish precipitate of hydrated manganese dioxide appears. Lower the safety-tube and then begin running slowly into the flask, through the dropping funnel, a mixture of alcohol
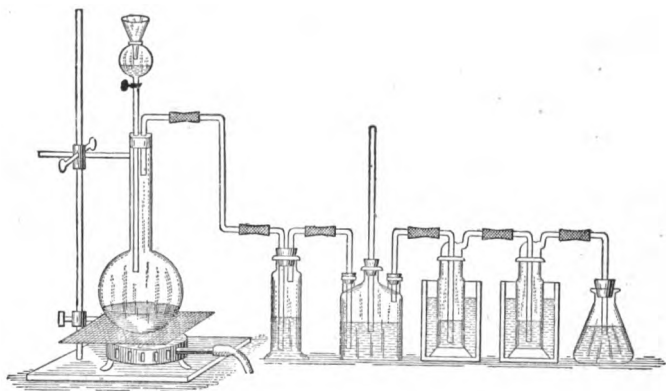
FIG. 24.

and sulphuric acid (100 c.c. of the former to 85 c.c. of the latter). Keep up a steady production of ethylene until the bromine is almost decolorized. The bromine bottles should stand in ice-water.

Disconnect the flask and then remove the flame.

[1] Von Baeyer's reagent is decolorized by formic and hydroxy-benzoic acids, by malonic ether, phenols, aldehyde, benzalde-hyde, aldehyde bisulphite, acetone, acetophenone, glycerol, and some sugars (because of oxidation of these substances), as well as by unsaturated compounds.

Wash the ethylene bromide with water in a separating funnel, and finally shake it with NaOH solution. Draw off the bromide into a flask, add dry calcium chloride, and cork. After a day or so distill, noting the boiling-point (130.3°, but 129.5° at 730 mm.). Also take the specific gravity (2.1785 at 20°). The bromide is easily solidified, melting at 9.5°.

(2) Bubble coal gas into Von Baeyer's reagent, as above.

Allyl alcohol (propenol), $CH_2 \!\!=\!\! CH \cdot CH_2OH$, is an unsaturated alcohol corresponding to the hydrocarbon propene, $CH_2 \!\!=\!\! CH \cdot CH_3$. Its radicle, C_3H_5, is called *allyl*. This alcohol can be made from glycerol.

Acrolein (acrylic aldehyde), $CH_2 \!\!=\!\! CH \cdot CHO$, is the aldehyde from the above alcohol. It is produced from glycerol (see p. 202):

$$\underset{\text{(Glycerol)}}{CH_2\!\!-\!\!CH\!\!-\!\!CH\!\!-\!\!O} \overset{\overset{\displaystyle OH \quad OH \quad H \quad H}{\diagup \cdots \diagup \cdots \diagup \cdots \diagup \cdots}}{} = \underset{\text{(Acrolein)}}{CH_2\!\!=\!\!CH\!\!-\!\!CHO} + 2H_2O.$$
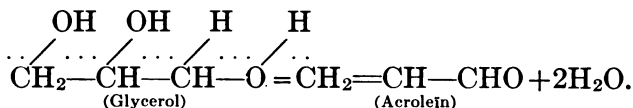
EXPERIMENT. In a dry test-tube mix 4 c.c. glycerol and 0.3 c.c. of 85% phosphoric acid. Fit the tube with a stopper and bent delivery tube. Dip the end of this tube in 2 c.c. of water in a small test-tube. Heat the glycerol to a high temperature. Finally test the solution for reducing power and with Schiff's reagent (aldehyde tests).

By oxidation it becomes **acrylic acid,**

$$CH_2 \!\!=\!\! CH \cdot COOH.$$

Crotonic acid is $CH_3 \cdot CH \quad CH \cdot COOH$.

Oleic acid is a member of the acrylic acid series. It has the formula,

$$CH_3(CH_2)_7CH = CH(CH_2)_7COOH.$$
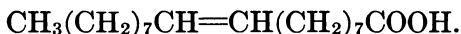
It is contained in combination with glycerol as glyceryl trioleate, in many oils, as in olive oil and whale oil, and in animal fats. Oleic acid forms crystals, melting at 14°. Hydriodic acid converts it into stearic acid; this is brought about by addition of hydrogen, thus:

$$C_{18}H_{34}O_2 + 2H = C_{18}H_{36}O_2.$$
$$\text{(Oleic acid)} \qquad \text{(Stearic acid)}$$
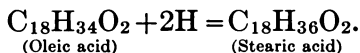
This reaction is now taken advantage of commercially in the process of *hydrogenation* of oils, by which they are converted into solid fats. In this process hydrogen gas is used, and a catalyzer (generally nickel) is employed to facilitate reaction with the olein. Fusion with caustic potash results in the formation of palmitic and acetic acids.

EXPERIMENTS. (1) Dissolve two drops of oleic acid in a few cubic centimeters of ether in a test-tube; shake with a little Von Baeyer's reagent (see p. 301).

(2) Shake some ether with a little bromine water; the ether becomes yellow. Add a few drops of oleic acid and shake. The bromine is taken up, so that the color is lost.

Erucic acid, $CH_3(CH_2)_7 \cdot CH = CH(CH_2)_{11}COOH$, is present in some oils, as cod-liver oil.

Linoleic acid, $C_{17}H_{31} \cdot COOH$, is believed now to be an acid somewhat similar to oleic acid, but it has two double linkings instead of one. Its molecule takes up four Br atoms, producing tetrabromstearic acid. Its glyceryl ester is contained in linseed oil. It has the power of taking up oxygen from the air and becoming a hard solid substance, hence its use in paints.

Ricinoleic acid,

$$CH_3(CH_2)_5CH(OH) \cdot CH_2 \cdot CH{=}CH(CH_2)_7COOH,$$
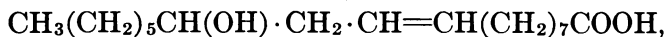
is present in castor oil in combination with glycerol.

ACETYLENES

These hydrocarbons, C_nH_{2n-2}, form a series of which few members are known.

Acetylene, $CH{\equiv}CH$, is the only important member. Small quantities are synthesized directly from carbon and hydrogen when a stream of hydrogen is passed between the carbon poles of an electric arc-light, a small quantity of methane being formed at the same time. It is formed when a Bunsen burner " snaps back." The gas is made most easily and cheaply by the action of water on calcium carbide,

$$C_2Ca + 2H_2O = C_2H_2 + Ca(OH)_2.$$
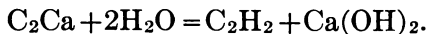
When used with a special burner, it gives a brilliant light, and is used as an illuminating gas. It is a colorless gas of unpleasant odor. It is very soluble in acetone.

EXPERIMENTS. (1) Put 10 gm. of calcium carbide in a dry flask or bottle, cork with a two-holed cork. By one hole suspend a dropping funnel containing water, and into the other hole fit a bent delivery tube. Let the water drop on the carbide very slowly. Bubble the acetylene into Von Baeyer's reagent until the test is secured. Then connect with a platinum-tipped glass tube such as is used for burning hydrogen. Light the acetylene; a brilliant flame is obtained.

(2) Test the acetylene by inverting a beaker moistened inside with a solution of cuprous chloride in ammonia over the stream of gas; a red precipitate of copper acetylide, C_2Cu_2, is formed.

Repeat the experiment, causing a Bunsen burner to strike back, thus producing acetylene.

The cuprous chloride is easily prepared as follows: dissolve 0.5 gm. of copper sulphate in a little water, add 2 c.c. of concentrated ammonium hydroxide, then 1.5 gm. hydroxylamine hydrochloride, and dilute to 25 c.c.

SULPHUR DERIVATIVES

SULPHUR may take the place of oxygen in alcohols or ethers, forming **sulphur alcohols** and **ethers, as**

$$CH_3 \cdot SH \text{ (cf. } CH_3OH),$$
$$CH_3 \cdot S \cdot CH_3 \text{ (cf. } CH_3OCH_3).$$
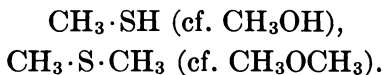
Sulphur alcohols are called mercaptans or thioalcohols. The ethers are dialkyl sulphides. When they are oxidized, as with nitric acid, **sulphonic acids** are formed, $CH_3 \cdot SH + 3O = CH_3 \cdot SO_3H$. The sulphonic acid group is SO_3H.

Sulphonic acids may be looked upon as sulphuric acid in which an hydroxyl group is replaced by an organic group:

$$SO_2 \Big\langle \begin{matrix} OH \\ OH \end{matrix} \qquad SO_2 \Big\langle \begin{matrix} C_2H_5 \\ OH \end{matrix} \; .$$

(Sulphuric acid)   (Ethylsulphonic acid)
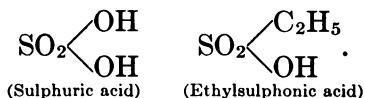
β-**Hydroxyethylsulphonic acid** (isethionic acid), $CH_2(OH) \cdot CH_2 \cdot SO_3H$, enters into the synthesis of taurin (see p. 272).

A *sulphone* is obtained if the hydroxyl of the SO_3H group be replaced by an organic radicle. Three aliphatic sulphones are of importance, because they are used as hypnotics.

Sulphonal (sulphonemethane, diethylsulphonedi-methylmethane), $\begin{matrix} CH_3 \\ CH_3 \end{matrix} > C < \begin{matrix} SO_2C_2H_5 \\ SO_2C_2H_5 \end{matrix}$, is made from acetone and ethyl mercaptan. It forms colorless crystals, slightly soluble in cold water, but, more soluble in hot water.

Trional (sulphonethylmethane) is diethylsulphonemethylethylmethane,

$$\begin{matrix} C_2H_5 \\ CH_3 \end{matrix} > C < \begin{matrix} SO_2C_2H_5 \\ SO_2C_2H_5 \end{matrix}.$$
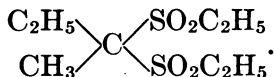
Tetronal is diethylsulphonediethylmethane,

$$\begin{matrix} C_2H_5 \\ C_2H_5 \end{matrix} > C < \begin{matrix} SO_2C_2H_5 \\ SO_2C_2H_5 \end{matrix}.$$
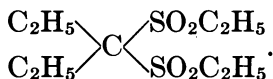
Ichthyol consists for the most part of a mixture of the ammonium salts of certain sulphonic acids derived from a peculiar tar, obtained by distillation of a bituminous shale (found in the Tyrol) containing the fossil remains of fishes. It is said to contain about 10% of sulphur.

There are several unsaturated compounds containing sulphur that are of interest. These are allyl derivatives.

Allyl sulphide, $(C_3H_5)_2S$, is contained in oil of garlic. It has a disagreeable odor.

Allyl isothiocyanate, $C \Big\langle \begin{matrix} N{-}C_3H_5 \\ S \end{matrix}$, is a mustard

oil.   It is contained in glucosidal combination in black mustard and horse-radish.

Allyl thiourea (allyl sulphocarbamide, thiosina-mine), $S=C \begin{cases} NH_2 \\ NH \cdot CH_2 \cdot CH=CH_2 \end{cases}$, is used as a remedy.

CYCLIC AND BICYCLIC COMPOUNDS

THESE form a transitional group between the fatty and the aromatic compounds.[1] They contain one or two closed carbon chains, differing from typical aromatic compounds in that their C atoms either have their full valence obviously satisfied (saturated) or have a double linking which causes the compound to respond to the tests for unsaturation (cf. benzene, p. 321).

CYCLIC COMPOUNDS

Certain hydrocarbons with the general formula C_nH_{2n} have properties quite different from those of the ethylene series; indeed, they behave quite like members of the methane series. Thus, they do not reduce Von Baeyer's reagent. Therefore, instead of representing them as composed of an open chain with double linkings, their formulæ are written as closed chains (and hence they are called cyclic compounds); for example, cyclopropane,

$$
\begin{matrix} CH_2 \\ | \quad \diagdown \\ \quad\quad CH_2; \\ | \quad \diagup \\ CH_2 \end{matrix}
\quad \text{cyclopentane,} \quad
\begin{matrix} CH_2\!-\!CH_2 \\ | \quad\quad\quad \diagdown \\ \quad\quad\quad\quad CH_2, \quad \text{etc.} \\ | \quad\quad\quad \diagup \\ CH_2\!-\!CH_2 \end{matrix}
$$
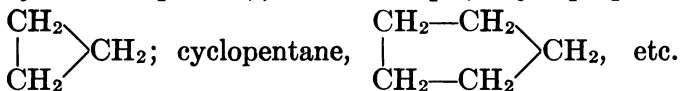
[1] Cyclic and aromatic compounds have been classed together as *homocyclic*.

They are given the same names as the members of the methane series, with the prefix cyclo. They are also called polymethylenes, and the individual compounds are trimethylene, pentamethylene, etc. Certain of these cyclic compounds have been found in petroleum.

Cycloses. There are a number of hydroxy derivatives of the cyclic hydrocarbons; these are cyclic alcohols or cycloses (OH attached to C of the ring). The most important of these is inosite.

Inosite, $C_6H_{12}O_6$, hexahydroxycyclohexane, has the same empirical formula as the hexoses; however, it is not a sugar. It occurs in animal tissues and in urine, being from this source optically inactive; *d* and *l* and *dl* varieties of inosite are said to occur in plants.

BICYCLIC COMPOUNDS. TERPENES AND CAMPHORS

In the volatile oils obtained from coniferous trees (and in various other natural products) there are hydrocarbons having the empirical formula $C_{10}H_{16}$. These are called terpenes They decolorize Von Baeyer's reagent (see p. 301), and they combine directly with one or two molecules of HCl. They therefore possess the general properties of unsaturated compounds, but they differ from these in many respects and may be considered to belong to the class of cyclic compounds since they contain a closed chain of carbon atoms. By mild oxidation many of them can be converted into cymene (paramethylisopropyl benzene) (see p. 332), and by further oxidation into paratoluic acid (see p. 362).

Thus they show a distinct relationship to aromatic compounds, although they are not true aromatic compounds.

The terpenes and camphors include many bodies of medical and commercial value, and of these the following are important:

Pinene, $C_{10}H_{16}$, the principal constituent of oil of turpentine, has the structural formula given below, and is optically active. It is dextrorotatory. Its boiling-point is 155°. When combined with hydrochloric acid it forms pinene hydrochloride, $C_{10}H_{17}Cl$, which, since it resembles camphor, is known as *artificial camphor* (see exp. below). Artificial camphor can be converted into true camphor. *Oil of turpentine* is obtained by incising the bark of fir-trees; the crude oil contains, in addition to turpentine, which is separated by distillation, residues constituting rosin. By destructive distillation or by steam distillation of resinous waste wood (pine and fir) there are obtained wood turpentine and pine oils. Turpentine boils at 160°, and has a specific gravity of 0.85. It hastens the oxidation of linseed oil, because it takes up oxygen readily from the air. Pinene can be converted by alcohol and nitric acid into **terpin**. It is not bicyclic like pinene, its formula being
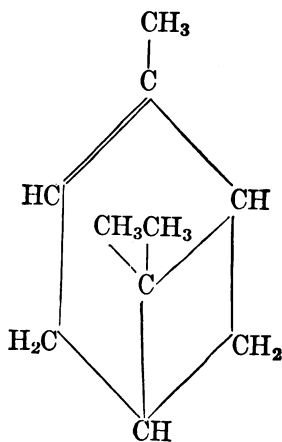
$$
\begin{array}{c}
CH_3 \\
| \\
C \\
\diagup\diagup\quad\diagdown\diagdown \\
HC\qquad\qquad CH \\
\;\;CH_3CH_3\; \\
\diagdown\;|\;\diagup \\
C \\
| \\
H_2C\qquad\qquad CH_2 \\
\diagdown\qquad\diagup \\
CH
\end{array}
$$

$$CH_3$$
$$|$$
$$C—OH$$

H_2C \\ CH_2

H_2C / CH_2

$CH—C(OH)$ $< \begin{matrix} CH_3. \\ CH_3. \end{matrix}$
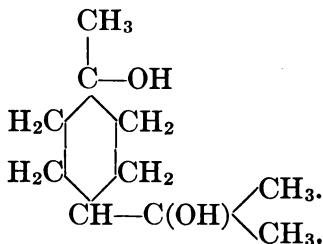
By taking up a molecule of water, *terpin hydrate* is formed, which is a crystalline substance used as a medicine.

EXPERIMENTS. (1) Prepare artificial camphor. Into 10 c.c. of freshly distilled turpentine that is free of water (treat with calcium chloride before distilling) contained in a flask kept cool by a freezing mixture, bubble dry HCl gas until crystals of pinene hydrochloride appear. Make the HCl by heating in a retort a mixture of dried NaCl and C.P. H_2SO_4. Collect the crystals on a filter and examine them.

(2) Shake some turpentine with Von Baeyer's reagent. Is there evidence of unsaturated linking?

Camphor, $C_{10}H_{16}O$. This is a gum obtained by distilling with steam the finely chopped wood of the camphor tree. Its chemical structure has recently been worked out, and it is now produced by synthetic processes on a commercial scale. Camphor contains a ketone group, so that it may be called a terpene ketone having the formula as shown below. In solution it is dextrorotatory.

$$CH_3$$
$$|$$
$$CH_2——————C——————CO$$
$$|\quad\quad CH_3—C—CH_3\quad |$$
$$|$$
$$CH_2——————CH——————CH_2$$
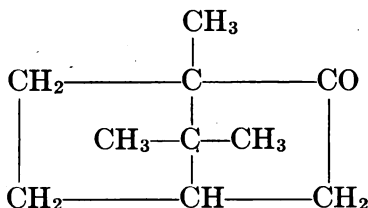
Borneol is a secondary terpene alcohol corresponding to camphor having CHOH instead of the CO group.

Camphor is convertible into carvacrol (isomer of thymol) by the loss of two atoms of hydrogen. By warming with phosphorus pentoxide it is converted into cymene. It melts at 176.4°, and sublimes, the sublimate forming crystals. *Hydroxycamphor* (oxy-camphor) has a secondary alcohol group in the place of a CH_2 group of camphor. It is one of the newer remedies. *Camphor monobromide* is $C_{10}H_{15}BrO$. Camphor can be oxidized to *camphoric acid*.

$$CH_3$$
$$|$$
$$CH_2——————C——————COOH$$
$$|\quad\quad CH_3—C—CH_3\quad\quad .$$
$$|$$
$$CH_2——————CH——————COOH$$
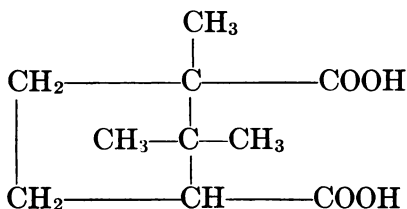
Menthol is a monocyclic terpene alcohol containing a secondary alcohol group CHOH. Its formula is given below. Like camphor, it contains no unsaturated linkings. Menthol is a white crystalline substance melting at 42°, and is the chief constituent of oil of peppermint. Its solution is lævorota-

tory. It is useful as a medicine. It is excreted in combination with glycuronic acid (p. 221).

$$
\begin{array}{c}
CH_3 \\
| \\
CH \\
\diagup \quad \diagdown \\
H_2C \qquad CH_2 \\
| \qquad \quad | \quad \diagup H \\
H_2C \qquad C \\
\diagdown \quad \diagup \quad \diagdown OH \\
CH\!\!-\!\!CH \diagdown \begin{array}{c} CH_3. \\ CH_3 \end{array}
\end{array}
$$
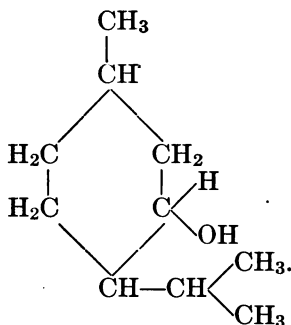
Eucalyptol (cineol) is a camphor-like liquid obtained from oil of eucalyptus. Its formula is

$$
\begin{array}{c}
CH_3 \\
| \\
C\!\!-\!\!-\!\!-\!\!-\!\!-\!\!O \\
H_2C \diagup \quad \diagdown CH_2 \qquad \quad | \\
H_2C \diagdown \quad \diagup CH_2 \qquad | \quad CH_3 \\
CH\!\!-\!\!-\!\!-\!\!-\!\!C \diagdown CH_3 \cdot
\end{array}
$$
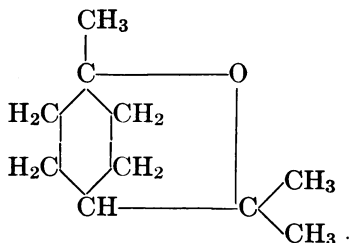
Sandalwood oil contains two isomeric unsaturated primary alcohols, one being bicyclic and the other tricyclic. They have the formula, $C_{15}H_{24}O$.

Polyterpenes have two or more terpene rings.

SUBSTANCES ALLIED TO TERPENES

Caoutchouc or **rubber** contains a terpene-like substance. Rubber is the hardened milky juice of certain tropical plants. Synthetic rubber, having

similar properties to natural rubber, has been prepared by causing isoprene,

$$CH_2 = C(CH_3)CH = CH_2,$$

to polymerize. Pure rubber is believed to be $(C_{10}H_{16})_n$. In solution it is in the colloidal condition. **Gutta-percha** is similar to rubber.

Cholesterol (cholesterin), $C_{27}H_{46}O$, is an important constituent of bile. It is also present in egg yolk, cod-liver oil and lanolin. It belongs to a class of compounds called *sterins*, which includes also isocholesterol, koprosterol, phytosterol, and other substances. It has an unsaturated linking and a secondary alcohol group:

$$\begin{matrix} CH_3 \\ \\ CH_3 \end{matrix} \!\!\!> CH \cdot (CH_2)_2 \cdot C_{17}H_{26} \cdot CH = CH_2.$$

$$CH_2 \cdot CHOH \cdot CH_2.$$
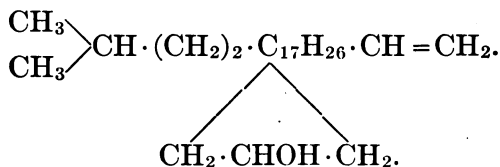
The portion $C_{17}H_{26}$ is believed to be related to the polyterpenes. Its crystalline form is characteristic. It melts at 145–146°. In ether solution it is lævorotatory.

Koprosterol, $C_{26}H_{46} \cdot CHCH$, is a similar compound occurring in the fæces.

Phytosterol is of vegetable origin, being most abundant in leguminous seeds and in vegetable oils. It can be detected and distinguished from cholesterol by the fact that its ester with acetic anhydride has a higher melting-point (125°) than the similar ester from cholesterol (114.5°).

CHAPTER XXIV

THE AROMATIC HYDROCARBONS

NEARLY all of the substances that we have so far studied are represented in their formulæ as composed of open chains of carbon atoms. A few of them, such as the anhydrides of hydroxy-acids, lactones, and the purin derivatives, have to be represented as composed of closed chains. It is, however, only in the case of the aromatic bodies and the cyclic compounds, that each link in the closed chain is represented by a C atom. In connection with the paraffin derivatives containing closed chains, it will be remembered that their closed chain is readily opened; e.g., an anhydride of an acid can easily be converted into the corresponding acid, etc.

We come now to a group of organic substances— the largest group, indeed—the members of which are composed of closed chains that cannot readily be opened. In the older chemical nomenclature the bodies belonging to this group were called aromatic bodies on account of the presence of an agreeable aroma, and by this name they are still known. They may all be looked upon as derivatives of a substance called benzene, C_6H_6, just as all the fatty substances may be represented as derivatives of methane. Many of the derivatives of benzene are indeed quite analogous with those of methane,

undergoing similar reactions and possessing much the same properties. Unlike the fatty series, few of them are useful as foods; many of them, however, have very pronounced physiological actions. Commercially they are of very great value.

There are four simple reactions in which the two groups—the aromatic and the fatty—give very different results:

1. With concentrated nitric acid the aromatic hydrocarbons readily form nitro compounds, which on reduction with nascent hydrogen yield amino-derivatives. Paraffins are unaffected by HNO_3.

$a.$ $C_6H_5|H + HO|NO_2 = C_6H_5NO_2 + H_2O.$
(Benzene)   (Nitrobenzene)

$b.$ $C_6H_5NO_2 + 6H = C_6H_5NH_2 + 2H_2O.$
(Aniline)
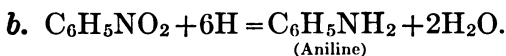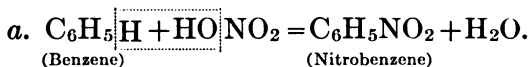
2. With concentrated sulphuric acid they form sulphonic acids (see p. 306). Paraffins are unaffected by H_2SO_4.

$C_6H_5|H + HO| \cdot SO_3H = C_6H_5SO_3H + H_2O.$
(Benzene sulphonic acid)
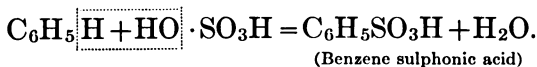
3. Chlor- and brom-benzene are very stable and do not readily react with KOH, whereas in the case of methyl chloride, etc., hydroxyl can readily be substituted for the Cl (see p. 137).

4. When a benzene substitution product with one or more side chains of carbon atoms is oxidized, the side chain or chains become oxidized in such a way as to form simply carboxyl.

BENZENE

At the outset we must study the structure of benzene, since, as has been noted, this is the mother substance of the aromatic bodies. We must furnish evidence that its formula is correctly represented as having a closed chain.

Benzene [1] (benzol), C_6H_6. When coal is heated in gas retorts in the preparation of artificial gas, there passes out with the gas a vapor which is condensed in specially arranged condensers. The condensed vapors constitute coal-tar. The ammonia and pyridine bases that are also given off from the retorts are dissolved in water. The tar is a mixture of hydrocarbons, neutral bodies, several phenols, and a small quantity of basic bodies, and also contains particles of carbon in suspension (hence its blackness). The tar products are separated partly by fractional distillation and partly by chemical means. The crude tar is distilled into four fractions, as follows:

(1) Light oil (fraction up to 150°).
(2) Carbolic oil (150–210°).
(3) Heavy or creosote oil (210–270°).
(4) Anthracene oil (above 270°).

The heavy oil sinks in water; it contains a large amount of naphthalene.

In the United States coal-tar is more commonly distilled into two fractions, the light oil to about 200°, and the heavy oil above 200°. By this method part of the phenols and naphthalene pass

[1] Different from benzine (see p. 121).

over into the light oil. If distillation is continued at a temperature above 270°, anthracene is obtained.

The residue contains a large amount of carbon, it is called pitch.

The light oil is purified by treatment with dilute acid and then with alkali and by subsequent distillation. It is in the light oil that most of the benzene and its homologues are contained. The benzene can be further purified by fractional distillation, then by treatment with concentrated H_2SO_4 to remove thiophene (C_4H_4S), and finally by freezing it and pouring off the liquid portion.

Benzene may also be obtained: (1) By distillation of a salt of an aromatic acid with soda-lime, a reduction which, it will be remembered, is analogous with that employed for the preparation of methane:

$$C_6H_5COONa + NaOH = Na_2CO_3 + C_6H_6.$$

(2) By passing acetylene (C_2H_2) through a red-hot tube. This method illustrates how synthesis of aromatic out of fatty hydrocarbons can be accomplished.

(3) By heating potassium in a current of CO. A synthesis occurs resulting in the formation of $C_6(OK)_6$, potassium carbonyl. This is a derivative of benzene and can be converted into benzene by distillation with zinc dust in the presence of water.

Benzene is a colorless liquid of aromatic odor, boiling at 80.3° (corrected) (at 80.12° at 757.3 mm.). Its melting-point is 5.5°. Its specific gravity is

0.8736 at $\frac{20°}{4°}$.   It can be used for molecular weight
determinations (see p. 60).   Benzene is inflammable
and immiscible with water.   It is a good solvent
for many substances.

It is soluble in water only to the extent of 0.1%
and it takes up about 0.03% of water.

EXPERIMENTS.   (1) Mix thoroughly 25 gm. of
benzoic acid and 50 gm. of powdered quicklime,
and put into a dry retort (cf. preparation of methane,
p. 120).   Connect with a condenser and heat grad-
ually.   Treat the distillate with dry calcium chloride
and redistill from a small fractionating flask (an air-
condenser will do).   Note the boiling-point.   Put
the distillate into a dry test-tube and cool in a freez-
ing-mixture until crystallization occurs.   Remove
from the mixture and warm the test-tube with the
fingers while stirring the crystals with a thermometer.
At what point does the temperature remain constant
while the crystals are melting?

(2) Determine the specific gravity of some pure
benzene at 15° with the Westphal balance.

(3) Shake a few cubic centimeters of benzene with
Von Baeyer's reagent.   Does it act like an unsat-
urated compound?

Structure of Benzene.   From its empirical formula,
C_6H_6, one would expect to find benzene giving re-
actions like those of acetylene or other unsaturated

hydrocarbons,[1] that is to say, reactions indicating the existence of double bonds between the carbon atoms. Such, however, is not the case. Benzene does not readily combine with halogens, i.e., form addition products; it is not sensitive toward oxidizing agents; it does not decolorize a solution of potassium permanganate containing sodium carbonate. Unsaturated compounds readily give all these reactions. It is evident, therefore, that the formula for benzene cannot be represented as containing double bonds between the carbon atoms. Further, the formula must represent all the hydrogen atoms as similarly combined with the carbon atoms, *for there are no isomers of the monosubstitution products of benzene:* there is only one monobrombenzene, one monochlorbenzene, etc. This important fact can be shown in a variety of ways. Perhaps the simplest is as follows: If we treat benzene with bromine, one of the six hydrogen atoms is replaced by bromine. Numbering the hydrogen atoms thus:
$\overset{1}{H}\,\overset{2}{H}\,\overset{3}{H}\,\overset{4}{H}\,\overset{5}{H}\,\overset{6}{H}$, let us suppose that $\overset{1}{H}$ is replaced. Our problem is to see whether the monobrombenzene thus formed is identical with that formed by replacement of $\overset{2}{H}$, $\overset{3}{H}$, etc. To do this we must replace another H in the compound, $C_6\,\overset{1}{Br}\,\overset{2}{H}\,\overset{3}{H}\,\overset{4}{H}\,\overset{5}{H}\,\overset{6}{H}$, by some group which can then

[1] Cf. dipropargyl, C_6H_6, $CH{\equiv}C{-}CH_2{-}CH_2{-}C{\equiv}CH$. This has a distinctly greater heat of combustion than benzene; therefore the kind of linking that we have in benzene must be quite different from that in ordinary unsaturated compounds.

be replaced by Br, the Br originally present being meanwhile replaced by H. This can be accomplished by treating monobrombenzene with nitric acid, the resulting compound having the formula $C_6H_4BrNO_2$. Let us suppose that $\overset{2}{H}$ is replaced by the NO_2 group, thus: $\overset{1}{C_6}\overset{}{Br}\overset{2}{NO_2}\overset{3}{H}\overset{4}{H}\overset{5}{H}\overset{6}{H}$. By the action of nascent H the NO_2 group becomes an amino group, NH_2 (see p. 376), and the Br is replaced by H. The formula for our substance is then $\overset{1}{C_6}\overset{2}{H}(\overset{}{NH_2})\overset{3}{H}\overset{4}{H}\overset{5}{H}\overset{6}{H}$ (aniline). By treating a salt of aniline (p. 384) with nitrous acid the diazonium salt is formed, which by treatment with hydrobromic acid (see p. 385) yields a monobrombenzene in which the Br atom stands in place of $\overset{2}{H}$, and yet this is found to be identical in properties with that monobrombenzene in which Br was in place of $\overset{1}{H}$. By similar reactions the various H atoms may be replaced one by one, the resulting monosubstitution product being always the same.

This fact makes it evident that we cannot represent the C atoms as linked together in an open chain, for then there would necessarily be two or three varieties of monosubstitution products, depending upon the particular C atom in the chain to which the substituting group is linked (cf. alcohols, p. 109). On this account Kekulé, who had been a mechanical engineer before he became a chemist, conceived the notion that the C atoms must be represented as

forming a ring, and that the formula for benzene must be

$$
\begin{array}{c}
\text{CH} \\
\text{HC} \quad\quad \text{CH} \\
\text{HC} \quad\quad \text{CH} \\
\text{CH}
\end{array}
$$
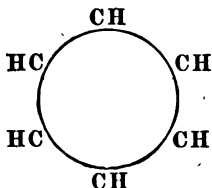
or, as it is more usually written,

$$
\begin{array}{c}
\text{CH} \\
\text{HC} \quad \text{CH} \\
\text{HC} \quad \text{CH} \\
\text{CH}
\end{array}
$$
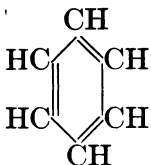
To satisfy the quadrivalence of the C atom, it is necessary, as shown in the second formula, to assume that certain of these bonds are double. We have, however, seen that when double bonds between carbon atoms exist, the resulting body is unsaturated. To explain this apparent inconsistency, Kekulé supposes that in benzene there are really no double bonds in the same sense as they exist in unsaturated hydrocarbons, but that the double bond is *dynamic*, changing about from place to place, and is really unrepresentable in a formula.[1]

---

[1] The centric formula ⬡ has been proposed to indicate pictorially this self-saturation of the carbon atoms of the ring without definite extra linkings. This formula also has the advantage of emphasizing the distinguishing difference of all aromatic from other organic compounds.

Collie has made an extremely interesting suggestion as to the spatial relations of the C atoms in benzene. His model represents each C atom as at the center of a tetrahedron, and neighboring carbons are attached by bands, while an H atom is
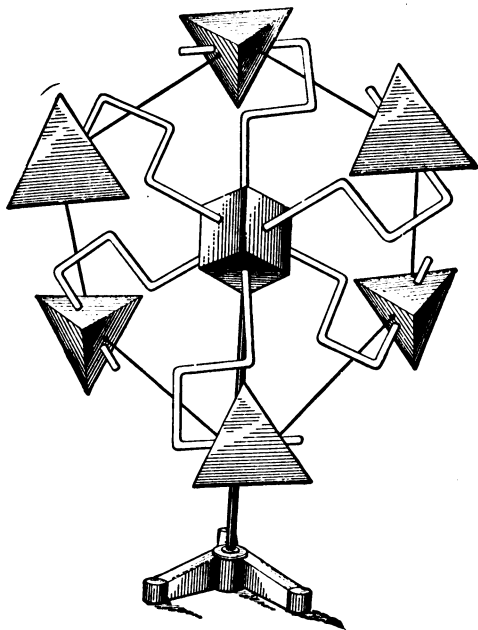
Fig. 25.

attached to each C through the center of a face not at an angle of the tetrahedron. The rest of the model is mechanical serving for support (see Fig. 25).

Such an arrangement permits rotation of two kinds, (1) the tetrahedra can rotate on their own axes simultaneously, and (2) the three pairs of

tetrahedra can rotate on the axes passing through
the center of the model. This possibility of double
rotation conforms very well to the idea that the
benzene molecule must be conceived as a system
in vibration. By those rotations the model can be
made to correspond successively to the following
formulæ:
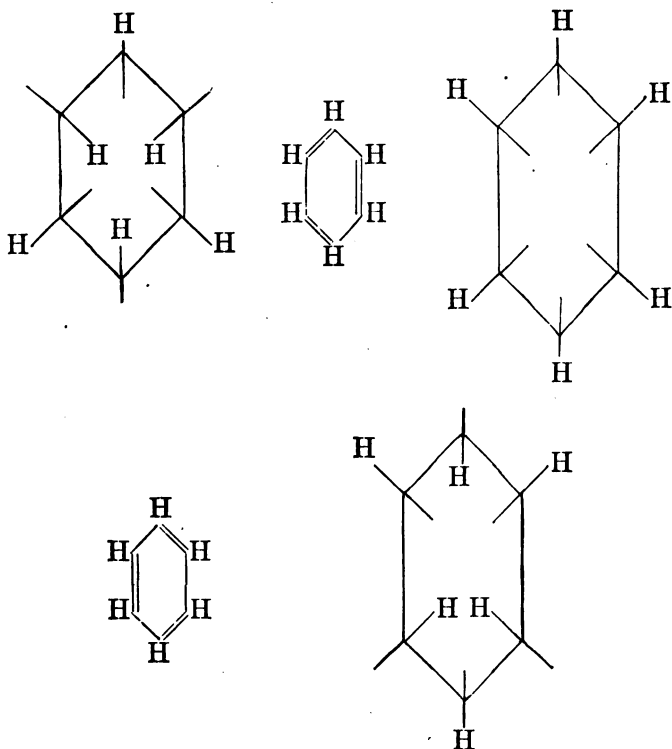
The first and last would indicate that there are
two sets of H atoms. Possibly this explains why,

in the substitution of certain groups for H, there is a tendency to displace alternate H atoms instead of successive ones; for instance, nitric acid forms
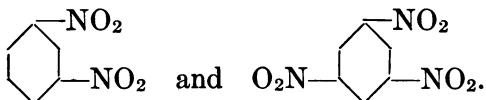
In perfect harmony with this conception of a ring is the fact that there are *three kinds of disubstitution products*. That three and only three are possible will be evident from the following formulæ, where x represents some substituting group:

A (ortho)   B (meta)

C (para)
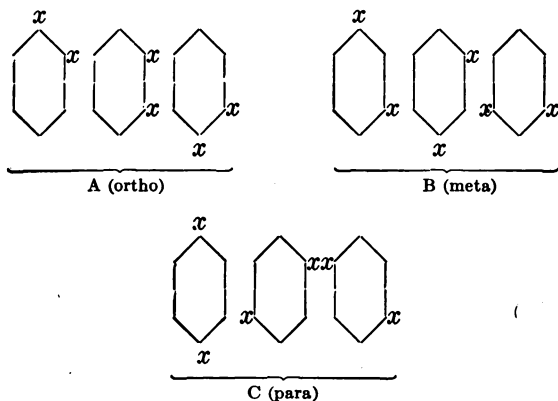
The substituting groups may replace neighboring hydrogens, as in the formulæ marked A; or be so arranged that a carbon of the ring intervenes, as in B or with two such atoms intervening, as in C. Bodies exhibiting the first arrangement are called *ortho*, the second *meta*, and the third *para*.[1]   For certain

---

[1] The abbreviations *o, m*, and *p*, are used for these terms.

of the simple disubstitution products of benzene it
has been definitely established which is ortho, which
meta, and which para. To ascertain to which of
these groups an unknown substance belongs it is
necessary to transform it into one of the known sim-
pler forms, it being considered that the unknown
substance contains the same arrangement of its
side chains as does the simpler substance which it
yields. It remains for us to see, therefore, how it is
possible to tell to what class some simple disub-
stitution product of benzene belongs. This is done
by a study of the number of isomeric compounds
which can be produced by replacing still another
hydrogen atom of the ring by a group different from
the other two groups. Suppose y to represent this
third group. In an *ortho* compound we might have
y attached next to x,

, or one carbon atom removed from it,

; that is to say, there might be two
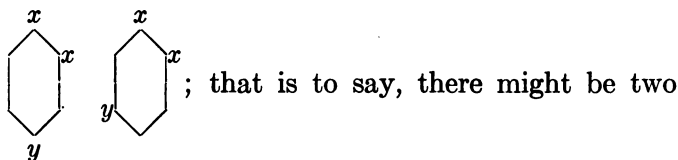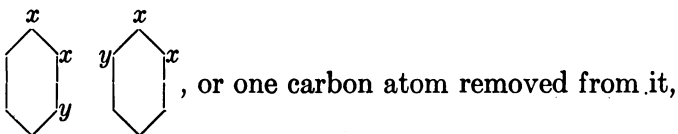
trisubstitution products which on removal of y
would yield the same disubstitution product. In
a *meta* compound y might occupy three different
positions; thus, between the two x's as in A, or
beyond but next to them as in B, or separated

from them by carbon atoms of the ring as in C, thus:

A   B   C

That is to say, there are three trisubstitution products which yield the same disubstitution product. In a *para* compound y could occupy only one position, i.e., next to an x; therefore there is only one trisubstitution product that could be converted into it, thus:
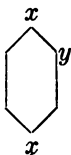
. To take an example: There are six diamino-

benzoic acids with the formula $C_6H_3{<}{=}{NH_2 \atop COOH}^{NH_2}$.

By removal of the carboxyl group three of these yield diaminobenzenes which are identical in properties (melting-point 63°), and which must therefore be meta; two others yield another variety of diaminobenzene (melting-point, 102°) which must be ortho; and the remaining one yields yet another diaminobenzene (melting-point 140°) which must be para.

For convenience of description it is customary

to number the carbon atoms in the benzene ring thus:
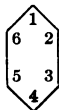
When three similar groups (e.g., three hydroxyls) are attached to the benzene ring, only three isomers are possible, *symmetrical* (positions 1, 3 and 5), *unsymmetrical* (1, 3, 4), and *adjacent* (1, 2, 3).

Analogous to the alkyl radicles of paraffin hydrocarbons is the phenyl group, C_6H_5. This is sometimes designated by the Greek letter ϕ.

Reaction by addition.—When hydrogen is mixed with benzene vapor and the mixture is passed over powdered nickel, the H adds on to each carbon, forming C_6H_{12}. This does not act like an aromatic compound; it is cyclohexane (p. 309).

HOMOLOGUES OF BENZENE

Toluene (toluol), $C_6H_5 \cdot CH_3$, boiling-point 110°, specific gravity 0.8656 at $\frac{20°}{4°}$, can be separated from light oil or can be prepared synthetically by treating a mixture of monobrombenzene and methyl iodide with sodium (cf. synthesis of paraffins, p. 117).

$$C_6H_5Br + CH_3I + 2Na = NaI + NaBr + C_6H_5CH_3.$$
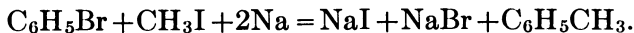
This reaction clearly illustrates its structure as methyl benzene. By oxidation the CH_3 group

becomes carboxyl, *benzoic acid*, C_6H_5COOH, being therefore formed.

Xylenes, $C_6H_4(CH_3)_2$. Since they are disubstitution products of benzene, there are three of them. The boiling-point of ortho is 141.9°, meta 139.2°, para 138°; the specific gravity at $\dfrac{20°}{4°}$ of ortho is 0.8766, meta 0.8655, para 0.8635. The xylenes can be prepared from light oil. By oxidation they give first *toluic acids*, $C_6H_4\underset{COOH}{\overset{CH_3}{\big<}} \left\{ \begin{array}{l} o \\ m, \\ p \end{array} \right.$

and then *phthalic acids*, $C_6H_4\underset{COOH}{\overset{COOH}{\big<}} \left\{ \begin{array}{l} o \\ m. \\ p \end{array} \right.$ The

xylol, which is extensively used in histological work and as a fat-solvent, is a mixture of the xylenes.

Isomeric with the xylenes is **ethyl benzene,** $C_6H_5 \cdot C_2H_5$, which on oxidation yields benzoic acid, C_6H_5COOH, instead of toluic or phthalic acid.

Mesitylene, $C_6H_3(CH_3)_3$, boiling-point 164.5°, specific gravity 0.8694 at $\dfrac{9.8°}{4°}$, is also contained in light oil, and can likewise be obtained by a most interesting and important synthesis, viz., by distilling a mixture of acetone and sulphuric acid (see exp. below). Three acetone molecules no doubt enter into the synthesis, the sulphuric acid removing a molecule of water from each and causing them to condense into a ring as represented in the following formula:
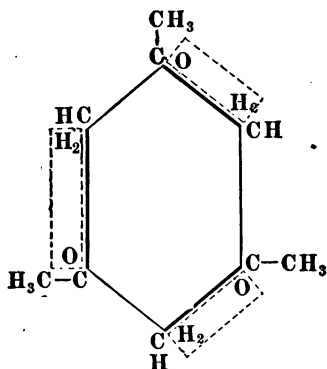
Mild oxidation of mesitylene yields *mesitylenic*

acid, $C_6H_3 \diagdown \begin{matrix} CH_3 \\ CH_3 \\ COOH \end{matrix}$, and if this be heated with soda-

lime and the COOH group be thus removed (see p. 319), metaxylene is obtained, furnishing corroborative proof that metaxylene has the formula
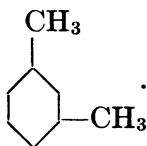
EXPERIMENT. *Preparation of a benzene hydrocarbon (mesitylene) from a fatty compound (acetone).* Into a 500-c.c. flask put 100 gm. of clean sand, 50 c.c. of acetone, and a cooled mixture of 65 c.c. of C.P. H_2SO_4 and 30 c.c. of water. Mix thoroughly and allow to stand for at least two days. Filter with the aid of suction, using a hardened filter-paper. Distill the filtrate, heating the flask in an oil bath. Shake the distillate with dilute alkali, then with

water. Separate the oily layer, dry it with cal-
cium chloride, and distill. Collect the fraction
coming over above 150°. Notice the aromatic
odor. Test it as follows: Place a few small crystals
of anhydrous aluminum chloride in a dry test-tube;
heat gradually until a thin coating of sublimate is
secured in the upper part of the tube. When cool
add a solution of a few drops of the mesitylene in
about 2 c.c. of chloroform and cork the tube. Most
aromatic hydrocarbons and some of their derivatives
give a color reaction under the conditions of this
test, at least on standing.

Cymene is paramethylisopropyl benzene,

$$C_6H_4 \diagdown \begin{matrix} CH_3 \\ CH \end{matrix} \diagdown \begin{matrix} CH_3. \\ CH_3 \end{matrix}$$
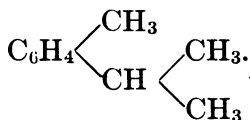
It can be obtained by warming camphor, $C_{10}H_{16}O$,
with phosphorus pentoxide, or by treating pinene,
$C_{10}H_{16}$ (from turpentine), with chlorine. It is a
constituent of certain ethereal oils, as oil of *eucalyptus*
and oil of *thyme*.

Of Benzene. As already explained, there is only one kind of monohalogen substitution product of benzene. *Chlor- and brombenzene* can be prepared by treating benzene with chlorine or bromine. *Iodobenzene* is prepared with greater difficulty, it being necessary to have an oxidizing agent present (I_2 with HIO_3). By prolonged action more than one hydrogen atom of the benzene molecule becomes replaced by the halogen, and of course there are *o-*, *m-*, and *p*-disubstitution products; indeed, all the H atoms may be replaced, hexachlor- (or brom-) benzene being formed, C_6Cl_6 (or C_6Br_6). If the reaction takes place in direct sunlight, addition products, instead of substitution products, are obtained, such as $C_6H_6Cl_6$ and $C_6H_6Br_6$. These readily decompose into the halogen acid and trisubstitution products of benzene:

$$C_6H_6Cl_6 = 3HCl + C_6H_3Cl_3.$$

In contrast to the halogen derivatives of the paraffins, the halogen substitution products of benzene are

[1] It will be advisable for the student to look over the synopsis of aromatic compounds (p. 423) frequently in studying the following pages.

very stable and do not readily give up their halogen atoms to be replaced by hydroxyl, a cyanide group, an amido group, etc., as alkyl halides do.

Of Toluene. There are four bodies with the empirical formula C_7H_7Cl. One of these, called *benzyl chloride*, has a very disagreeable odor and readily yields up its Cl atom when heated with hydroxides, cyanides, etc. It behaves in this respect like a fatty derivative. These facts suggest that the Cl atom is in the side chain, thus $C_6H_5CH_2Cl$. That this is really so is proved by the fact that when oxidized it yields benzoic acid, C_6H_5COOH. It is formed when toluene is treated at boiling temperature or in direct sunlight with the halogen.

The three other bodies are called *chlortoluenes* and have agreeable aromatic odors. They do not give up their Cl atom when heated with hydroxides, etc. They behave in this respect like chlorbenzene, so that the Cl atom must be present in direct connection with the benzene nucleus itself, thus:

$$C_6H_4\Big\langle {{CH_3}\atop{Cl}} \Big. .$$
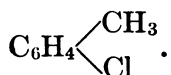
The three varieties are ortho, meta, and para. When they are oxidized the Cl atom is not removed, but the CH_3 side chain becomes converted into COOH, a substituted benzoic acid being thus formed, i.e., a chlorbenzoic acid. They are prepared by treating toluene in the cold, and in diffused light, with chlorine, the reaction being greatly accelerated by the presence of antimony trichloride or some other halogen-carrier.

In the same way with the di- and trihalogen sub-
stitution products of toluene, substitution may occur
in either the phenyl [1] or the methyl groups.   The
other substitution products of toluene exhibit a
similar isomerism.

[1] Phenyl is the name given to the radicle C_6H_5.

AROMATIC HYDROXY COMPOUNDS

ONE or more of the H atoms of benzene may be displaced by a hydroxyl group—OH, the resulting body being called a phenol. Phenols manifest faintly acid properties, so that some of them are called acids; thus, monohydroxybenzene is carbolic acid, and trihydroxybenzene, pyrogallic acid. Their acidity indicates that in solution a few H· ions are liberated. Compare the acid power of phenol with that of weak organic acids, as shown in the table (appendix, p. 451). When brought into contact with alkaline hydroxides, salts, called phenolates or phenoxides, are formed, e.g., C_6H_5ONa sodium phenolate. Such phenolates can be obtained by dissolving the phenol in a solution of the hydroxide and evaporating to dryness. They are, therefore, stable in the presence of water and thus differ from the alcoholates, which are decomposed by water and can be formed only by acting on alcohol with the alkali metals. By union with phenyl, therefore, the hydroxyl group—OH comes to possess quite different properties from those that it has when combined with a paraffin (see p. 137).

On the other hand, even such weak acids as carbonic (H_2CO_3 or $CO_2 + H_2O$) are more strongly acid than phenol and can decompose phenolates, liberat-

ing the phenol. The percentage dissociation for a decinormal solution of phenol is only 0.0037, that of carbonic acid being 0.174.

In other respects phenols behave like tertiary alcohols (cf. tertiary alcohol group

$$-\overset{|}{\underset{|}{C}}-OH \text{ with } \text{(benzene ring)} C-OH$$
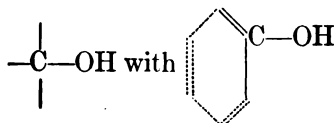
of phenol), thus: they form ethers and ethereal salts, but do not yield aldehydes, ketones, or acids on oxidation (see p. 112). The OH group can be removed by treatment with PCl_5. Using the same classification as for alcohols, we may, therefore, subdivide them into mon-, di-, and triacid phenols.

MONACID PHENOLS

Phenol (carbolic acid), C_6H_5OH. This important substance is extracted from the carbolic oil fraction of coal-tar by shaking with a solution of alkali, the carbolic acid in the resulting solution being then precipitated by sulphuric acid and redistilled (see exp. below). It is purified by recrystallizations. It may also be prepared by fusing potassium benzene sulphonate with caustic potash:

$$C_6H_5SO_3K + KOH = C_6H_5OH + K_2SO_3,$$
(Potassium benzene sulphonate)
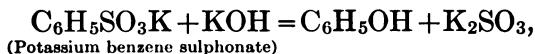
or by boiling a diazonium salt with water (see p. 385):

$$C_6H_5N_2 \cdot NO_3 + H_2O = C_6H_5OH + HNO_3 + N_2.$$
(Benzene diazonium nitrate)
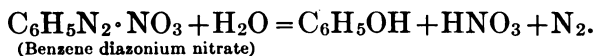
EXPERIMENTS. (1) Extract phenol from heavy oil (carbolic oil) in the following manner: Dissolve 2 c.c. in ether, add 10 c.c. of 5% NaOH and shake for five minutes. Draw off the bottom layer with a pipette and filter through a wet filter. Acidulate the filtrate with HCl, cool, and shake with ether vigorously. Remove the ether layer with a pipette, transferring it to an evaporating dish. Evaporate on a steam-bath away from a flame. Note the odor of the residue and test it for phenol (see tests, 3).

(2) *Prepare phenol from aniline.* Into a freshly made (hot) solution of 12 c.c. of C.P. H_2SO_4 in 50 c.c. of water put 10 c.c. of aniline, allowing it to flow down the wall of the beaker. Mix well and dilute with 100 c.c. of water. Cool with running water, then add sodium nitrite solution (8.5 gm. in 40 c.c. of water) until a drop of the mixture well diluted gives a blue color to starch-potassium-iodide paper (soak filter-paper in boiled starch solution containing potassium iodide, dry it, and cut up into strips), showing the presence of free nitrous acid. This procedure is called *diazotizing*, because the nitrous acid changes the aniline salt into a diazonium salt. Transfer to a half-liter flask, heat to 40–50° in a water-bath for half an hour, then distill with steam (see p. 16). The phenol passes over into the condenser with the steam. Saturate the distillate with sodium chloride and shake with several small portions of ether. Dry the separated ethereal extract over dehydrated sodium sulphate for several days in a corked flask. Distill off the ether (away from a flame if possible, a steam-bath being safest);

finally draw a stream of air through the hot flask with a suction-pump. Distill the phenol, using an air-condenser. Collect the phenol by fractions, testing the first fractions as in (3) below. When a drop of distillate, on cooling with water, crystallizes, collect samples.

$$C_6H_5NH_2 + H_2SO_4 \qquad = C_6H_5NH_2 \cdot H_2SO_4,$$
<div align="center">(Aniline)　　　　　　　(Aniline sulphate)</div>

$$C_6H_5NH_2 \cdot H_2SO_4 + HNO_2 = C_6H_5 \cdot N_2 \cdot OSO_3H + 2H_2O$$
<div align="center">(Benzene diazonium sulphate)</div>

$$C_6H_5 \cdot N_2 \cdot OSO_3H + H_2O \quad = C_6H_5OH + N_2 + H_2SO_4.$$
<div align="center">(Phenol)</div>
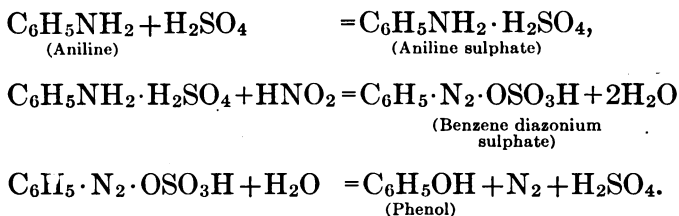
(3) *Tests.* (*a*) To half a test-tube of phenol solution add bromine water until a white precipitate of *tribromphenol* forms. (*b*) Test some solution with a drop of ferric chloride solution, a violet color is obtained. (*c*) To a few cubic centimeters of solution add Millon's reagent and boil; a red color develops. (*d*) To 10 c.c. of phenol solution add a few cubic centimeters of ammonia, then small portions of bleaching-powder, shaking after each addition, until the mixture turns blue.

Phenol, when pure, forms colorless rhombic needles melting at 42° and boiling at 182.9°. Its specific gravity is 1.039 at 58.5°. It becomes reddish on exposure to light. It dissolves in 15 parts of water at 17°; in other words, by shaking phenol crystals with water and allowing them to stand at room temperature, an approximately 6.5% solution is obtained, and the crystals, by taking up water,

will liquefy and form an oily layer at the bottom of
the bottle.   It mixes with glycerol, alcohol and ether
in all proportions.   The easiest way to prepare a
5% phenol solution is by diluting the proper quan-
tity of a 50% solution in glycerol.   Phenol is
extensively used in surgery as an antiseptic.   It is
produced in the intestine by the action of micro-
organisms on the aromatic groups in protein; the
phenol thus produced is absorbed in the blood and
unites with potassium sulphate, to be excreted into
the urine as potassium phenol sulphate,

$$C_6H_5 \cdot OSO_2OK.$$

It can also combine with glycuronic acid.   Phenol
uncombined with alkali is poisonous.   It is often
taken with suicidal intent.

The **derivatives of phenol** are (1) the ethers and
ethereal salts and (2) the substitution products.

The **ethers** are of two classes: (*a*) the
aromatic-fatty ethers, such as phenyl ethyl ether,
$C_6H_5 \cdot O \cdot C_2H_5$, and (*b*) the *true aromatic* ethers,
such as phenyl ether, $C_6H_5 \cdot O \cdot C_6H_5$.   The aromatic-
fatty ethers may be obtained by allowing an alkyl
halide to act on a phenolate:

$$\cdot C_6H_5O \overline{|Na+I|} C_2H_5 = C_6H_5 \cdot O \cdot C_2H_5 + NaI.$$
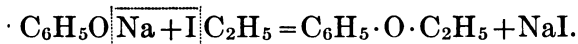
The chief members of this class are *anisole* (phenyl
methyl ether) and *phenetole* (phenyl ethyl ether)
They are both liquids having pleasant odors.   The
true aromatic ethers cannot be prepared by this
reaction since a halogen cannot easily be displaced
from phenyl.   They may, however, be obtained

by heating phenol with a dehydrating agent such as aluminium chloride:

$$C_6H_5O\underline{H + HO}C_6H_5 = C_6H_5 \cdot O \cdot C_6H_5 + H_2O \ .$$
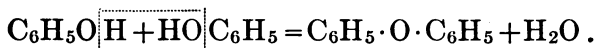
The **ethereal salts.** *Phenyl acetate,* $C_6H_5 \cdot OOCCH_3$,

is a type of these and is prepared by the action of acetyl chloride on phenol:

$$C_6H_5O\underline{H + Cl}OCCH_3 = C_6H_5 \cdot OOCCH_3 + HCl.$$
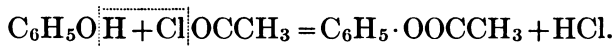
The **substitution products of phenol.** In these one or more hydrogens of phenyl, C_6H_5, are replaced by some radicle, but the hydroxyl group remains intact. They form a large class, but only a few of the compounds will be discussed here, the most important of the others being considered later.

Tribromphenol, $C_6H_2Br_3OH$, is precipitated by treating phenol with bromine water (see exp. above).

Mononitrophenol, $C_6H_4(NO_2)OH$, may be ortho or para and is prepared by the action of dilute nitric acid on phenol.

Trinitrophenol, $C_6H_2(NO_2)_3OH$, or **picric acid,** is prepared by allowing strong nitric acid to act on phenol (see exp. below). The NO_2 groups are symmetrically attached to the benzene ring, thus:

$$O_2N\overset{\displaystyle -OH}{\underset{\displaystyle NO_2}{\bigcirc}}NO_2.$$
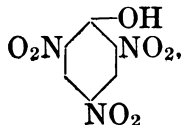
It forms yellow prismatic crystals, has a bitter taste, and is very poisonous. In watery solution it stains

silk and wool yellow, and is used in histology for staining elastic fibers and also zymogen granules in gland cells. Like nitroglycerol, it is an explosive and its potassium and ammonium salts are extensively employed for this purpose. The substitution of three H atoms by the negative NO_2 groups in picric acid evidently increases its acidity, i.e., its dissociability into H ions (cations) and anions of the rest of the molecule (see exp. below).

Picric acid has an anæsthetic action on burns.

By the action of phenolsulphonic acid on nitrates production of picric acid results. This is the basis of one of the methods of estimating small quantities of nitrates, as in water for drinking purposes.

$$C_6H_4(OH)SO_3H + 3HNO_3 = C_6H_2(OH)(NO_2)_3$$
$$+ H_2SO_4 + 2H_2O.$$
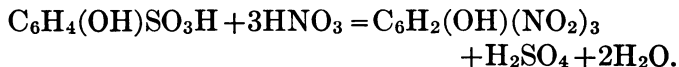
EXPERIMENTS. (1) *Prepare picric acid.* Put 10 gm. of C.P. HNO_3 into a flask, and add slowly 10 gm. of phenol. When the action has subsided, add 30 gm. of fuming nitric acid and boil until the liquid becomes yellow. Avoid boiling down to dryness, since an explosion will result. Cool, dilute the crystalline mass with water, and filter with suction. Wash the crystals with water, and recrystallize from a considerable quantity of hot water acidulated with 5 drops of H_2SO_4:

$$C_6H_5OH + 3HONO_2 = C_6H_2(NO_2)_3(OH) + 3H_2O.$$
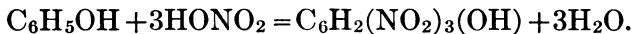
(2) Warm gently a little picric acid with 5 c.c. of petroleum ether in a test-tube; a colorless solution is

secured (no ionization). Pour the petroleum ether into water and shake; the water becomes yellow from the picric acid dissolved in it (ionization).

(3) Immerse pieces of woolen, silk, and cotton cloth in picric acid solution for fifteen minutes. Wash them thoroughly with running water. Which are dyed?

Aminophenols (see p. 382).

Phenolsulphonic acids (see p. 393).

Cresols   (hydroxytoluenes), $C_6H_4\Big\langle\begin{matrix}CH_3\\OH\end{matrix}$.   In accordance with the theory it is possible, by starting from the corresponding toluene-sulphonic acids or toluidines, to obtain three cresols, viz., ortho, meta, and para. The mixture of cresols is called *tricresol* or cresylic acid. Cresol is also produced in the intestine by the action of micro-organisms on protein. Cresol (chiefly para) may be excreted in the urine in combination with sulphuric acid, exactly as in the case of phenol (p. 340). **Lysol** is a mixture of cresols with soap, and is said to be as strongly germicidal as phenol but less irritating. **Creolin** forms with water an emulsion of cresols. These substances possess antiseptic properties and are less poisonous than phenol. They are extensively used for disinfecting purposes.
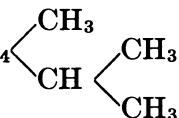
Parahydroxytolyl mustard oil, obtained by hydrolysis of **sinalbin** (p. 253), is a thiocyanate derivative of para cresol, $C_6H_4\Big\langle\begin{matrix}OH\\CH_2-CNS\end{matrix}$.

Thymol and carvacrol are isopropyl cresols.

That this is so is shown by the fact that they can both be converted into cymene, $C_6H_4\begin{cases} CH_3 \\ CH\begin{cases} CH_3 \\ CH_3 \end{cases} \end{cases}$ (by removal of OH). They also give the reactions of phenols, and might therefore be considered as hydroxycymenes. Thymol is isopropylmetacresol,

$$C_6H_3\begin{cases} CH_3 \ (1) \\ OH \ (3) \\ C_3H_7 \ (4) \end{cases} \text{ or }$$
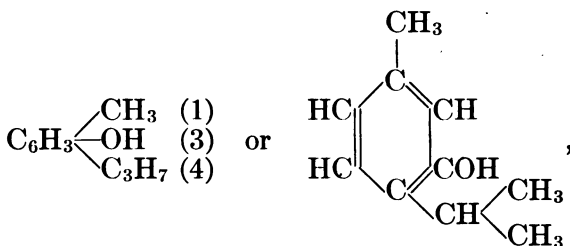
and carvacrol is isopropylorthocresol,

$$C_6H_3\begin{cases} CH_3 \ (1) \\ OH \ (2) \\ C_3H_7 \ (4) \end{cases} \text{ or }$$
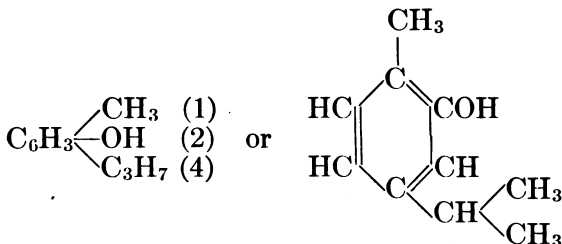
Thymol is contained in oil of thyme and is an antiseptic, being less poisonous than phenol. The melting-point of its crystals is 49.4° (corrected). In spite of the fact that it dissolves only to the extent of about 0.1% it is an efficient preservative agent. Carvacrol is contained in *oil of caraway*.

Aristol (thymol iodide) is dithymol di-iodide. It is an antiseptic powder.

DIACID PHENOLS

These are ortho, meta, and para. There is a gradation in melting-points, o 104°, m 119°, and p 169°. (Not all o, m, p compounds show consistent rise in melting-point in this manner.) They all have more or less marked reducing properties, and on this account some of them (especially hydroquinol) are used as developers in photography. With ferric chloride they all give color reactions by becoming partially oxidized.

Orthodihydroxybenzene, pyrocatechol (1, 2-phendiol, *pyrocatechin*, catechol),
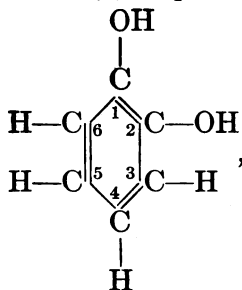
can be made by fusing orthophenol-sulphonic acid with caustic potash. It is soluble in water. By introducing a methyl radicle in place of a hydrogen atom of one hydroxyl group, **guaiacol** (monomethyl ether of pyrocatechol, $C_6H_4\left\langle\begin{smallmatrix}OCH_3\\OH\end{smallmatrix}\right.$) is obtained. This latter can also be separated from beech-wood tar by distillation and crystallization, and is sometimes used, particularly as one of its compounds, in the treatment of phthisis. Guaiacol benzoate, or **benzosol**, and guaiacol carbonate, or **duotal**,

$(C_6H_4 \cdot OCH_3O)_2CO$, have also been much used as remedies for tuberculosis.

The most important constituents of *creosote* are guaiacol and *creosols*, $C_6H_3 \underset{\diagdown OCH_3}{\overset{\diagup CH_3}{\underset{}{\longleftarrow OH}}}$.

Metadihydroxybenzene, resorcinol (1, 3-phendiol,

resorcin),

, is made by fusing
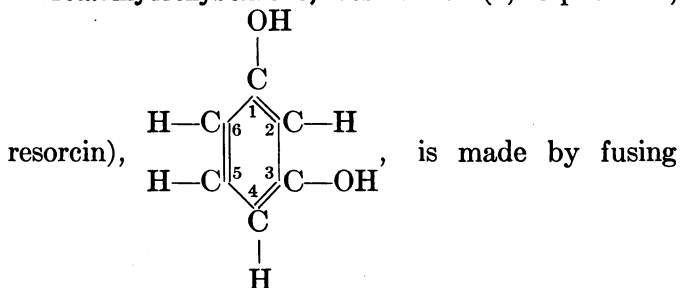
metabenzene-disulphonic acid with caustic potash. It is soluble in water, and its solutions have a sweetish taste. When heated with phthalic acid it forms fluorescein (see exp., p. 372), and with sodium nitrite a blue pigment, *lacmoid*, solutions of which turn red with acids.

Paradihydroxybenzene,   hydroquinol (hydroquinone, quinol, 1,4-phendiol),
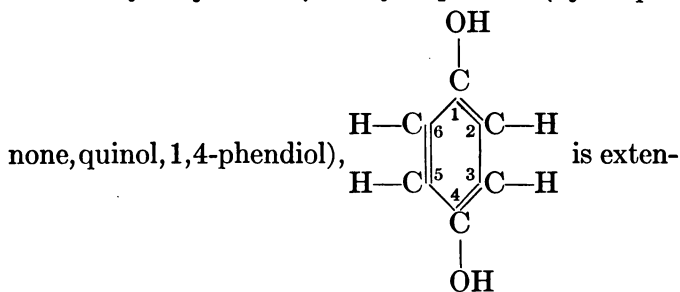
is exten-

sively used in photography.

Dihydroxytoluene, orcinol (orcin), $C_6H_3 \!\!\begin{array}{l} \diagup CH_3 \quad 1 \\ -OH \quad 3, \\ \diagdown OH \quad 5 \end{array}$

is prepared by fusing 1, 3, 5-chlortoluene-sulphonic acid with caustic potash. On treatment with ammonia it absorbs oxygen from the air and is converted into *orcein*, $C_{28}H_{24}N_2O_7$, which dissolves in alkalies to form a dark-red dye. Orcein is used in histology. It is contained in the natural dye archil, which is prepared, like litmus, by exposing powdered lichens suspended in ammoniacal solution to the action of the air.

Unsaturated derivatives of diacid phenols.

Eugenol, or parahydroxy-metamethoxy-allyl-benzene,

$$\begin{array}{c} \diagup C \!\!=\!\! CH_2 \!-\! CH \!\!=\!\! CH_2 \\ HC \diagup \quad \diagdown CH \\ \parallel \quad \quad \mid \\ HC \diagdown \quad \diagup COCH_3 \\ C \!\!-\!\! OH \end{array}$$

, is the chief substance in *oil of cloves*, and is contained in other drugs.

Eugenol acetamide, eugenol carbinol, eugenol iodide, and benzeugenol have been put on the market as medicinal preparations.

Safrol is contained in oil of sassafras and camphor oil. It is the methylene ether of allyl pyrocatechol:

$$C_6H_3 \!\!\begin{array}{l} \diagup CH_2 \cdot CH \!\!=\!\! CH_2 \ (1) \\ -O \diagdown \\ \diagdown O \diagup CH_2 \ (3 \text{ and } 4). \end{array}$$

Apiol has the same formula as safrol, except that it has OCH_3 groups in the place of H in positions 2 and 5.

Pyrogallol (*pyrogallic acid*, 1, 2, 3–phentriol) is 1, 2, 3 (*adjacent*, see p. 329) trihydroxbenzene, $C_6H_3(OH)_3$, and can be prepared by the dry distillation of gallic acid (see exp. below):

$$C_6H_2 \begin{cases} (OH)_3 \\ COOH \end{cases} = C_6H_3 {<} \begin{matrix} OH \ (1) \\ OH \ (2) \\ OH \ (3) \end{matrix} + CO_2.$$

(Gallic acid)   (Pyrogallol)
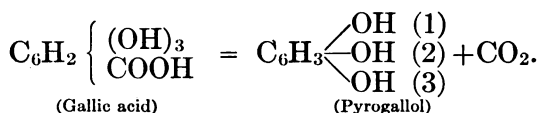
It forms fine needle-shaped crystals and is easily soluble in water. The solution when made alkaline greedily absorbs oxygen from the air, so that it is used for this purpose in gas analysis (see exp. below). Carbonates and acetates along with some carbon monoxide gas are produced by the oxidation. It is also extensively employed as a developer in photography.

Phloroglucinol (*phoroglucin*, 1, 3, 5-phentriol), $C_6H_3(OH)_3$, is 1, 3, 5 (*symmetrical*) trihydroxybenzene, and is obtained by the action of caustic potash on *phloretin*, which is split off from the glucoside phloridzin (see p. 252) by boiling the latter with acids.

Phloroglucinol is also employed along with vanillin in alcoholic solution as an indicator (*Günzberg's reagent*) for free mineral acid. When a drop of this reagent, mixed with the acid solution, is evaporated to dryness, it gives a deep-red stain if mineral acid is present.

Hydroxyhydroquinol is asymmetrical tri-hydroxy-benzene.

EXPERIMENTS. (1) Carefully heat 5 gm. of dry gallic acid in a retort or sublimation apparatus; carbon dioxide is evolved and pyrogallol sublimes. Test some of the latter with dilute ferric chloride solution; an intense blue-black color is obtained.

(2) Put 1 gm. of pyrogallol into a dropping funnel, add 10 c.c. of strong NaOH solution, cork tightly, and shake vigorously for a few minutes. Connect the stem of the funnel (after filling the stem with water) with a burette, the burette and tubing being full of water; open the cock, whereupon the water rises to take the place of the oxygen that has been absorbed.

Level up the water in the burette and the funnel, then read from the burette how much water was required to replace the oxygen that was absorbed. By finding how much more water is needed to fill the funnel completely, the volume of unabsorbed air (N_2) is easily determined.

(3) Test solutions of resorcinol and pyrocatechol with ferric chloride; color reactions are obtained.

AROMATIC ALCOHOLS (ALDEHYDES AND KETONES)

Besides the above, we may also have hydroxy derivatives of benzene in which the hydroxyl group instead of replacing one of the hydrogens of the benzene nucleus, is connected with a side chain. The best example is **benzyl alcohol,** $C_6H_5 \cdot CH_2OH$, which is *phenyl carbinol.* In their reactions such alcohols differ entirely from phenols and indeed possess all the properties of fatty primary alcohols. Thus, benzyl alcohol can be prepared by boiling

benzyl chloride for some time (6–8 hours) with water (cf. synthesis of methyl alcohol, p. 137):

$$C_6H_5CH_2\underset{\text{(Benzyl chloride)}}{|Cl+H|}OH = C_6H_5 \cdot CH_2OH + HCl.$$
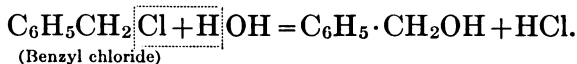
The Cl group, being in this case connected with a side chain and not with the benzene nucleus, is easily replaceable by OH. Benzyl alcohol may also be made by treating benzoic aldehyde (oil of bitter almonds) with nascent hydrogen:

$$\underset{\text{(Benzoic aldehyde)}}{C_6H_5 \cdot CHO} + 2H = C_6H_5 \cdot CH_2OH.$$
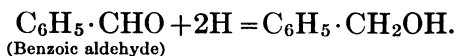
The reactions of this alcohol agree with those of fatty alcohols: oxidation yields first an aldehyde (benzaldehyde) and then an acid (benzoic); ethers, such as benzyl methyl ether ($C_6H_5 \cdot CH_2O \cdot CH_3$), and ethereal salts, such as benzyl acetate

$$(C_6H_5CH_2 \cdot OOCCH_3),$$
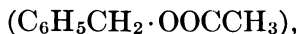
are easily obtained. There are also substitution products (which, however, are not obtained by direct treatment) where one or more of the H atoms of the nucleus are replaced, e.g., chlorbenzyl alcohol, $C_6H_4Cl \cdot CH_2OH$.

Benzyl alcohol, however, differs in many respects from aliphatic alcohols; for instance, it does not form an ester with sulphuric acid. Its boiling-point is 206.5°.

The *homologues* of benzyl alcohol are of two kinds: (*a*) those in which the phenyl group remains unchanged, but the alcoholic side chain contains some higher fatty radicle, and (*b*) those in which the alco-

holic side chain remains unchanged (i.e., remains as carbinol), but one or more of the H atoms of the benzene nucleus become replaced by radicles, as in

tolyl carbinol, $C_6H_4{<}^{CH_3}_{CH_2OH}$.
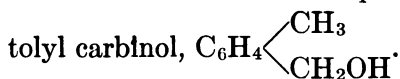
These alcohols, since they contain the primary alcohol group, can be oxidized to aldehydes and acids.

Benzoic aldehyde (benzaldehyde, oil of bitter almonds), $C_6H_5 \cdot CHO$, is an important substance, being very reactive and therefore much employed for organic synthesis. Besides being produced by oxidation of benzyl alcohol, it can be obtained by the action of a hydrolyzing ferment—emulsin—on amygdalin, a glucoside contained in bitter almonds, the stone of the peach, etc. (see p. 252). The emulsin is usually present along with the amygdalin. Hydrocyanic acid is also produced during the reaction:

$$C_{20}H_{27}NO_{11} + 2H_2O =$$
(Amygdalin)
$$= C_6H_5 \cdot CHO + HCN + 2C_6H_{12}O_6.$$
(Benzaldehyde)   (Dextrose)
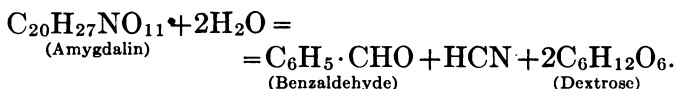
It can also be prepared by distilling a mixture of a benzoate and a formate, and by heating benzal chloride, $C_6H_5CHCl_2$, with water and milk of lime under pressure:

$$C_6H_5C{<}^{H}_{\substack{Cl + H\ O\ H \\ Cl + H\ O\ H}} = C_6H_5 \cdot CHO + 2HCl + H_2O.$$
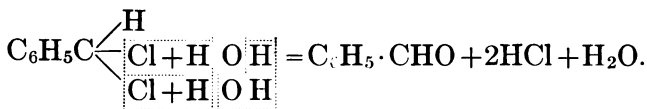
Commercially it is made from benzyl chloride. It is an oil of a pleasant odor, boiling at 179° and

having a specific gravity of 1.0504 at 15°.   Although relatively insoluble in water, it is used as a flavoring agent.   It is not poisonous.   Like other aldehydes, it forms addition products with such substances as hydrocyanic acid and acid sulphites.   It also combines with alcohols, acids, ketones, etc., and forms a hydrazone (see p. 388) with phenylhydrazine, $C_6H_5 \cdot CH = N \cdot NH \cdot C_6H_5$.   When a solution of benzyl aldehyde in dilute alcohol containing some potassium cyanide is boiled, two molecules of it condense, forming *benzoin*, $C_6H_5 \cdot CHOH \cdot COC_6H_5$.   In contact with air benzaldehyde readily oxidizes to benzoic acid, and with nascent hydrogen it combines to form benzyl alcohol.

When benzaldehyde is treated with acetic anhydride, *benzoyl acetyl peroxide*,

$$C_6H_5 \cdot CO—O—O—OC \cdot CH_3,$$
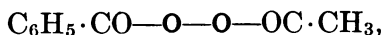
is produced.   The formula is comparable to that of hydrogen peroxide, $H—O—O—H$.   This is called **acetozone** (or benzozone) and is believed to have strong germicidal powers by virtue of being a peroxide.   It is used therapeutically for intestinal disorders.

Any aromatic aldehyde when shaken with strong KOH and allowed to stand, undergoes oxidation and reduction simultaneously, the product being equal quantities of alcohol (reduction) and acid (oxidation).

EXPERIMENTS.   (1) To 5 c.c. of benzyl chloride in a small flask add 50 c.c. of water and 5 gm.

barium nitrate, also some capillary tubes (to prevent bumping). Attach to a reflux condenser and boil for two hours. If unchanged benzyl chloride is still present, filter. Cool, add a few c.c. of ether, and draw off the bottom layer with a pipette. Shake with three portions of ether in a separating funnel. Evaporate the ether. Note the oily drops and the odor of benzaldehyde. Add some Schiff's reagent and warm; a beautiful color is developed, which is intensified on heating, because benzaldehyde is soluble in hot water, but only slightly soluble in cold water.

$$2C_6H_5 \cdot CH_2Cl + Ba(NO_3)_2 =$$
$$= 2C_6H_5 \cdot CHO + BaCl_2 + NO + NO_2 + H_2O.$$
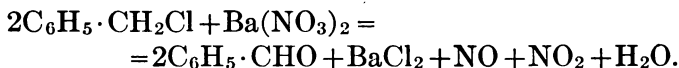
(2) To some solution of phenylhydrazine in acetic acid add a little water and a few drops of benzaldehyde. Collect the precipitate and crystallize it from alcohol. The crystals of hydrazone melt at 152°.

(3) Spread a drop of benzaldehyde on a watch-glass, and let it stand until crystals of benzoic acid appear.

(4) Mix 10 c.c. of benzaldehyde and 12 c.c. of alcohol in a small flask. Add 10 c.c. of 10% KCN solution; now heat, using a reflux condenser, for thirty minutes. Cool, filter off the crystals of benzoin, and recrystallize from hot alcohol.

(5) To a solution of amygdalin add emulsin, cork the tube, and keep at 40° for some hours. Note the odor; also test with Schiff's reagent.

Cinnamic aldehyde has the formula

$$C_6H_5—CH=CH—CHO.$$
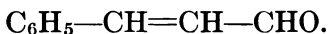
It is the essential constituent of *cinnamon oil*. Synthetic cinnamic aldehyde is displacing the natural oil.

Saligenin is both an alcohol and a phenol; it is an ortho compound having the formula,

$$C_6H_4\left<{OH \atop CH_2OH}\right..$$
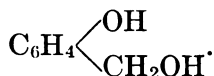
It is combined with dextrose in the glucoside salicin (see p. 252).

Ketones. The CO group may be attached to two phenyl groups (aromatic ketones), or linked to a phenyl and fatty group (mixed aromatic fatty ketones).

These are prepared by methods analogous with those already studied in connection with aliphatic ketones, thus:

a. By distilling calcium benzoate, diphenyl ketone or *benzophenone* is produced:

$$\begin{array}{c}C_6H_5CO\;O \\ C_6H_5\;COO\end{array}\Big>Ca = \begin{array}{c}C_6H_5 \\ C_6H_5\end{array}\Big>CO + CaCO_3.$$
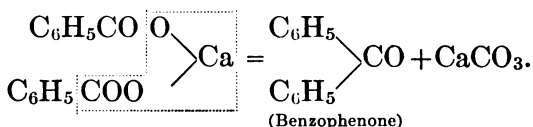
(Benzophenone)

b. By distilling salts of two different aromatic acids, such as a salt of benzoic and one of toluic acid:

$$\begin{array}{c}C_6H_4\!<\!\!{CH_3 \atop COOM}\;^1 \\ + \\ C_6H_5COOM\end{array} = \begin{array}{c}C_6H_4\!<\!\!{CH_3 \atop CO} \\ C_6H_5\end{array} + M_2CO_3.$$

(Phenyltolylketone)
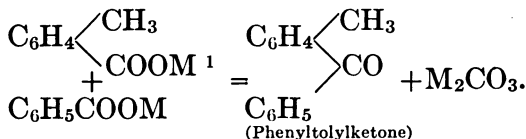
[1] The salt usually employed is that of calcium. M means a metal.

c. By distilling a salt of an aromatic acid with one of a fatty acid:

$$\begin{matrix} C_6H_5COOM \\ + \\ CH_3COOM \end{matrix} = \begin{matrix} C_6H_5 \\ \\ CH_3 \end{matrix} \Big\rangle CO + M_2CO_3.$$

(Methyl phenyl ketone or acetophenone)
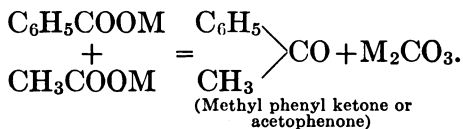
Acetophenone may also be obtained by adding aluminium chloride to a mixture of benzene and acetyl chloride. It is a crystalline substance melting at 20.5°, and is slightly soluble in water. It is used in medicine as a hypnotic under the name of *hypnone.*

CHAPTER XXVII

AROMATIC ACIDS

MONOBASIC ACIDS

AROMATIC acids are in general analogous with those of the paraffins, being monobasic, dibasic, etc. The representative *monobasic* acid is **benzoic,** $C_6H_5 \cdot COOH$. This acid is of great commercial value and of much physiological interest, since, as will be explained later, it is the end product of the oxidation in the animal body of a large number of benzene derivatives having oxidizable side chains.

It can be prepared by numerous reactions, the most important of which are as follows:

1. By oxidation of *any* benzene derivative with a single fatty side chain. It follows from this that if an aromatic substance yields benzoic acid on oxidation, it must contain only one side chain. When two side chains exist, a dibasic acid (phthalic) is obtained. Thus the hydrocarbons of the benzene series, $C_6H_5CH_3$, $C_6H_5C_2H_5$, $C_6H_5C_3H_7$, their monacid alcohols and aldehydes, $C_6H_5CH_2OH$, $C_6H_5CH_2CH_2OH$, C_6H_5CHO, etc., and their halogen derivatives where the halogen is situated in the side chain, all yield benzoic acid when oxidized.

2. By hydrolysis of benzonitrile, C_6H_5CN (see

p. 256). The reagent can be obtained by substituting the CN group for an H of benzene, either by distilling potassium benzene sulphonate with potassium cyanide,

$$C_6H_5SO_3K + KCN = C_6H_5CN + K_2SO_3,$$
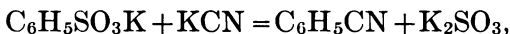
or by heating a diazonium salt with $Cu_2(CN)_2$ (see p. 385).

3. By treating *benzoyl chloride* (see p. 359) with water, $C_6H_5CO|Cl + H|OH$.

4. By treating boiling toluene with chlorine, whereby *benzotrichloride*, $C_6H_5CCl_3$, is produced, which is then boiled with water (see exp. below):

$$C_6H_5C \begin{cases} Cl \quad H \quad O\,H \\ Cl + H \quad O\,H \\ Cl \quad H \quad O\,H \end{cases} = C_6H_5COOH + 3HCl + H_2O.$$
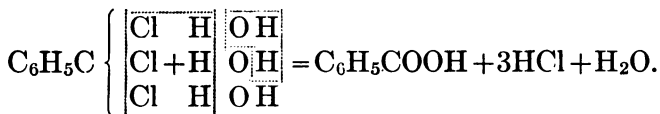
This is the ordinary commercial method.

5. By sublimation or treatment of gum benzoin with alkalies.

6. By heating hippuric acid (see p. 360) with hydrochloric acid (hydrolysis):

$$C_6H_5C{\overset{\displaystyle O}{\diagup}}NH \cdot CH_2COOH + H_2O =$$
(Hippuric acid)

$$= C_6H_5COOH + CH_2{\diagdown}{\overset{NH_2}{\diagdown COOH}}.$$
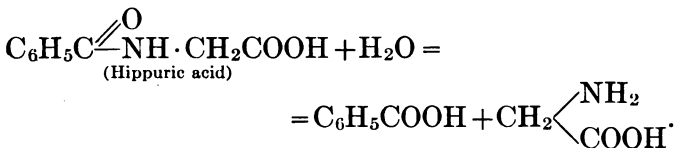
Benzoic acid forms needle-shaped crystals, which melt at 121.3° (corrected) and readily sublime. It is slightly soluble in cold water, but its solubility increases with rise in temperature until, at 90°,

the water contains 11.2% of the acid, and the crystals that remain undissolved liquefy and form a layer beneath the water. When the temperature is further raised in a closed tube, the two layers gradually mix till, at 116°, a homogeneous liquid is obtained. Salicylic acid (p. 363) behaves in a similar manner. The lower liquid layer is a solution of water in the acid, not melted acid. It is soluble in alcohol and ether, and volatilizes with steam. Its salts and derivatives are very numerous, and are analogous with those of acetic acid. Most of them are soluble in water.

Of the *metallic salts* those of sodium and ammonium are employed as medicines.

The *ethereal salts* are prepared in the same way as are those of acetic acid (see exp. (1) (*a*)).

Balsams (e.g., balsam of Tolu and balsam of Peru) contain as their important constituents benzoic and cinnamic acids, both as free acids and as their esters in combination with benzyl alcohol. *Gum benzoin* is a balsam containing less cinnamic acid than other balsams.

EXPERIMENTS. (1) *Preparation of benzoic acid.* Put into a flask 5 c.c. of benzotrichloride, 100 c.c. of water, and small pieces of pumice. Attach to a reflux condenser and boil for two hours. Before cooling add 200 c.c. of hot water and filter at once. Cool, collect the crystals on a filter, recrystallize from hot water, and make the ethyl benzoate test on the dried crystals as follows: to some of the dried benzoic acid add 1 c.c. of alcohol and about 3 c.c.

of concentrated H_2SO_4. Heat; just as it begins to boil, notice the peppermint-like odor of ethyl benzoate. Save a sample of benzoic acid.

(2) Heat together 1 c.c. of benzaldehyde and an excess of potassium permanganate solution until the odor of benzaldehyde is imperceptible. Add permanganate as required to maintain a pink color. Decolorize with a few drops of alcohol. Cool, filter, and add HCl to the filtrate; benzoic acid crystallizes out:

$$C_6H_5CHO + O = C_6H_5COOH.$$
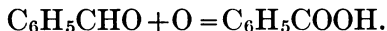
(3) Sublime benzoic acid from impure benzoic acid, (see p. 13).

BENZOIC ACID DERIVATIVES

Benzoyl chloride, the acid chloride of benzoic acid, C_6H_5COCl, can be obtained by the action of chlorine on benzaldehyde, or by the action of PCl_5 on benzoic acid: $C_6H_5COOH + PCl_5 = C_6H_5COCl + POCl_3 + HCl$. It is more stable than acetyl chloride, not being decomposed by water in the cold. It resembles acetyl chloride, however, in that it reacts with the hydroxyl group of alcohols to form esters of benzoic acid. The presence of caustic alkali greatly facilitates this reaction. It reacts thus with the hydroxyl groups in dextrose, the resulting ester being insoluble in water and in dilute alkali.

EXPERIMENT. To 10 c.c. of 10% NaOH add 4 drops of glycerol and 1 c.c. of benzoyl chloride. Cork the tube, and shake until a curdy precipitate

forms, cooling the tube frequently. Add 10 c.c. of water, shake and filter. Crystallize the glyceryl tribenzoate from 15 c.c. of hot 65% alcohol.

The *substitution products* of benzoic acid are numerous, for of each there may be an ortho, meta, and para variety. They can be made by oxidizing the corresponding substituted toluenes, or by direct substitution of one or more of the hydrogens of the phenyl radicle in benzoic acid, the methods being the same as are used for the substitution products of benzene. The chlorbenzoic acids, the nitrobenzoic acids, the aminobenzoic acids, and the sulphobenzoic acids are examples (see p. 394). The aminobenzoic acids are weaker than benzoic acid, while the nitrobenzoic acids are stronger.

Novocaine is a derivative of para-aminobenzoic acid, $C_6H_4(NH_2)COO—CH_2 \cdot CH_2—N(C_2H_5)_2 \cdot HCl$. It is built up from ethane by substitution of an H in each CH_3 group, diethylamine hydrochloride being the second substituting group. It is a local anæsthetic, introduced as a substitute for cocaine.

Stovaine and *alypin*, local anæsthetics of somewhat similar nature, are also benzoic acid derivatives.

An important compound of benzoic acid, from a biochemical standpoint, is **hippuric acid**. This is benzoylaminoacetic acid, $C_6H_5CO \cdot NH \cdot CH_2COOH$. It is present in the urine of herbivorous animals, being produced in the kidney by synthesis from glycin and benzoic acid. It also appears in human urine when benzoic acid is administered, or when

foods yielding it in the organism are ingested. It may be prepared in the laboratory by several methods:

1. Heating glycocoll and benzoic acid to 160° in a closed tube.

2. Shaking glycin dissolved in sodium hydroxide solution with benzoyl chloride (see exp. below):

$$C_6H_5CO|Cl+H|HNCH_2COOH =$$
$$= C_6H_5CO \cdot NH \cdot CH_2COOH + HCl.$$
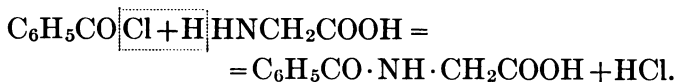
3. Heating *benzamide* with chloracetic acid (benzamide is analogous to acetamide, see p. 274):

$$C_6H_5CONH|H+Cl|CH_2COOH =$$
$$= C_6H_5CO \cdot NH \cdot CH_2COOH + HCl.$$
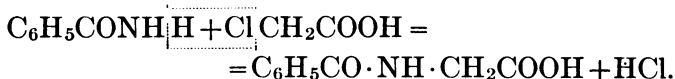
Hippuric acid is relatively insoluble in cold water, alcohol, and ether, and forms long rhombic crystals, having a melting-point of 187.5° (corrected). It is readily decomposed by boiling with acids or alkalies, and also decomposes when urine containing it undergoes fermentation.

EXPERIMENTS. (1) *Synthesize hippuric acid.* Shake together 4 c.c. of benzoyl chloride and a solution of 2.5 gm. of glycocoll in 30 c.c. of 10% NaOH (keeping the flask corked) until the odor of the chloride has disappeared. Cool whenever the mixture gets hot. Filter, and acidulate the alkaline filtrate with HCl. Collect the hippuric acid on a filter, wash with a little water, press dry between filter-paper, and recrystallize from hot water. Save a sample. Test part of it as follows.

(2) (*a*) Test the solubility of hippuric acid in petroleum ether (compare benzoic acid). (*b*) Heat a little dry hippuric acid in a test-tube; benzoic acid sublimes, while the residue becomes reddish.

Corresponding to *toluene* there are four monobasic **toluic acids**. Three of these (*o-*, *m-*, *p-*) have the formula $C_6H_4\diagup^{CH_3}_{COOH}$ and are made by oxidizing the corresponding xylenes with nitric acid. The fourth has the formula $C_6H_5CH_2COOH$, and might properly be called **phenyl-acetic acid**. It is obtained by treating benzyl chloride, $C_6H_5CH_2Cl$, with potassium cyanide and hydrolyzing the resulting nitrile ($C_6H_5CH_2CN$):

$$C_6H_5CH_2CN + 2H_2O = C_6H_5CH_2COOH + NH_3.$$
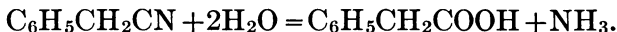
A homologue of this is phenyl-propionic or **hydrocinnamic acid,** $C_6H_5CH_2CH_2COOH$.

Cinnamic acid is an unsaturated compound, its formula being $C_6H_5 \cdot CH = CH \cdot COOH$. It is used therapeutically.

Mandelic acid is a hydroxy acid, its formula being $C_6H_5 \cdot CHOH \cdot COOH$.

Mesitylene yields only one acid, **mesitylenic,** $C_6H_3\diagup^{CH_3}_{\diagdown^{CH_3}_{COOH}}$. This is of importance because it can be converted into metaxylene by distillation with lime (cf. benzene, p. 319):

$$C_6H_3\diagup^{CH_3}_{\diagdown^{CH_3}_{COOH}} + CaO = C_6H_4\diagup^{CH_3}_{\diagdown CH_3 \, (m)} + CaCO_3.$$
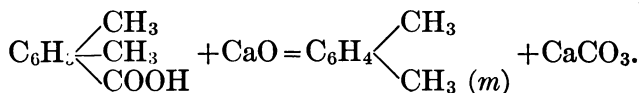
PHENOLIC MONOBASIC ACIDS

An acid group may exist along with one or more phenolic hydroxyl groups. According to the number of the latter groups we may have mono-, di-, and tri-hydroxybenzoic acids.

A. *Monohydroxybenzoic acids,* $C_6H_4 {<} {OH \atop COOH}$.

The *ortho* variety of this is **salicylic acid,** an extremely important medicinal substance. Oxidation of the alcohol saligenin (above) yields salicylic acid. It may be prepared by a variety of reactions, the chief of which are as follows:

(1) By saponifying methyl salicylate (oil of wintergreen) with caustic potash,

$$C_6H_4 {<} {COO\overline{CH_3} \atop OH} + \overline{OH}K = C_cH_4 {<} {COOK \atop OH} + CH_3OH.$$
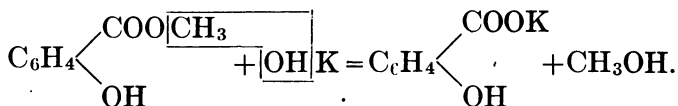
The potassium salicylate thus formed can be decomposed by acidifying with hydrochloric acid (see exp. 1, p. 366).

(2) By subjecting sodium phenolate to the action of carbon dioxide under pressure (and at 140°), sodium phenyl carbonate, $C_6H_5OCOONa$, is formed, which by heating to 140° in an autoclave, becomes converted into sodium salicylate (an intramolecular change taking place):

$$C_6H_5{-}O{-}COONa = C_6H_4 {<} {COONa \atop OH}.$$
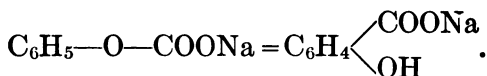
This method is used commercially.

. (3) By fusing orthotoluene-sulphonic acid, ortho-cresol, or orthosulphobenzoic acid with caustic potash. In the case of the first two bodies oxidation of the methyl side chain occurs. The replacement of the sulphonic group by hydroxyl has already been explained (cf. p. 337).

(4) By converting orthoaminobenzoic acid into the diazonium salt and boiling this with water (see p. 384).

Salicylic acid crystallizes in needles and melts at 159° (corrected). It is readily soluble in hot water, but only sparingly so in cold. Its aqueous solutions give an intense violet color with ferric chloride. It is readily soluble in fat-solvents. Solutions of salicylic acid possess antiseptic properties, and, having no odor, it is therefore employed for preserving wines, foods, etc. Its sodium salt, $C_6H_4\begin{smallmatrix} \diagup COONa \\ \diagdown OH \end{smallmatrix}$, has great medicinal value in the treatment of rheumatism.

There are also *meta* and *para* hydroxybenzoic acids, which can be prepared from the corresponding amino- or sulphonic-benzoic acids. They do not react with ferric chloride.

The meta and para acids are weaker acids than salicylic acid, and have a somewhat different physiological action. The introduction of OH in the ortho position increases the acid power of the molecule, so that salicylic acid is much stronger than benzoic acid.

Salicylic acid forms various salts, the salicylates, many of which are important. **Methyl salicylate,**

$C_6H_4{\Large\langle}^{OH}_{COOCH_3}$, is the chief constituent of oil of wintergreen. It can be made synthetically by heating methyl alcohol with sulphuric acid and salicylic acid. A very interesting compound of salicylic acid is phenyl salicylate, $C_6H_4{\Large\langle}^{OH}_{COOC_6H_5}$ · or **salol.** It is produced by heating salicylic acid alone to 200°–220° (see exp. 3).

$$2C_6H_4{\Large\langle}^{OH}_{COOH} = C_6H_4{\Large\langle}^{OH}_{COOC_6H_5} + CO_2 + H_2O;$$
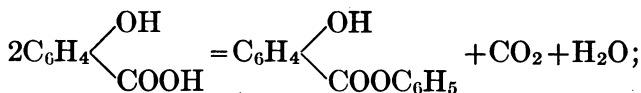
or by heating phenol and salicylic acid in the presence of phosphorus oxychloride:

$$3C_6H_4{\Large\langle}^{OH}_{COOH} + 3C_6H_5OH + POCl_3 =$$

$$= 3C_6H_4{\Large\langle}^{OH}_{COOC_6H_5} + H_3PO_4 + 3HCl.$$
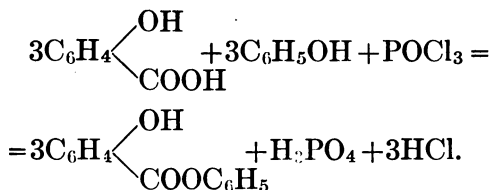
Salol is a white crystalline powder, somewhat aromatic in odor and melting at 43°. It is insoluble in water and unaffected by dilute acids. Alkalis readily saponify it, however, and yield salicylate and phenol. Taken internally it will therefore remain undecomposed till it reaches the intestine, when the phenol and salicylate liberated by action of the alkali will act as antiseptics. On this account it has been used for intestinal antisepsis.

EXPERIMENTS. *Salicylic acid.* (1) Saponify 5 c.c. of oil of wintergreen by boiling with 100 c.c. of 20% NaOH, using a reflux condenser, until the oil has disappeared. Cool, acidulate with HCl, collect the crystals on a filter, and wash them with a small quantity of water. Dissolve the salicylic acid in a little hot alcohol, and filter the solution into a beaker half full of cold water. Collect the crystals.

(2) Tests. (*a*) Add ferric chloride solution to some salicylic acid solution; a violet-blue color is produced. Compare the similar phenol test. Try ferric chloride with alcoholic solutions of phenol and of salicylic acid. (*b*) Mix a little salicylic acid with some soda-lime and heat in a dry test-tube until the odor of phenol is noticed.

(3) *Prepare salol* as follows: Fill a dry test-tube one-third full of salicylic acid, and fit the test-tube with a cork having a piece of small glass tubing eight inches long passing through it. Now heat gradually, boil the melted salicylic acid for five minutes, and, removing the cork, pour the hot liquid into some cold water in a beaker. Collect the insoluble material, and heat it with some water in a test-tube, when it soon melts and sinks as dark-colored drops. Decant off the water, and add 2 c.c. of H_2SO_4; on heating a reddish color develops.

There are several derivatives of salicylic acid among the newer remedies, as **sanoform** or diiodomethyl salicylate, **salophen** or acetyl-para-

minóphenyl salicylate, and **salipyrin,** a combination of salicylic acid with antipyrin.

More important are the drugs which act as local anæsthetics on raw surfaces, the orthoforms, anæsthesin and nirvanin.

Orthoform is the methyl ester of aminohydroxy-benzoic acid, $C_6H_3\begin{cases} NH_2 & (1) \\ OH & (2) \\ COOCH_3 & (4) \end{cases}$. A *new* ortho-form has been prepared in which the positions of OH and NH_2 are reversed.

Anæsthesin has been proposed as a remedy to be used in the place of orthoform; it is the ethyl ester of para-amino benzoic acid. **Nirvanin** is the methyl ester of diethylglycocoll-aminosalicylic acid,

$$C_6H_3\begin{cases} NH \cdot OCCH_2N(C_2H_5)_2 & (1) \\ OH & (3) \\ COOCH_3 & (4) \end{cases}$$
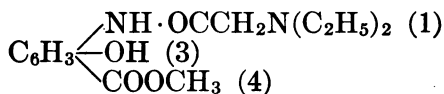
Aspirin is acetyl-salicylic acid, $C_6H_4\begin{cases} OOCCH_3 \\ COOH \end{cases}$.

Novaspirin is a citric acid derivative,
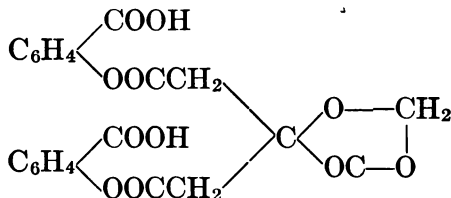
Both of the aspirins are invaluable substitutes for sodium salicylate.

Betol is the β-naphthol ester of salicylic acid, ·

$$C_6H_4(OH)COO \cdot C_{10}H_7.$$

B. *Dihydroxybenzoic acid.* **Protocatechuic acid,**

$$C_6H_3 \diagdown \begin{matrix} COOH & (1) \\ OH & (3) \\ OH & (4) \end{matrix} .$$
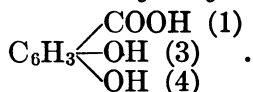
Its monomethyl ether, $C_6H_3 \diagdown \begin{matrix} COOH \\ OCH_3, \\ OH \end{matrix}$

is vanillic acid, which is derived from vanillin, the

corresponding aldehyde, $C_6H_3 \diagdown \begin{matrix} CHO \\ OCH_3, \\ OH \end{matrix}$ by oxidation.

Vanillin, contained in the vanilla-bean, is extensively employed as a flavoring agent. It is used, with phloroglucin, as an indicator for free mineral acid (see p. 402). Synthetically it can also be prepared by treating guaiacol, $C_6H_4 \diagdown \begin{matrix} OCH_3 \\ OH \end{matrix}$, with chloroform and caustic soda.

C. *Trihydroxybenzoic acid* is the important compound gallic acid, $C_6H_2 \begin{cases} COOH & (1) \\ OH & (3) \\ OH & (4) \\ OH & (5) \end{cases}$ $(+H_2O)$. This

is contained in certain plants, but is most readily obtained by boiling tannin with dilute mineral acid, or by fermenting oak gallnuts. **Tannic acid** (tannin), obtained from nutgall, consists of two molecules of gallic acid minus one molecule of water; it is therefore a condensation product.

Tannic acid will be seen to bear a relation to gallic

acid similar to that which disaccharides bear to monosaccharides:

$$C_{14}H_{10}O_9 + H_2O = 2C_7H_6O_5.$$

$$\text{(Tannic acid)} \qquad\qquad \text{(Gallic acid)}$$
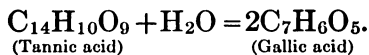
The following structural formulæ have been proposed for tannic acid:
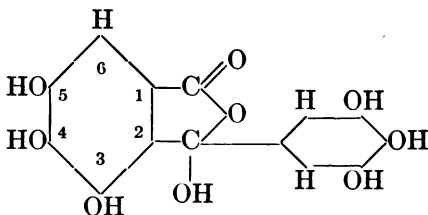
and
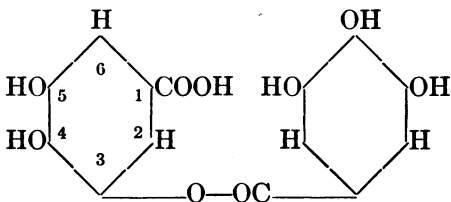
Its constitution is still under discussion.

That gallic acid has the structural formula given to it above is proved by the fact that it can be prepared by fusing bromprotocatechuic acid with KOH:
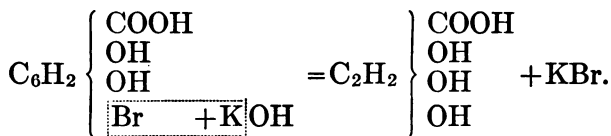
Gallic acid is almost insoluble in cold water, but soluble in hot water, alcohol, and ether; and with

ferric chloride its solutions give first a precipitate
and then form a dark-green solution. A *blue-
black ink* is made by adding gallic acid to a slightly
acid solution of ferrous sulphate to which indigo
carmine has also been added. When this dries on
paper it oxidizes, giving a heavy black precipitate.
When distilled, gallic acid yields pyrogallic acid
and carbon dioxide (see p. 349). **Airol** and **dermatol**
are combinations of gallic acid with bismuth.

Tannic acid is much more soluble than gallic,
the solution being colloidal. It gives the same reac-
tion with ferric chloride. Tannic acid solution is
slightly dextrorotatory. It has a very extensive
commercial use in tanning, in which process it forms
insoluble and tough compounds with the protein,
etc., in skin. It is also employed, on account of
its astringent properties, in medicine. Many de-
rivatives of tannic acid have been prepared as sub-
stitutes for it, such as **tannalbin, tannacol, tannigen,
tannoform,** etc.

There are many substances of vegetable origin
similar in properties to tannic acid, but having dif-
ferent chemical structure. These are classed to-
gether as *tannins.* When acted upon by molten
KOH some of these yield gallic acid, while others
yield protocatechuic acid. The tannin of tea and
that of coffee are not identical with tannic acid.

EXPERIMENTS. (1) Test solutions of gallic acid
and tannic acid with ferric chloride.

(2) Add tannic acid solution to some gelatin solu-
tion; the gelatin is precipitated.

(3) To a solution of quinine bisulphate (quinine dissolved in very dilute H_2SO_4) add tannic acid solution; the quinine is precipitated.

D. *Other phenolic acids.* **Tyrosin** is a phenol having an α amino acid side chain. It is parahydroxyphenyl-α-aminoproprionic a c i d , $C_6H_4\diagdown\begin{smallmatrix}OH\\CH_2 \cdot CHNH_2 \cdot COOH\end{smallmatrix}$. Tyrosin is derived from protein. Being a phenol it gives a test with Millon's reagent. Proteins that contain no tyrosin (as gelatin, certain albumoses, etc.) do not give this test. It occasionally occurs in the urine as characteristic crystals. **Phenylalanin** is closely related to tyrosin, differing only in not being a phenol; its formula is $C_6H_5 \cdot CH_2 \cdot CHNH_2 \cdot COOH$. **Homogentisic acid** is dihydroxyphenylacetic acid, $C_6H_3\diagdown\begin{smallmatrix}OH\ (5)\\OH\ (2)\\CH_2 \cdot COOH\ (1)\end{smallmatrix}$. It has been found in the urine in cases of alcaptonuria, being derived from tyrosin and phenylalanin.
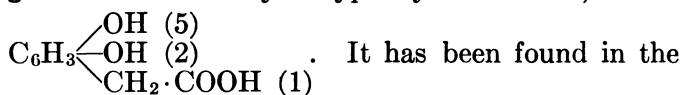
DIBASIC ACIDS

In agreement with theory, there are three of these. They are called **phthalic acids.** Orthophthalic acid is prepared by oxidizing naphthalene (see p. 409) with sulphuric acid, or by oxidizing *o*-toluic acid with potassium permanganate. When heated it decomposes into water and an anhydride,

$$C_6H_4\diagdown\begin{smallmatrix}COOH\\COOH\end{smallmatrix}_{(o)} = C_6H_4\diagdown\begin{smallmatrix}CO\\CO\end{smallmatrix}\diagup O + H_2O,$$
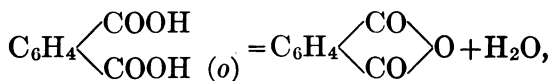
which latter, when heated with phenol in the presence of H_2SO_4, yields phenolphthalein (see exp. 3), a body of complicated structure used extensively as an indicator in volumetric analysis, being red in alkaline and colorless in acid solution (see p. 399). It is also used now as a cathartic.

The meta- and paraphthalic acids do not form anhydrides. Certain iodine derivatives of phenolphthalein, as *nosophen, eudoxine,* and *antinosine,* are used as medicines.

When phthalic anhydride is acted upon by ammonia, an acid imide, *phthalimide,*

$$C_6H_4 \diamond \begin{matrix} C=O \\ NH, \\ C=O \end{matrix}$$
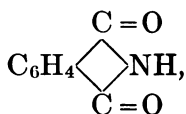
is formed.

EXPERIMENTS. (1) Heat some phthalic acid in a sublimation apparatus (see p. 13); the sublimate is phthalic anhydride.

(2) To some phthalic anhydride add an equal quantity of resorcinol and 1 c.c. of concentrated H_2SO_4, then warm until deep red. Dilute with 100 c.c. of water and render alkaline with NaOH. The resulting solution of *fluorescein* is pinkish to transmitted light, but shows a marked greenish fluorescence to reflected light:

$$C_6H_4 \diamond \begin{matrix} CO \\ CO \end{matrix} O + 2C_6H_4 \diamond \begin{matrix} OH \\ OH \end{matrix} = C_6H_4 \diamond \begin{matrix} CO \\ C \end{matrix} O + 2H_2O$$

$$HO \cdot H_3C_6 \quad C_6H_3 \cdot OH$$

$$O$$

(Fluorescein)
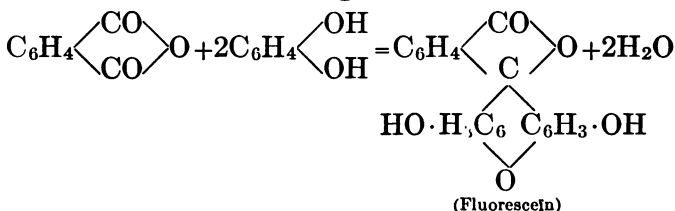
(3) Mix equal quantities of phthalic anhydride and phenol, add a little C.P. H_2SO_4, and warm until strongly colored. Pour into a large quantity of water. This solution of phenolphthalein becomes red when it is made faintly alkaline:

$$2C_6H_5OH + C_6H_4{\overset{CO}{\underset{CO}{\diagup\diagdown}}}O =$$

$$= C_6H_4{\overset{C-}{\underset{CO}{\diagup\diagdown}}}O (C_6H_4OH)_2 + H_2O.$$

(Phenolphthalein)
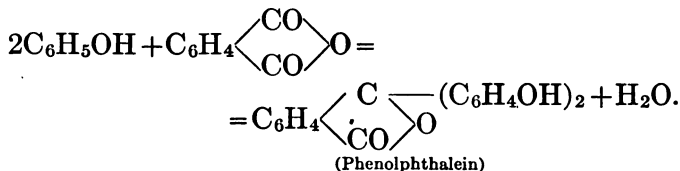
(4) Prepare eosin. To 2.5 gms. of fluorescein add 10 c.c. of alcohol, then add, a drop at a time, 2 c.c. of bromine, shaking the mixture after each addition. When enough bromine has been added to form dibromfluorescein, the latter goes into solution, then as tetrabromfluorescein is formed it crystallizes out. After the mixture has stood for an hour, filter and wash the crystals with a little cold alcohol. To a little of the eosin add NaOH solution; the eosin now dissolves, forming a solution of characteristic red color.

Eosin is an acid dye, being the potassium or sodium salt of **tetrabromfluorescein,**
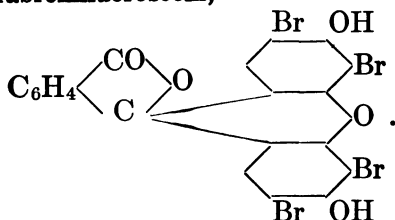
There is a *hexabasic* acid, viz., **mellitic,** $C_6(COOH)_6$, which is present in the mineral mellite in combination with aluminium.

CHAPTER XXVIII

AROMATIC NITROGEN DERIVATIVES

THERE is very little similarity between the nitrogen compounds of the aromatic bodies and those of the paraffins. The nitro compounds of the paraffins we have seen to be of little importance; those of the aromatic bodies, on the other hand, are of prime importance, because they are readily produced and are easily converted into other nitrogenous derivatives. On this account *nitration* forms the first step in many organic syntheses.

NITRO COMPOUNDS

By shaking benzene in the cold with a mixture of pure nitric and sulphuric acids, **mononitrobenzene,** an oily liquid, is obtained.[1] The sulphuric acid absorbs the water produced:

$$C_6H_6 + HNO_3 = C_6H_5NO_2 + H_2O$$
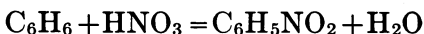
Its boiling-point is 210°, melting-point 5°, and its specific gravity 1.2033 at $\dfrac{20°}{4°}$.

EXPERIMENT. To 80 c.c. H_2SO_4 in a flask add, while shaking, 70 c.c. of colorless HNO_3. Cool thor-

[1] Mononitrobenzene has the odor of bitter almonds and is known as essence of mirbane. It is poisonous.

oughly. Add (a little at a time) 20 c.c. of benzene, keeping the temperature of the mixture below 30° and shaking frequently. Take 30 minutes for the work of adding the benzene. Attach a vertical air-condenser tube; heat for an hour in a bath kept at 60°, shaking occasionally. Cool, dilute with 120 c.c. of water, pour into a separating funnel, draw off the bottom layer of acid, and wash the oil with water (the nitrobenzene becomes the bottom layer). Warm gently with dry calcium chloride in a flask on a water-bath. Distill in a fractionating flask; when the temperature rises above 100° attach an air-condenser, and observe the boiling-point. Note the odor of the distillate.

If, on the other hand, the reaction be allowed to proceed at boiling temperature and with fuming nitric acid the product is **dinitrobenzene,** a crystalline substance (needles) melting at 90° (corrected) and boiling at 297°.

$$C_6H_5NO_2 + HNO_3 = C_6H_4{\Large\langle}{{NO_2}\atop{NO_2}} + H_2O.$$
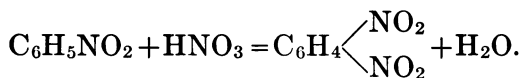
Although three varieties of this are possible, it is almost exclusively the meta form that is produced.

EXPERIMENT. *Prepare   dinitrobenzene   (meta).* Mix in a beaker 25 c.c. of C.P. H_2SO_4 and 25 c.c. of fuming HNO_3. Immediately add very slowly 5 c.c. of benzene from a pipette. After the action subsides, boil for a while and then pour the mixture into 250 c.c. of cold water. Filter off the precipitate,

press between filter-paper, and crystallize from alcohol. Make a melting-point determination with dried crystals. Save a sample of the crystals.

Toluene and the xylenes react with nitric acid in the same manner. In fact, the more alkyl groups there are attached to the benzene nucleus, the more easily can nitro groups be introduced into it. The nitro compounds are very stable.

Trinitrotoluene has recently come into use as an explosive.

AMINO COMPOUNDS

The most important reaction of nitro compounds is that with nascent hydrogen, whereby they become converted into amino compounds, of which **aniline** (phenylamine) is the representative:

$$C_6H_5NO_2 + 6H = C_6H_5NH_2 + 2H_2O.$$
$$\text{(Aniline)}$$
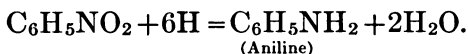
Commercially, aniline is produced by mixing nitrobenzene with iron filings and hydrochloric acid in an iron cylinder provided with a stirring apparatus, and, when the action is over, adding lime and distilling the aniline. It is a colorless liquid boiling at 183.7° (corrected); its specific gravity at 16° is 1.024. If not perfectly pure it becomes colored on standing. It is soluble in about 30 parts of water, and one part of water is soluble in about 20 parts of aniline at 25°. It is readily soluble in alcohol. It gives several important color reactions, described in the experiments below. A blue coloring matter is produced by the action of

potassium dichromate and sulphuric acid (see 2*b*); this is the same substance as the first artificial dye-stuff that was produced (in 1856). Aniline may be considered as NH_3 in which one H is displaced by C_6H_5. Like all such bodies (see p. 258), it directly combines with acids to form (aniline) salts, e.g., $C_6H_5NH_2.HCl$; $C_6H_5NH_2.HNO_3$; $C_6H_5NH_2.H_2SO_4$. The hydrochloride is technically known as *aniline salt*. In watery solution, however, aniline is not alkaline towards litmus and scarcely conducts an electrical current; in other words, it does not become ionized (see p. 65). It is, therefore, quite different in this respect from aliphatic amines, which with water form bases, some of which are stronger even than ammonia (cf. p. 260). Phenyl (C_6H_5) diminishes the basic properties of the amino (NH_2) group, but fatty residues increase the basic properties of NH_2. Whereas nitrous acid decomposes fatty amines with liberation of nitrogen (p. 260), it converts aromatic amines into diazonium compounds (p. 384).

Aniline can be liberated from the acid in its salts by distilling with caustic alkali:

$$C_6H_5NH_2 \cdot HCl + KOH = C_6H_5NH_2 + KCl + H_2O.$$
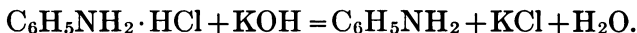
It can also be obtained by distilling indigo (hence its name, *anil* being the Spanish for indigo). It is an extremely important substance in organic synthesis.

EXPERIMENTS. (1) *Preparation of aniline.* Put 30 gm. of granulated tin and 15 c.c. of nitrobenzene into a large flask, add gradually (in portions of

5 c.c. each) 100 c.c. of C.P. HCl, and cool the flask whenever the action becomes very vigorous.   When all the acid has been added, heat on a water-bath for one hour, using a vertical air-condenser.   Now dilute with 50 c.c. of water, cool to room temperature, pour into a separating funnel, and shake with ether to remove unchanged nitrobenzene.   Add 50% NaOH until strongly alkaline; cool the flask if the mixture boils.   Distill with steam, until the distillate comes clear.   Add to the distillate 25 gm. NaCl for each 100 c.c.; shake in a separating funnel with three portions of ether.   Dry the ether extract with solid potassium hydroxide.   Next empty the liquid into a fractionating flask, distill off the ether, then distill the aniline, using an air-condenser.

(2) *Tests.*   (a) Dissolve a *little* $KClO_3$ in 0.5 c.c. H_2SO_4; adding a few drops of aniline solution causes a blue-violet color to appear; diluting with water changes it to red;   then adding ammonia restores the blue.   (b) To a solution of aniline in H_2SO_4 add a few drops of potassium dichromate solution; a blue color appears.   (c) To some aniline solution (in water) add a filtered solution of bleaching-powder; a purple color develops.

Derivatives of Aniline.   The *homologues* include three **toluidines,** $C_6H_4\!\!<^{CH_3}_{NH_2}$, of which the ortho and para varieties are important, and six **xylidines,** $C_6H_3\!\!<^{(CH_3)_2}_{NH_2}$, this large number of isomers being due to differences in the relative positions of the

amino and methyl groups. When a mixture of aniline and paratoluidine is treated with oxidizing agents, a compound known as para-rosaniline is obtained. Many of the aniline dyes are derivatives of this substance. *Fuchsin* is methyl para-rosaniline,
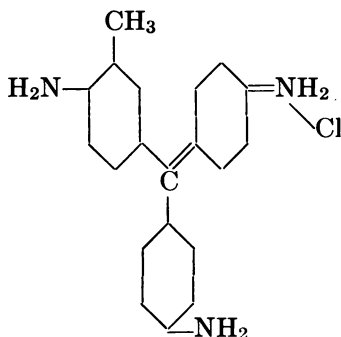
Acid fuchsin is a sulphonic acid derivative.

Dyes that have this structure are called the triphenylmethane dyes.

EXPERIMENT. Heat together in a test-tube 1 c.c. of aniline, 1 gm. of paratoluidine, and 3 gm. $HgCl_2$ until dark red in color (15 minutes at 180–200°). Cool partly, and extract with alcohol; a deep-red solution is obtained. Filter, and evaporate the filtrate.

Replacement of one or more of the H atoms of the NH_2 group in aniline can be effected in various ways.

By reaction with alkyl halides secondary and tertiary *mixed aromatic fatty amines* are obtained.

Thus methyl iodide produces methyl aniline and dimethyl aniline:

$$C_6H_5NH\overline{H+I}CH_3 = C_6H_5NHCH_3 \cdot HI$$

and $C_6H_5NHCH_3 + ICH_3 = C_6H_5N\diagup^{CH_3}_{\diagdown CH_3} \cdot HI.$
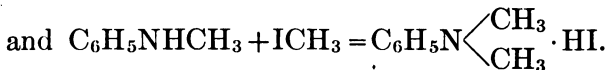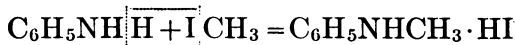
Some quaternary base is also formed by the reaction.

Dimethyl aniline is commercially the most important of these mixed amines and is prepared by heating aniline hydrochloride with methyl alcohol, methyl chloride being first formed, which then reacts as above.

Dimethyl aniline is oxidized to **methyl violet,** by the action of cupric chloride in the presence of potassium chlorate, acetic acid, and sodium chloride; the copper salt acting as an oxygen carrier. Methyl violet 2B has the following formula:

$$C\diagup^{C_6H_4N(CH_3)_2}_{\diagdown C_6H_4 = N(CH_3)_4.}$$
$$\diagdown Cl$$
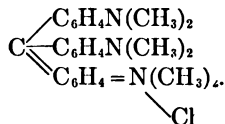
This is a triphenylmethane dye; its relationship to fuchsin is indicated by the chemical name hexamethylpararosaniline. Methyl violet B is pentamethylpararosaninile. Both of these are present in commercial methyl violet.

Methyl violet is also called *pyoktanin*.

In a similar manner replacement with phenyl groups may occur, di- and triphenylamine being produced.

Diphenylamine, $C_6H_5NHC_6H_5$, is obtained by heating aniline with aniline hydrochloride to 200°:

$$C_6H_5NH\overline{H+HClNH_2}C_6H_5 =$$
$$= C_6H_5NHC_6H_5 + NH_4Cl.$$
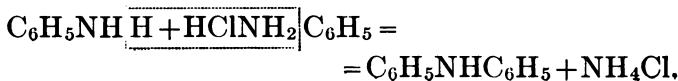
Dissolved in concentrated sulphuric acid, it is a reagent which detects traces of nitric acid by formation of a deep blue color. It is changed to tetra-phenylhydrazine.

With acid chlorides, aniline forms *anilides*, which are analogous with the acid amides (see p. 273):

$$CH_3CO \overline{|Cl+H|} HNC_6H_5 = CH_3COHNC_6H_5 + HCl.$$
$$\text{(Acetanilide)}$$
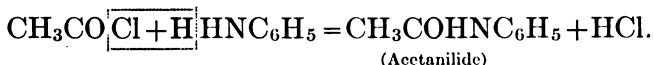
One of these, **acetanilide** (phenylacetamide), is of very great therapeutic interest on account of its antipyretic properties. It is the active drug in many proprietary headache medicines (antikamnia, antifebrine, orangine powders, etc.). These remedies are not entirely harmless, since acetanilide acts as a circulatory depressant. Acetanilide is easily prepared by heating aniline with glacial acetic acid (see exp.):

$$C_6H_5NH \overline{|H+HO|} OCCH_3 =$$
$$= C_6H_5 \cdot NH \cdot OCCH_3 + H_2O.$$
$$\text{(Acetanilide)}$$
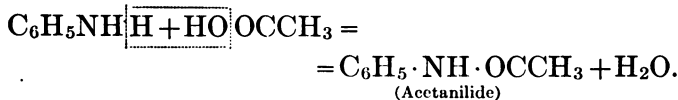
EXPERIMENT. Mix 10 c.c. each of aniline and glacial acetic acid in a small flask; fit with a long glass tube as a reflux condenser (this allows some of the water of reaction to escape, but condenses the acetic acid); boil for two hours. Dilute with 100 c.c. of boiling water and filter at once, using a hot funnel. On cooling, acetanilide crystallizes out. Recrystallize from hot water. Save a sample.

Acetanilide is very slightly soluble in cold water and crystallizes from hot water in colorless plates. It melts at 114.2° (corrected). Two other anti-

pyretic drugs are closely related to acetanilide. In
one of these, **exalgin** (methyl acetanilide), the hydro-
gen atom of the amido group is replaced by methyl,
$C_6H_5NCH_3COCH_3$. In the other, **benzanilide** (ben-
zoyl anilide), the acetyl radicle is replaced by ben-
zoyl, $C_6H_5 \cdot NH \cdot OCC_6H_5$.

Phenol and amino groups exist in the amino-
phenols, which are prepared by reducing the mono-
nitrophenols. The *para* variety is of therapeutic
interest. Its ethyl ether is known as *paraphenet-*
idin, $C_6H_4 \big\langle {}^{OC_2H_5}_{NH_2}$, and if this is treated with
glacial acetic acid, acetaminophenetole is formed,
$C_6H_4 \big\langle {}^{OC_2H_5}_{NH \cdot OCCH_3}$ which is known in medicine as
phenacetin (or acetphenetidin) and is perhaps the
safest antipyretic. Phenacetin is a white crystal-
line substance, sparingly soluble in water, and with a
melting-point of 135°.

A number of other phenetidin derivatives are
used in medicine, particularly holocain, lactophenin,
and phenocoll. **Holocain** is

$$C_6H_4 \big\langle {}^{OC_2H_5}_{NH} \big\rangle C - CH_3.$$
$$C_6H_4 \big\langle {}^{N}_{OC_2H_5}$$
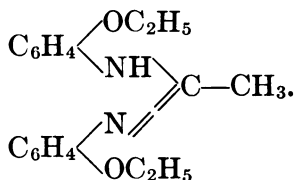
Lactophenin is lactylphenetidin,

$$C_6H_4 \big\langle {}^{OC_2H_5}_{NH \cdot OC \cdot CHOH \cdot CH_3}.$$
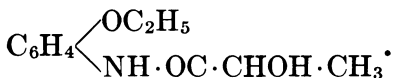
Phenocoll is aminoacetphenetidin (glycocoll phenetidin).

$$C_6H_4 \Big\langle \begin{matrix} OC_2H_5 \\ NH \cdot OC \cdot CH_2 \cdot NH_2 \end{matrix} .$$
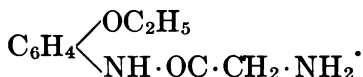
Acid and amino groups. By reducing the nitrobenzoic acids with tin and hydrochloric acid (nascent hydrogen) amino derivatives of benzoic acid may be obtained (cf. reduction of nitrobenzene to aniline, p. 376). The ortho variety of these is known as *anthranilic acid,* $C_6H_4 \Big\langle \begin{matrix} COOH \\ NH_2 \end{matrix}$. It is produced as an intermediate product in the preparation of aniline by boiling indigo with caustic alkali.

One of the most important nitrogenous aromatic compounds is an amine derivative of pyrocatechol. **Epinephrin** (adrenalin, suprarenin) has the following structural formula:
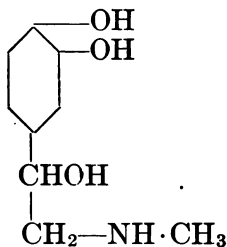
Epinephrin is the active principle in the extract from the suprarenal capsule, and when its solution is injected into the circulation of an animal, several important effects are observed, chief of which is rise of blood-pressure. It is optically active,

(α) D is -50.4 to $51.4°$. *d. l.* Suprarenin has been prepared synthetically. By treating this with tartaric acid, crystals can be obtained, from which *l.* suprarenin is secured. This is found to be identical with natural epinephrin. Synthetic *l.* suprarenin is now a commercial product. It is advisable to reserve the term *suprarenin* for the synthetically produced substance. The physiological action of racemic suprarenin is weak compared with that of *l.* suprarenin.

DIAZO AND DIAZONIUM COMPOUNDS

When fatty amino derivatives are treated with nitrous acid (see p. 260), nitrogen is evolved and a hydroxyl group takes the place of the amino group; with the aromatic amines, on the other hand, nitrous acid at low temperatures has quite a different action. It converts them into **diazo compounds,** so called because they contain two nitrogen (nitrogen $=$ *azote* (French)) atoms linked together. The *diazonium salts* are of very great importance in organic synthesis on account of the readiness with which they can be converted into other bodies. They are prepared by treating an ice-cold solution of an aniline salt with nitrous acid.

The diazonium salts are believed to contain the linking $-N-$.
$$\overset{\displaystyle -N-}{\underset{\displaystyle N}{\vert\vert\vert}}$$
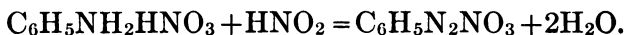
$$C_6H_5NH_2HNO_3 + HNO_2 = C_6H_5N_2NO_3 + 2H_2O.$$
(Benzene diazonium nitrate)

If a diazonium salt be dried and struck with a hammer, it explodes. Its important reactions are as follows:

1. *With water* it forms phenol and nitrogen:

$$C_6H_5N_2Cl + H_2O = C_6H_5OH + N_2 + HCl.$$
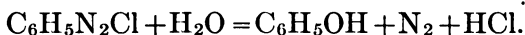
To obtain this result the diazonium salt is best prepared by treating a cold, acidified solution of an aniline salt with an equivalent quantity of sodium nitrite, and then boiling (see exp. 2, p. 338).

2. Boiling *with alcohol* causes replacement of the N_2 group either by ethoxy ($-O-C_2H_5$) or by hydrogen. In the first case phenyl ethyl ether or *phenetole* is formed:

$$C_6H_5N_2Cl + C_2H_5OH = C_6H_5OC_2H_5 + N_2 + HCl;$$
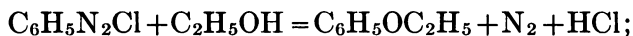
in the second case benzene and aldehyde:

$$C_6H_5N_2Cl + C_2H_5OH = C_6H_6 + CH_3CHO + N_2 + HCl.$$

3. Heating *with a halogen acid* or, better still, with an acid solution of the corresponding cuprous salt of the acid causes replacement of the N_2 group by the halogen:

$$C_6H_5N_2Cl + HCl = C_6H_5Cl + N_2 + HCl.$$
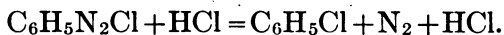
4. Heating *with cuprous cyanide* replaces the N_2 group by cyanogen:

$$C_6H_5N_2Cl + Cu_2(CN)_2 = C_6H_5CN + Cu_2{\Large\langle}^{CN}_{Cl} + N_2.$$
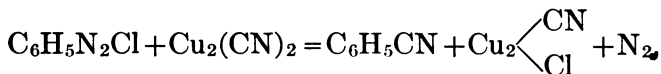
and the resulting nitrile can be hydrolyzed to form benzoic acid (see p. 356).

5. Nascent H changes a diazonium salt to phenyl-hydrazine (p. 388).

Other replacements by hydrocarbon residues, sulphur groups, etc., can also be effected.

EXPERIMENTS. (1) Prepare benzene diazonium nitrate. Put 50 gm. of arsenic trioxide into a flask; provide a funnel-tube, as in other gas-generators, and a delivery-tube which is connected with an empty bottle or cylinder standing in cold water. Mix 10 gm. of aniline nitrate with 12 c.c. of cold water in a graduate or large test-tube standing in ice-water, and immerse in the liquid a delivery-tube coming from the condenser-bottle of the gas apparatus. Through the funnel add 50 c.c. of concentrated HNO_3 to the As_2O_3; heat as is necessary to keep up an evolution of nitrogen oxides. Bubble the gas into the aniline nitrate mixture until complete solution is secured. Add to the solution an equal volume of alcohol cooled to 0°, then some cold ether. An abundant precipitate of benzene diazonium nitrate is obtained.[1] Filter quickly with suction. Test for the following reactions at once:

(2) (*a*) Dissolve some in water and let it stand. It

[1] A less troublesome method of preparation is as follows: dissolve 5 gm. aniline hydrochloride in 35 c.c. absolute alcohol which contains a few drops of concentrated HCl. Cool to 5°; add 4 c.c. ethyl nitrite very slowly while shaking and cooling. Test for HNO_2 with starch iodide paper. Add more ethyl nitrite if necessary. Let it stand a while, then add cold ether.

decomposes, as is shown by change of color. (*b*) Boil some with water; notice the phenol odor. (*c*) Boil some with alcohol in a test-tube; it is decomposed with production of phenetole. (*d*) Add some to a little concentrated HCl and boil. Chlorbenzene is formed: on adding water this sinks to the bottom. (*e*) The dried salt is explosive; place a small particle on a piece of iron and strike it with a hammer.

In all the above cases the N_2 group is replaced. Diazo compounds, however, exhibit another type of reaction in which the N_2 group is retained and a new substance of greater stability is produced. The more important of these substances are:

a. **Diazoamino Compounds.** In these, one of the hydrogens of an amino group is replaced by a diazo residue. A type of the class is *diazoaminobenzene*, $C_6H_5 \cdot N{=}N \cdot NH \cdot C_6H_5$, which is prepared by bringing together aniline and diazonium chloride in neutral solution. It forms yellowish crystals, which are insoluble in water but soluble in alcohol. By heating with aniline, and in various other ways, diazoaminobenzene becomes converted by a rearrangement of atoms into

b. **Aminoazobenzene,** $C_6H_5 \cdot N{=}N \cdot C_6H_4 \cdot NH_2$, which is the amino derivative of a substance called azobenzene.

Dimethylaminoazobenzene is a derivative, having the formula,

$$C_6H_5 \cdot N_2 \cdot C_6H_4 \cdot N(CH_3)_2.$$

It is used as an indicator for free acid, giving a pink color in the presence of the latter (see p. 402).

c. **Azobenzene,** $C_6H_5 \cdot N{=}N \cdot C_6H_5$.   Azobenzene can be obtained by partial reduction of nitrobenzene.   It forms orange-red crystals and is soluble in water, but the resulting solution is not a dye (see, p. 407).   The azo group is present, however, in many dyes.   It has been calculated that the number of azo dyes that can theoretically be prepared runs up into the millions.

d. **Hydrazobenzene,** $C_6H_5NH{-}NHC_6H_5$, is obtained by reducing azobenzene; it is colorless.   Hydrazobenzene is the diphenyl derivative of *hydrazine,* $NH_2{-}NH_2$.

Benzidine is produced from hydrazobenzene by the action of strong acids, the latter causing intramolecular rearrangement.   Its formula is

$$NH_2 \cdot C_6H_4 \cdot C_6H_4 \cdot NH_2.$$
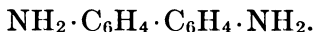
e. **Phenylhydrazine,** $C_6H_5NH{-}NH_2$, is the most important hydrazine derivative.   It forms hydrazones (see p. 352) with aldehydes, and osazones with sugars (see p. 235).   It is obtained by reduction of diazonium salts (see exp.):

$$C_6H_5N_2Cl + 4H = C_6H_5NH{-}NH_2 \cdot HCl.$$
$$\text{(Phenylhydrazine hydrochloride)}$$
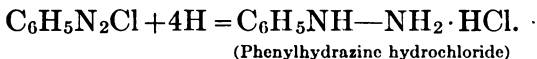
EXPERIMENT.   To 18 c.c. of freshly distilled aniline add, while stirring, 100 c.c. of concentrated HCl.   Cool in a freezing mixture to 0°, add 150 gm. of ice, then add slowly from a dropping funnel (have

the tip dipping in the ·mixture), while shaking, a solution of sodium nitrite (14 gm. in 70 c.c. of water), until testing with starch-potassium-iodide paper shows the presence of free nitrous acid (blue color). For the test dilute a drop of the acid mixture with 5 c.c. of water. During the diazotizing the temperature must keep below 5°. Add slowly an ice-cold solution of 60 gm. of stannous chloride in 50 c.c. of concentrated HCl. Add ice to keep the temperature at 0°. Mix thoroughly and let it stand one hour. Filter through muslin, using suction. Transfer to a porous plate, press out the phenylhydrazine hydrochloride crystals in a thin layer, and set away to dry out:

1. $C_6H_5NH_2 \cdot HCl + HNO_2 = C_6H_5N_2Cl + 2H_2O$.

2. $C_6H_5N_2Cl + 4H = C_6H_5NH \cdot NH_2 \cdot HCl$.
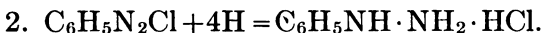
Free phenylhydrazine may be extracted by treating the hydrochloride with an excess of NaOH solution and shaking with ether. After dehydrating the ethereal extract, evaporate the ether; phenylhydrazine remains behind as a liquid which readily solidifies on cooling.

Phenylhydrazine is a colorless oil at ordinary temperature and boils at 242°, meanwhile undergoing some decomposition. It melts at 19°. It is poisonous. It becomes dark colored on exposure to air. Its salts, e.g., the hydrochloride, are solid and are sometimes employed in place of the base itself for producing osazone crystals, the hydrochloric acid being neutralized by sodium acetate.

The relationship of these bodies to nitrobenzene and aniline will be evident from an examination of the following formulæ:

$$C_6H_5NO_2 \quad \begin{array}{c} C_6H_5 \cdot N \\ \| \\ C_6H_5 \cdot N \end{array} \quad \begin{array}{c} C_6H_5 \cdot NH \\ | \\ C_6H_5 \cdot NH \end{array} \quad \begin{array}{c} C_6H_5 \cdot NH \\ | \\ NH_2 \end{array} \quad C_6H_5NH_2$$

(Nitroben-   (Azoben-   (Hydrazo-   (Phenylhydrazine)   (Aniline)
zene)   zene)   benzene)
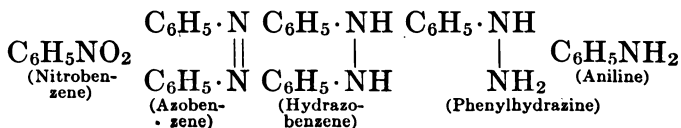
SULPHUR AND ARSENIC DERIVATIVES

SULPHUR DERIVATIVES

Sulphonic acids. With sulphuric acid the benzenes form sulphonic acids, thus:

$$C_6H_6 + H_2SO_4 = C_6H_5SO_3H + H_2O$$
(Benzene-sulphonic acid)

and $C_6H_5CH_3 + H_2SO_4 = C_6H_4\begin{smallmatrix}CH_3\\SO_3H\end{smallmatrix} + H_2O.$
(Toluene-sulphonic acid)
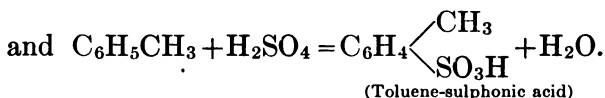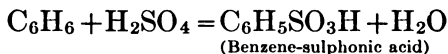
It is of importance to note that in this respect they behave quite differently from paraffins. When an alkyl group (as in toluene), an amino group (as in aniline), or a hydroxyl group (as in phenol) is attached to the benzene nucleus, the sulphonic acid derivative is more easily formed than when benzene alone, or any of its other derivatives, is used.

The sulphonic acids are soluble in water and are strong acids, so that their salts are very stable, e.g., $C_6H_5SO_3Na$. Treated with phosphorus pentachloride the salts of sulphonic acids form sulphonic chlorides, which may be reduced to mercaptans:

1. $C_6H_5SO_3Na + PCl_5 =$
$$= C_6H_5SO_2Cl + POCl_3 + NaCl.$$

2. $C_6H_5SO_2Cl + 6H = C_6H_5SH + HCl + 2H_2O.$
(Thiophenol)
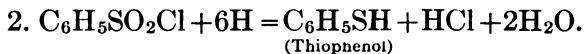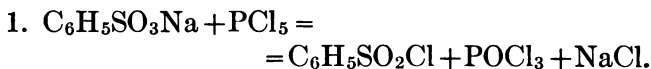
These reactions show us that sulphonic acids must possess an —OH group and that the S atom is in immediate connection with the benzene ring. The structural formula of benzene-sulphonic acid must therefore be $\begin{matrix} C_6H_5 \\ HO \end{matrix}\!\!\!\diagdown\!\!SO_2$ or sulphuric acid, $\begin{matrix} HO \\ HO \end{matrix}\!\!\!\diagup\!\!\diagdown\!\!SO_2$, in which one hydroxyl group is replaced by phenyl (cf. p. 306). They give several other reactions, the following of which are important:

1. *Fused with potassium hydroxide*, benzene-sulphonic acid yields phenol,

$$C_6H_5SO_3K + KOH = C_6H_5OH + K_2SO_3.$$
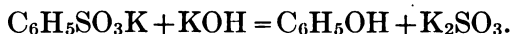
EXPERIMENTS. (1) To 75 gm. of fuming H_2SO_4 in a small flask to which an air-condenser is attached add, a little at a time, 20 gm. of benzene, shaking and cooling after each addition. Transfer to a dropping funnel, and run the mixture out, drop by drop, into 300 c.c. of cold saturated NaCl solution. Keep the salt solution cold with ice-water. On standing, crystals of sodium benzene sulphonate form. Crystallization may be hastened by strongly cooling some of the mixture in a test-tube and emptying the crystalline mass into the main liquid. Filter the pasty mass of crystals with suction and wash it with a little saturated salt solution. Press dry, and complete the drying in an oven at 110°.

(2) Weigh the dry powder (of 1); weigh five times as much KOH. Put the KOH in an iron dish, add a few cubic centimeters of water,

and melt. Then add slowly, while stirring with a spatula, the sodium benzene sulphonate. Keep fused for an hour. Dissolve in water, acidulate with HCl, shake with ether, and treat the ethereal solution of phenol in the same way as in the previous phenol experiments (see p. 338).

2. *Distilled with potassium cyanide*, cyanides are formed:

$$C_6H_5SO_3K + KCN = C_6H_5CN + K_2SO_3$$

and $C_6H_4 \Big\langle {}^{CH_3}_{SO_3K} + KCN = C_6H_4 \Big\langle {}^{CH_3}_{CN} + K_2SO_3.$
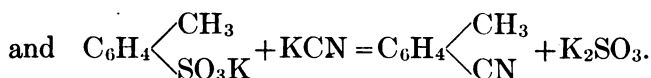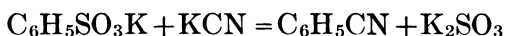
By hydrolysis these cyanides can be converted into acids:

$$C_6H_5CN + 2H_2O = C_6H_5COOH + NH_3.$$
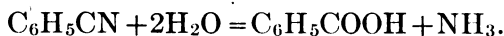
The toluene-sulphonic acids may be ortho or para. The meta variety is rare. The sulphonic acid group is present in many dyestuffs (see p. 407).

By the action of sulphuric acid on salicylic acid, **salicyl-sulphonic acid**, $C_6H_4 \Big\langle {}^{COOH\ (1)}_{OSO_3H\ (2)}$, is formed. This is a white crystalline deliquescent substance, readily soluble in water, the solution being a valuable precipitant for certain proteins. Its solutions on standing become colored red.

Phenol and sulphonic groups exist in phenol-sulphonic acid, $C_6H_4 \Big\langle {}^{SO_3H}_{OH}$ (*o* or *p*), which is commercially known as *aseptol* and used as a disinfectant.

The sodium salt of it is *sodium sulphocarbolate* (phenolsulphonate), and is used to arrest fermentation in the stomach.

Acid and sulpho groups. Metasulphobenzoic acid is produced by the action of sulphuric acid on benzoic acid. The important substance **saccharin** is the imide of orthosulphobenzoic acid,

$$C_6H_4 \underset{SO_2}{\overset{CO}{<}} > NH,$$
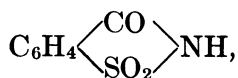
and is also called benzosulphinide. Its sodium salt (in which Na replaces H of NH) is called **soluble saccharin.** It is intensely sweet, and antiseptic; on account of these properties it is used as a medicine and a preservative.

Sulphonic and amino groups. By the action of sulphuric acid on aniline, aniline sulphate is formed, and then this becomes converted by heating into paraminobenzenesulphonic acid or **sulphanilic acid,** $C_6H_4 \underset{SO_3H}{\overset{NH_2}{<}}$, by dehydration:

$$C_6H_5NH_2 \cdot H_2SO_4 = C_6H_4 \underset{SO_3H}{\overset{NH_2}{<}} + H_2O.$$
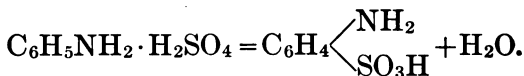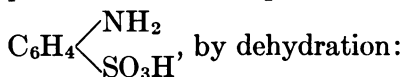
Sulphanilic acid is soluble in hot water, but only sparingly so in cold water. Its solution is acid in reaction, thus differing from that of taurin (amino-ethyl-sulphonic acid, see p. 272). It is used in the manufacture of dyes, in a large number of which there exists the sulphonic acid group along with a diazo group. Two of these dyes, viz., **methyl**

orange and **tropæolin OO,** are used as indicators in biochemistry.

EXPERIMENT. *Preparation of sulphanilic acid.* To 50 gm. of C.P. H_2SO_4 in a flask, add gradually 15 c.c. of aniline, and heat in an oil-bath at 180–190° for about four hours, until a test-drop, diluted with water and treated with NaOH, shows no unchanged aniline. Cool, and pour into a beaker of cold water while stirring the latter. Filter off the crystals. Evaporate the filtrate to small volume to secure more crystals. Recrystallize from hot water.

Helianthin is dimethylaminoazobenzene-sulphonic acid,

$$C_6H_4 \begin{cases} N{=}N{-}C_6H_4N(CH_3)_2 \ (1) \\ SO_3H \ (4) \end{cases},$$
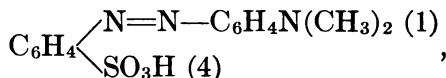
prepared by acting on benzene-diazonium-sulphonic acid with dimethylaniline. Its sodium salt is *methyl orange* (see indicators, p. 400).

Orange II is an azo dye, somewhat related to methyl orange in chemical structure:

$$C_6H_4 \begin{cases} N{=}N \cdot C_{1c}H_6 \cdot OH \\ SO_3H \end{cases}.$$
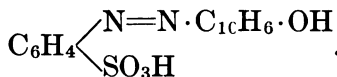
EXPERIMENT. Dissolve 10 gm. of dry sulphanilic acid in 100 c.c. of 2.5% Na_2CO_3 solution (made with anhydrous carbonate), and add 3.5 gm. of $NaNO_2$ dissolved in 20 c.c. of water. Cool with ice-water, gradually add diluted HCl (6 c.c. + 10 c.c. H_2O), and finally add an acid solution of dimethylaniline.

(6 gm. +6 c.c. HCl +20 c.c. H_2O).　Render the mixture alkaline with NaOH solution and add 20 gm. of NaCl.　Filter off the methyl orange precipitate and crystallize from hot water.　To a little dilute solution of methyl orange add some acid, a red color is obtained.　Save a sample of the crystals.

Tropæolin OO is diphenyl-aminoazobenzene-sulphonic acid, $C_6H_4{<}^{N_2—C_6H_4NHC_6H_5}_{SO_3H}$.　Its solution gives a violet color with free mineral acid; or, if its alcoholic solution be evaporated to dryness, the resulting residue, gives a violet color with free mineral acids.　Applied in this latter manner the test is very delicate.　It is thus used as an indicator in analysis of the gastric juice.

Methylene blue (methylthionin chloride) is a dye containing sulphur in the chromophore group (see p. 406).　It is a thiazine derivative, its formula being:

$$(CH_3)_2N— \underset{\displaystyle Cl}{\underset{|}{\overset{N}{\underset{S}{\bigcirc\bigcirc}}}} —N(CH_3)_2.$$
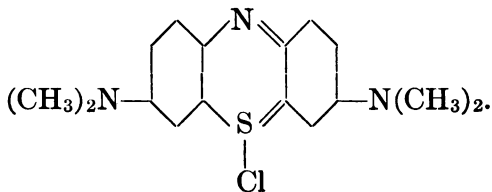
AROMATIC ARSENIC DERIVATIVES

An arsenic-containing derivative of ortho amino-phenol has been recently synthesized.　It is used as a remedy for syphilis.　Its trade name, **salvarsan** (*arseno-benzol* or " 606 "), gives little idea of its

composition.   It is the hydrochloride of dihydroxy-diamino-diarseno-(di-)benzene,

$$\underset{\underset{\text{OH}}{|}}{\overset{\overset{\text{As}=\text{As}}{|}}{\underset{\text{C}_6\text{H}_3}{\bigcirc}}}\text{—NH}_2 \quad \underset{\underset{\text{OH}}{|}}{\overset{\overset{}{|}}{\underset{\text{C}_6\text{H}_3}{\bigcirc}}}\text{—NH}_2$$
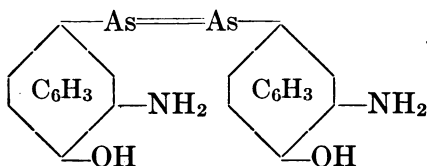
Another organic arsenic compound is *atoxyl*, in which an OH of monosodium arsenate is replaced by aniline,

$$\text{C}_6\text{H}_4 \Big\langle {}^{\text{NH}_2\ (1)}_{\text{AsO(OH) (ONa) (4)}}$$
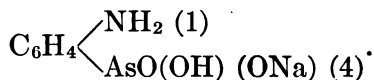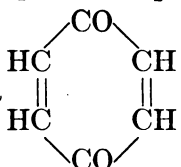
If the sodium be substituted by H, *arsanilic acid* is obtained.   *Arsacetin* is sodium acetyl arsanilate.

Quinones. These may be regarded as diketones. The best known of them is **benzoquinone** or *quinone*,

which has the structural formula

$$\underset{\displaystyle \diagdown CO \diagup}{\overset{\displaystyle \diagup CO \diagdown}{\underset{HC}{\overset{HC}{\underset{\|}{\overset{\|}{}}}} \quad \underset{CH}{\overset{CH}{\underset{\|}{\overset{\|}{}}}}} , \quad \text{and}$$

may be prepared by oxidizing various para derivatives of benzene, but not ortho or meta derivatives. Thus *p*-phenolsulphonic acid, *p*-sulphanilic acid, *p*-amino-phenol, etc., all yield quinone when oxidized. It is usually prepared, however, by oxidizing aniline with chromic acid or by oxidizing hydroquinol:

$$\underset{\underset{COH}{\overset{\|}{HC}} \quad \underset{CH}{\overset{\|}{CH}}}{\overset{COH}{\overset{\diagup\diagup}{\underset{HC}{\quad}\underset{CH}{\quad}}}} + O = \underset{\underset{C=O}{\overset{\|}{HC}} \quad \underset{CH}{\overset{\|}{CH}}}{\overset{C=O}{\overset{\diagup}{\underset{HC}{\quad}\underset{CH}{\quad}}}} + H_2O.$$
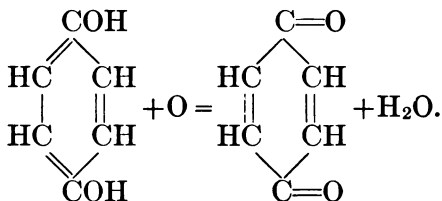
These reactions for its preparation (with the exception of its preparation from aniline) leave little doubt as to its structural formula.

The quinones are of a yellow color and possess a

398

pungent odor. In some particulars they behave like ketones, but in others very differently. They have oxidizing properties and are important in dye chemistry.

INDICATORS

At this stage it will be convenient to discuss briefly the **theory of the action of indicators.**

These must possess weak acid or basic properties, and be, therefore, undissociated when in a free state, but dissociated when present as salts. In the dissociated state the anion must have a different color from that of the undissociated compound.

Taking the three most commonly used indicators, phenolphthalein, methyl orange, and litmus, let us see in how far their actions can be thus explained.

(1) *Phenolphthalein.* This is of the nature of a very feeble acid, so that it is undissociated when in a free state, and when undissociated it is colorless. When dissociated, however, its anion has a red color. Dissociation occurs when it is converted into a salt. Thus, when we titrate an acid with sodium hydroxide, using phenolphthalein as indicator, what happens is this: In the presence of the acid the phenolphthalein is undissociated, and the solution is therefore colorless; as alkali is added the acid becomes gradually neutralized, until at last a trace of alkali in excess of that necessary to neutralize the acid is present; this trace combines with the phenolphthalein, forming a salt, which then dissociates, so that the anion imparts its red color to the solution.

The acid to be titrated must be distinctly stronger than phenolphthalein, for otherwise, before the former has all been neutralized, some of the salt formed will become hydrolyzed (see p. 70), and the base thus liberated will combine with the phenolphthalein and form a salt which, partially dissociating, will impart a pink tint to the solution. Thus, phenols cannot be titrated with phenolphthalein. On the other hand, such a feeble acid as carbonic is so much stronger than phenolphthalein that the latter can be employed as an indicator for titrating it. On this account carbon dioxide (carbonates) must be absent from the standard alkali used for titrating. Phenolphthalein can also be used for practically all organic acids.

The base used for neutralization must also be a strong one. Thus, if a feeble base such as ammonia is employed, then the salt which it forms with the phenolphthalein will be so feeble that it will be decomposed by the water (hydrolysis), and the end reaction will be indefinite, an excess of ammonia requiring to be present before the decomposing effect of the water is overcome. Phenolphthalein must not, therefore, be used when ammonia or ammonium salts are present in a solution.

Phenolphthalein is the ideal indicator for weak acids and acid salts, and should be employed along with a strong base.

(2) *Methyl Orange.* This is the sodium salt of a much stronger acid than phenolphthalein, and it dissociates readily in weak solution. When undissociated (as free acid) it is red, when dissociated

(as a salt) its anion is yellow. Its dissociation in water is prevented by the presence of a trace of stronger acid—such solutions are therefore red— but if alkali is added in sufficient amount just to neutralize this acid, then the methyl orange partially dissociates and the solution becomes much paler, and if a trace more alkali is added, still more dissociation occurs, so that the solution becomes bright yellow. Methyl orange is not affected by acid sodium phosphate (NaH_2PO_4), so that a weak acid such as this must be present in large excess before it can prevent the dissociation of methyl orange; therefore, for titrating acid salts this indicator is unsuitable; and for the same reasons it cannot be used for weak organic acids. On the other hand, it is suitable for practically all bases and carbonates, since with all of them it will immediately form dissociable salts, which do not hydrolyze so long as any of the base is available (i.e., uncombined with the acid that is being titrated, which must, of course, be stronger than methyl orange). Nitrous acid acts on methyl orange chemically, therefore nitrites must not be present.

Methyl orange is therefore especially useful for the titration of bases, including ammonia, and unsuitable for the weaker organic acids. Very weak organic bases (as aniline) cannot be titrated.

According to a recent theory the color change of phenolphthalein and methyl orange is due to intramolecular rearrangement and production of a tautomer having a quinoid structure (a CH group of benzene changed to CO). For example, the red

salt of phenolphthalein (in the presence of dilute alkali) is said to have the following quinoid formula:

$$C_6H_4 \underset{COONa}{\overset{\displaystyle C}{<}} C \underset{CH\ CH}{\overset{CH\ CH}{<\ \ \ >}} C=O$$
$$C_6H_4\ \rangle OH.$$
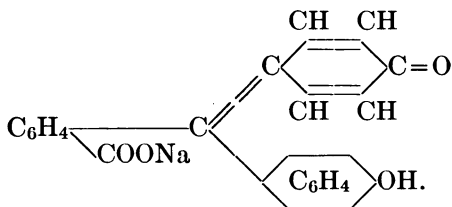
Compare this with the formula of non-ionizing phenolphthalein (p. 373).

It is supposed that methyl orange has a tautomeric quinoid structure in the presence of free acid. The quinoid substance is red in the case of both phenolphthalein and methyl orange.

The indicators used for the detection of mineral acid in the gastric contents belong to the same class as methyl orange, e.g., *Congo red* (p. 410) and *dimethylaminoazobenzene* (p. 387). While it is true that these indicators will not give an accurate titration value with organic acids, our experience (contrary to statements in clinical chemistry textbooks) is that methyl orange, Congo red, and dimethylaminoazobenzene give a distinct color reaction (as with mineral acids) even when used with very dilute organic acid solutions (see exp. p. 405). The phloroglucin-vanillin reagent (p. 348), however, reacts only to mineral acid and can be used as the indicator when making a quantitative estimation of mineral acid in the presence of organic acids.

(3) *Litmus.* This stands between phenolphthalein and methyl orange in its properties. In the

un-ionized state it is red, therefore red with acids; and in the ionized state blue, therefore blue with alkalies.

The importance to the student of thoroughly understanding the action of these three indicators will be evident from a single illustration, namely that urine reacts very differently towards them. Towards methyl orange urine (even when it is acid to litmus) reacts alkaline or neutral, towards phenolphthalein it reacts acid, while towards litmus paper urine reacts acid (usually), neutral, or alkaline. The cause of this difference in action lies in the fact that in this fluid we have a mixture of NaH_2PO_4 and Na_2HPO_4. Occasionally these two salts are present in equivalent quantities in the urine (normally in milk also); in such a case the urine reacts acid to blue litmus paper and alkaline to red litmus (amphoteric reaction). This is due to the fact that NaH_2PO_4 is acid to litmus, and Na_2HPO_4 is alkaline. In normal (acid) urine NaH_2PO_4 preponderates over the alkaline salt, therefore the urine reacts acid to litmus. Even the acid-reacting NaH_2PO_4, is but feebly dissociated (i.e., furnishes few ions) compared with the relatively strong acid in methyl orange; therefore it is unable to influence the degree of dissociation of methyl orange. Congo red acts in the same manner as methyl orange. Phenolphthalein, however, is so feeble an acid that these acid salts can readily keep it in the (practically) undissociated condition and do not allow the indicator to form its sodium salt, under which circumstances, as we have already stated, it remains colorless.

EXPERIMENTS. (1) Effect of ammonium salts on indicators. (*a*) Measure with a pipette 5 c.c. of decinormal H_2SO_4 containing ammonium sulphate and titrate with decinormal NaOH, using methyl orange as indicator. (*b*) Repeat (*a*) but use phenolphthalein as indicator.

(2) Organic acids. (*a*) Titrate 5 c.c. of decinormal

butyric acid with methyl orange; (*b*) with phenol-phthalein.

(3) Acid salts. (*a*) With litmus paper (both blue and red) test solutions of NaH_2PO_4 and Na_2HPO_4 (both being one-tenth gram molecular), then mix 4 c.c. of NaH_2PO_4 with 6 c.c. of Na_2HPO_4, and test with litmus (amphoteric). (*b*) Test the acidity of acid phosphate to methyl orange and to methyl red.

Determination of the H ion concentration of a solution may often be made by the use of indicators. This depends on the fact that different indicators suffer a color change in the presence of different degrees of acidity; thus rosolic acid gives a series of colors from yellow to red when added to various solutions of low acidity, solutions of somewhat greater acidity give colors with methyl red ranging from red to yellow, still more ‘acid solutions give similar color changes with methyl orange, while with solutions equivalent to $\dfrac{N}{100} - \dfrac{N}{500}$ HCl Tropæolin OO gives a gradation of colors from red to yellow (see exp. 1).

By using standard solutions of known H ion concentrations and adding the proper indicators, a basis is secured for colorimetric estimations. To the solution to be tested is added an indicator which gives with the solution one of the intermediate colors shown by the standard solutions to which the same indicator has been added. It may be necessary to try several indicators before the right one is found. The final determination is simply a

question of color matching; and the solution is said to have the same H ion concentration as the standard solution that most nearly resembles it in color.

EXPERIMENTS. (1) Select 12 test-tubes having practically the same diameter, and clean them thoroughly, rinsing with distilled water. Arrange them in three series of four tubes each. In each tube put 10 c.c. of the acid solution indicated.

For series 1 use $\dfrac{N}{50}$, $\dfrac{N}{100}$, $\dfrac{N}{250}$, and $\dfrac{N}{1000}$ HCl.

For series 2 use $\dfrac{N}{100}$, $\dfrac{N}{1000}$, $\dfrac{N}{2000}$, and $\dfrac{N}{5000}$ lactic acid.

For series 3 use $\dfrac{N}{1000}$, $\dfrac{N}{2000}$, $\dfrac{N}{5000}$, and $\dfrac{N}{10000}$ lactic acid.

To each tube of series 1 add 5 drops of .05% tropæolin OO (dissolved in 50% alcohol); for series 2 use 3 drops of .05% alcoholic solution of dimethylaminoazobenzene; and for series 3 use 3 drops of .02% methyl orange. After mixing note the gradation of colors obtained in each series.

(2) In order to illustrate the differing H ion concentrations obtained at the end-points of titration with different indicators, titrate successively 5 c.c. portions of one-tenth gram molecular NaH_2PO_4 solution, using methyl red, rosolic acid, and phenolphthalein. Explain why the titrations differ so widely.

DYES

Several of these have already been mentioned. All such bodies are supposed to owe their dyeing properties to the presence in them of a so-called *chromophore group*.

Most chromophore groups contain double linkings. The azo group $(N=N)$ is an *independent chromophore*, being sufficient of itself to impart color to a compound. The groups $C \Rightarrow O$, $CH = CH$ and $N = C$ are *dependent chromophore* constituents, since they require a certain environment in the structure of the molecule in order to enable them to impart color; the true chromophore group in these cases must, therefore, be more than the simple groups given above. The following give illustrations of chromophore groups:
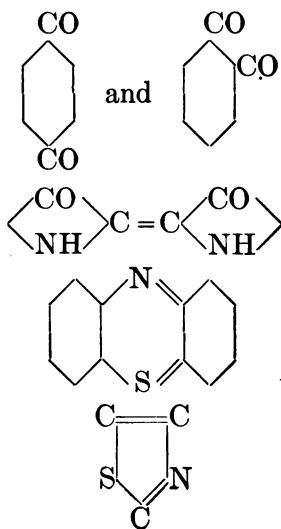
The presence in a substance of one of these groups alone is not, generally, sufficient to constitute it a dye, the substance is merely a chromogen; certain other groups, such as OH and NH_2, must, as a rule, be attached to a chromophore-containing compound to render it available as a dye. These assisting or auxiliary groups are called *auxochromes;* these confer salt-forming properties. The auxochrome has the effect of producing color in colorless chromogens, or of intensifying the color of other chromogens. The dye-stuff, when fully elaborated, will have basic or acidic properties. The sulphonic acid group is often introduced to render a dye soluble (and acidic).

In solution some dyes are emulsoid colloids, a few are semi-colloids, and others are crystalloids. The diffusible dyes can penetrate animal tissues, and, therefore, can be used as stains in the preparation of tissues for microscopical examination. The semi-colloids dialyze slowly, probably because a very small proportion of the substance is in true solution in equilibrium with that portion that is in colloidal solution.

If cloth is immersed in water its fibers acquire negative charges of electricity. Dyes that furnish electro-positive ions or electro-positive colloidal particles are adsorbed by the fibers, because the ions or particles are attracted, and after neutralization of electrical charges are precipitated on the fibers (see p. 95). In many cases the amount of dye taken up from a solution of a particular concentration indicates that there is an equilibrium be-

tween the fibers and the solution; this is the same sort of result as is obtained in recognized adsorption processes. Dyes that have electro-negative ions or colloidal particles may be adsorbed by fibers under special conditions, for instance, when electrolytes are present.

Basic dyes are salts of weak organic bases with strong acids, and, therefore, undergo hydrolytic dissociation (see p. 70). The base set free goes into colloidal solution, the particles being electro-positive. Acid dyes are mostly sodium salts of fairly strong organic acids; they do not hydrolyze appreciably, but they ionize. The ion of the acid (electro-negative) behaves like a colloid.

In the case of many dyes cotton fibers do not take up the color satisfactorily. *Mordants* are used as a preliminary step in the dyeing process, resulting in the coating of the cotton fibers with a colloidal substance which is capable of precipitating or absorbing the dye substance. For basic dyes tannic acid is largely used. For acid dyes acetates of aluminium, chromium, and iron are commonly employed, the cloth being soaked with the acetate and then steamed to decompose the salt and leave the colloidal hydroxide of the metal.

In some cases the dye may enter into chemical combination after adsorption.

AROMATIC COMPOUNDS HAVING CONDENSED
RINGS

Naphthalene ($C_{10}H_8$) contains two benzene rings
connected in the following manner:
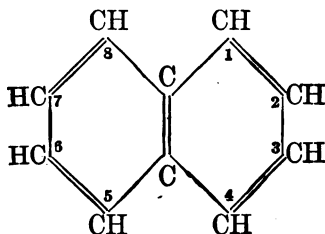
It forms white crystals melting at 80°, boiling at
218.1° and having a tar-like odor. It is volatile
and is contained in coal-gas, being also a con-
stituent of the distillate from coal-tar. It is an
antiseptic.

EXPERIMENTS. (1) Heat some naphthalene in a
sublimation apparatus.

(2) Try the reaction with aluminium chloride
given by some naphthalene dissolved in chloroform
(see p. 332).

The **naphthols**, $C_{10}H_7 \cdot OH$, correspond to phenols.
Alpha-naphthol (melting-point 95°) and beta-naph-
thol (melting-point 122°) are both of importance.

α Derivatives of naphthalene have some group introduced in position 1, 4, 5 or 8, while β derivatives have it in position 2, 3, 6 or 7. Ortho, meta and para naphthalene derivatives have two substituting groups attached to the same half of the formula (as in positions 1, 2, 3, 4).

Epicarin is β-naphthol-ortho-hydroxy-toluic acid,

$$C_6H_3 {\Large\langle} \begin{array}{l} COOH \\ OH \\ CH_2 \cdot OC_{10}H_7 \end{array} .$$
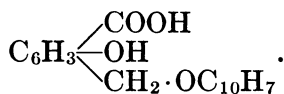
β-Naphthol benzoate, $C_{10}H_7$—$OOC \cdot C_6H_5$, is another of the newer remedies.

Orphol is bismuth β-naphtholate. All these substances are antiseptics.

Alpha- and *beta-naphthylamines*, $C_{10}H_7 \cdot NH_2$ are used as reagents. α-Naphthylamine is used to detect the presence of and to estimate the amount of traces of nitrites, as in drinking water. This test depends on the fact that a red compound, azo-benzene-naphthylamine-sulphonic acid, is produced.

Congo red is a complex diazonium derivative of naphthylamine-sulphonic acid. Its formula is

$$\begin{array}{l} NaO_3S \\ H_2N \end{array} {\Large\rangle} C_{10}H_5 \cdot N{=}N \cdot C_6H_4 \cdot C_6H_4 \cdot N{=}N \cdot C_{10}H_5 {\Large\langle} \begin{array}{l} SO_3Na \\ NH_2 \end{array} .$$
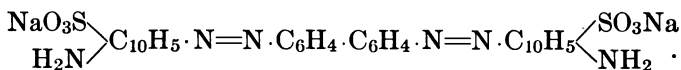
Its color becomes blue in the presence of free acids. It forms a colloidal solution, which will not dialyze. Electrolytes cause its molecules to aggregate.

Santonin, $C_{15}H_{18}O_3$, is a naphthalene derivative and is the inner anhydride or lactone of santonic acid. Its formula is probably,

C—CH$_3$ CH$_2$

OC   C   CH—CH$_3$

CH

H$_2$C   CH   O   CO

C

C—CH$_3$ CH$_2$
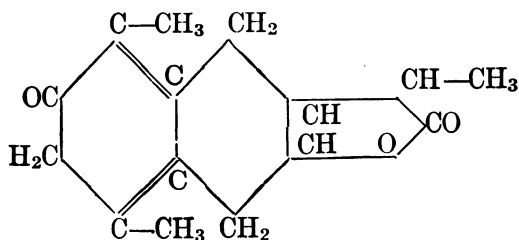
Elaterin, a neutral principle, is said to be a derivative of naphthalene.

Anthracene. $C_{14}H_{10}$, is a hydrocarbon containing three benzene rings condensed together:

CH   CH   CH

HC   C   C   CH

HC   CH

   C   C

CH   CH   CH

or

CH   CH   CH·

HC 7   8 C   9 C   1   2 CH

HC 6   3 CH

   5 C   10 C   4

CH   CH   CH
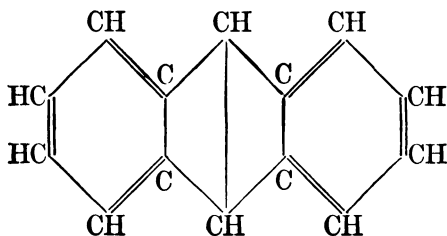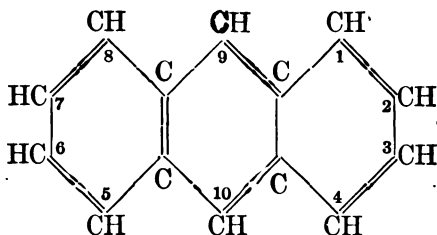
It occurs in coal-tar in small quantity and is used in manufacturing alizarin. Its crystals melt at 216.5° (corrected). Exposure to light changes it into dianthracene, which depolymerizes in the dark to anthracene, a reversible photo-chemical reaction:

$$2C_{14}H_{10} \rightleftarrows C_{28}H_{20}.$$
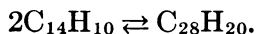
One of the important derivatives of anthracene is **anthraquinone,**

$, C_{14}H_8O_2.$
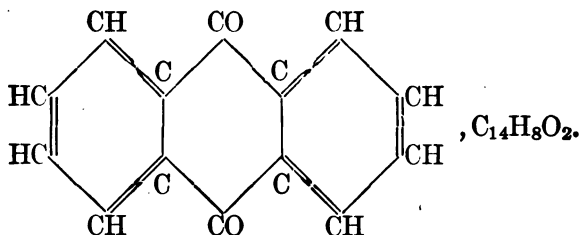
Dihydroxyanthraquinone is the very important dye **alizarin,** $C_{14}H_6O_2(OH)_2$:
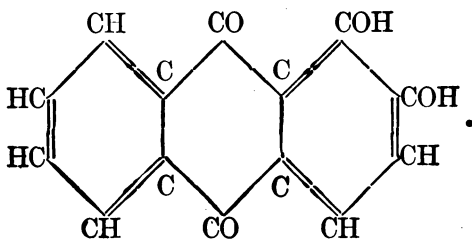
This was formerly obtained from a plant. It is now produced much more cheaply by synthetic means. Its synthesis on a commercial scale is one of the great achievements of organic chemistry.

Aloin is an anthraquinone derivative. Its formula may be (the position of the OH being uncertain):
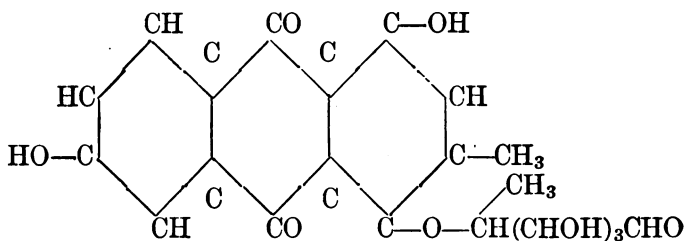
Chrysophanic acid, $C_{14}H_5O_2(CH_3)(OH)_2$, and **chrysarobin,** $C_{15}H_{12}O_3$, are anthracene derivatives of therapeutic importance, chrysophanic acid probably being monomethyl-dihydroxy-anthraquinone, and chyrsarobin monomethyl-trihydroxy-anthracene.

Emodin, $C_{15}H_{10}O_5$, is 2-monomethyl 3, 6, 7-tri-hydroxyanthraquinone.

Rhein, $C_{15}H_8O_6$, is also an anthraquinone derivative,

$$C_{14}H_5O_2 \begin{cases} COOH \ (1) \\ OH \ (3) \\ OH \ (5) \end{cases} .$$
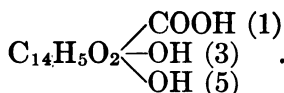
Isomeric with anthracene is **phenanthrene,** $C_{14}H_{10}$:
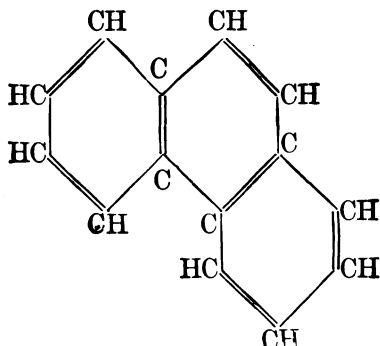
Some chemists think that it may be a derivative of diphenyl, the two benzene rings being linked to $CH = CH$, in addition to the direct linking, the formula being written:
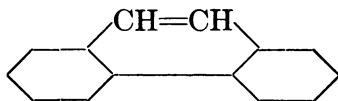
HETEROCYCLIC COMPOUNDS

HETEROCYCLIC compounds are related to the aromatic compounds, but contain at least one atom other than C atoms in the ring; this is generally N.[1]

Pyrrol has the formula HC— CH. *Iodol* is a

$$\begin{array}{c} HC-CH \\ \| \quad \| \\ HC \quad CH \\ \diagdown \diagup \\ NH \end{array}$$
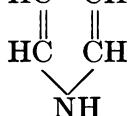
medicinal derivative; it is tetraiodopyrrol.

[1] Heterocyclic compounds of minor importance are thiophene,

$$\begin{array}{c} HC-CH \\ | \quad | \\ HC \quad CH \\ \diagdown \diagup \\ S \end{array},$$

pyrazole,

$$\begin{array}{c} HC-CH \\ | \quad | \\ HC \quad NH \\ \diagdown \diagup \\ NH \end{array}$$

imidazole,

$$\begin{array}{c} HC-N \\ \| \quad \| \\ HC \quad CH \\ \diagdown \diagup \\ NH \end{array},$$

and furan,

$$\begin{array}{c} HC-CH \\ \| \quad \| \\ HC \quad CH \\ \diagdown \diagup \\ O \end{array}.$$
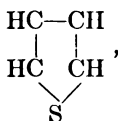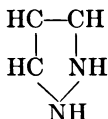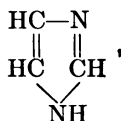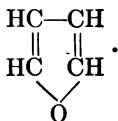
Pyrrolidine is the hydrogen addition derivative of pyrrol, H_2C——CH_2. This is the basis of certain alkaloids.

$$H_2C \overbrace{\underbrace{}_{1}}^{3 \quad 4} CH_2$$
$$H_2C \underset{1}{\overset{2 \quad 5}{\diagdown}} CH_2$$
$$NH$$
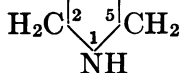
Prolin and **hydroxy-prolin** are pyrrolidine acids (p. 271).

Hæmatin, hæmin, and **hæmatoporphyrin** (from hæmoglobin) are supposed to contain four pyrrol rings in their molecules.

Antipyrin or *phenazone* is an important derivative of pyrazolone, which contains the pyrazole ring, its formula being:

$$HC = C - CH_3$$
$$OC \diagup N - CH_3.$$
$$N - C_6H_5$$
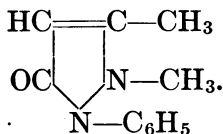
It is an antipyretic of value, and is a crystalline substance melting at 113°.

Two of its derivatives are used as remedies: *pyramidon* or dimethylamino-antipyrin, and *tussol* or antipyrin mandelate.

Furfuraldehyde is the chief derivative of furan; its formula is

$$HC = CH$$
$$| \qquad \diagdown O$$
$$HC = C \diagup CHO.$$
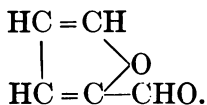
Pyridine Bases. These are ammonia derivatives and of great importance on account of their relationship to certain alkaloids which will be dis-

cussed presently. The simplest member of the series is pyridine, which has the structural formula,
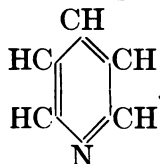
It may therefore be considered as benzene with a CH group replaced by nitrogen (C_5H_5N). There are several methyl pyridines.

The pyridines are contained in coal-tar, and are formed when bones are distilled, being produced by the action on one another at high temperatures of acrolein, ammonia, methylamine, etc.

Pyridine is a colorless liquid with an odor like tobacco-smoke. It boils at 115° C. It mixes readily with water, the resulting solution being strongly alkaline. Like other tertiary ammonia bases, it directly combines with acids to form crystalline salts. When it is warmed with alkyl halides, addition products are formed, and if these be treated with caustic potash a very pungent and disagreeable odor is evolved.

EXPERIMENTS. (1) Dissolve some pyridine in water; test alkalinity with litmus. Notice the odor.

(2) Then neutralize the solution with HCl, add a few drops of platinic chloride solution, and boil; a yellow precipitate of $(C_5H_5N)_2PtCl_4$ forms.

CONDENSED HETEROCYCLIC BENZENE COMPOUNDS

PYRROL DERIVATIVES OF BENZENE

Indol, $C_6H_4\diagup\!\!\!\diagdown\substack{CH\\NH}\!\!\!\diagdown CH$, contains the pyrrol nucleus, condensed with the benzene nucleus, and may be represented thus:
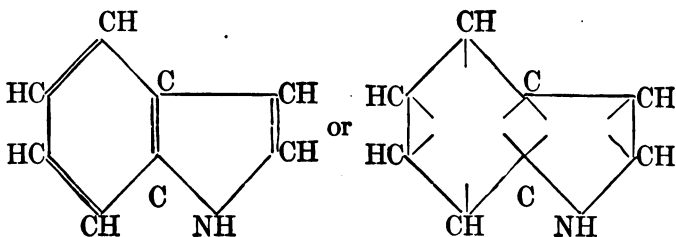
Skatol is methyl indol, $C_6H_4\diagup\!\!\!\diagdown\substack{C-CH_3\\NH}\!\!\!\diagdown CH$. Indol and skatol are contained in fæces, imparting the characteristic odor to the latter. They are produced in the intestine by the action of bacteria on the aromatic groups (tryptophan) in protein. They are volatile with steam.

Indican is the oxidation product of indol in combination with sulphuric acid as an ethereal sulphate, $C_6H_4\diagup\!\!\!\diagdown\substack{C=O-SO_2(OK)\\NH}\!\!\!\diagdown CH$. It is potassium indoxyl-sulphate. It is sometimes present in the urine in considerable quantity. The urine may also contain indoxyl glycuronic acid. The origin of these

bodies is indol absorbed from the bowel-contents. *Indigo* can be obtained from it; and indigo is deposited from urine containing much indican after ammoniacal decomposition sets in. To estimate the indican in the urine it is converted into indigo by various reagents, and this is then removed by shaking with chloroform. The blue chloroform solution can be compared with an indigo solution of known strength, and thus a colorimetric estimation may be made.

Skatoxyl-sulphuric acid is the corresponding derivative of skatol, $C_6H_4 <^{C \; =CH_3}_{NH} > C\!-\!O\!-\!SO_2(OH)$.

Tryptophan, $\quad C_6H_4 <^{C \; =CH_2 \cdot CH(NH_2) \cdot COOH}_{NH} > CH$

is β-indol α-amino-propionic acid. It is a decomposition product of protein, being produced during tryptic digestion. It, in turn, is attacked by bacteria in the intestines, giving rise to indol. It gives a color reaction with glyoxylic acid (see p. 220).

Directly related to indol is **isatin,** $C_6H_4 <^{CO}_{NH} > CO$,

dioxyindol, for the former can be obtained from the latter by reduction. **Indigo,** structurally, is a combination of two isatin molecules, the end oxygen atom of each molecule being eliminated, thus:

$$C_6H_4 <^{CO}_{NH} > C\!=\!C <^{CO}_{NH} > C_6H_4.$$
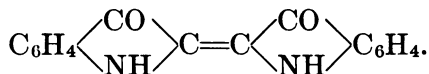
Indigo can be produced from isatin. It is a valuable blue dye. The synthesis of indigo on a com-

mercial scale is one of the great achievements of chemistry. Most of the indigo marketed nowadays is artificially produced, the cost of manufacture being only about one-fourth the cost of production of natural indigo. It will be of interest to give an outline of one of the recent commercial methods. Naphthalene is the starting-point of the synthesis. This is oxidized by fuming H_2SO_4 to phthalic acid, and the latter is converted into phthalimide by the action of ammonia gas; then by treatment with chlorine and caustic soda phthalimide becomes converted into anthranilic acid. This acid is condensed with monochloracetic acid,

giving
$$\text{C}_6\text{H}_4 \begin{cases} -\text{COOH} \\ \text{CH}_2\cdot\text{COOH} \\ \text{NH} \end{cases}$$
. Fusion with KOH
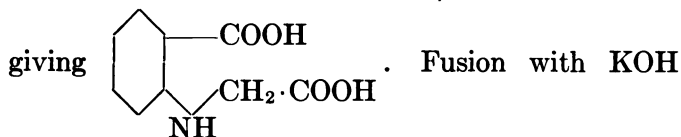
splits off CO_2 and water, producing

$C_6H_4 \begin{array}{c} \diagup CO \diagdown \\ \diagdown NH \diagup \end{array} CH$, which is then oxidized in alkaline
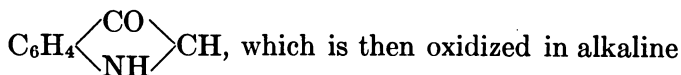
solution to indigo by a current of air.

In plants the indigo is contained in a glucoside combination, indican (p. 253). Reduction (adding H) changes indigo to *indigo white;* it is in this form that it is introduced in alkaline solution into cloth for dyeing; on exposure to air it oxidizes to the insoluble indigo blue. Indigo red, *indirubin*, is a structural isomer of indigo.

EXPERIMENT. Synthesize indigo. To 1 c.c. of water add 3 drops of acetone and a few crystals of orthonitrobenzaldehyde. Warm the mixture in a

bath kept at 50° for ten minutes. Cool, add a few. drops of 10% NaOH and shake. A yellow color appears first, then a green. When it is deep green add chloroform and shake. Indigo dissolves in the chloroform (blue solution). Remove the bottom layer with a pipette, and run it into a sample bottle. As the solvent evaporates indigo is deposited on the wall.

CONDENSED PYRIDINE-BENZENE COMPOUNDS

Quinoline (chinoline) is another tertiary ammonia base. It may be considered as naphthalene in which a CH group has been replaced by N:

$$CH \quad CH$$
$$HC \diagup \overset{C}{\diagdown} \diagup CH$$
$$HC \diagdown \quad \diagup CH \qquad , \ C_9H_7N.$$
$$CH \overset{C}{\diagdown} N$$
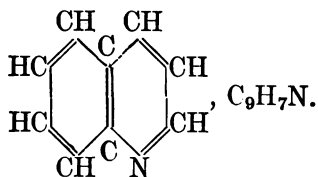
It is found in coal-tar. When certain alkaloids, particularly quinine and cinchonine, are distilled with potassium hydroxide, quinoline is obtained. Quinoline can be synthesized from aniline and glycerol in the presence of nitrobenzene and concentrated sulphuric acid (see exp. below): The reactions involved are as follows: the glycerol is dehydrated to acrolein; removal of a molecule of water from acrolein by further dehydration causes combination with aniline forming acrolein-aniline; and finally oxygen from nitrobenzene removes a hydrogen atom from the end of the chain and also

from the benzene ring, resulting in the closing of the pyridine ring.

(Acrolein-aniline)   (Quinoline)
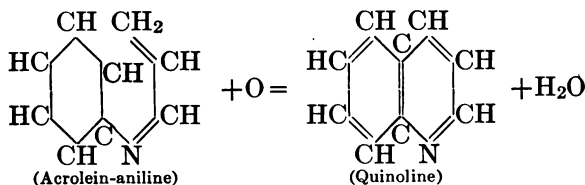
Quinoline is a liquid boiling at 240°. By proper treatment of quinoline, pyridine can be derived from it. Many alkaloids are quinoline derivatives.

Oxyquinoline Sulphate (chinosol), $(C_9H_7NO)_2 \cdot H_2SO_4$, is a substance used as an antiseptic, and is said to be non-toxic.

EXPERIMENT. *Synthesize quinoline.* In a liter flask mix 15 gm. of nitrobenzene, 24 gm. of aniline, and 75 gm. of glycerol; add 62 gm. of C.P. H_2SO_4 while agitating the mixture. Connect with an air-condenser having a diameter of 2 cm., and heat the flask very gradually on a sand-bath. Wrap the condenser with a damp rag. When the reaction begins (sudden bubbling) remove the flame. If the action is very vigorous, cool the upper part of the flask with an air stream from a bellows. When the mixture becomes quiet, heat for three hours on a sand-bath. Then dilute with 300 c.c. of water and distill with steam. When no more oily drops of nitrobenzene come over, stop the distilling. Cool partially, render the mixture alkaline with strong NaOH solution, and again distill with steam, thus

removing the quinoline and aniline. This last distillate is specially treated to convert the aniline into phenol, as was directed in the experiment under phenol (see p. 338). Diazotize the cooled liquid after rendering it distinctly acid with dilute H_2SO_4, warm in a bath, make alkaline (the phenol becomes fixed as a phenolate, while quinoline is set free), and distill with steam. Extract the quinoline from the distillate with ether and proceed just as was done with phenol.

Thalline, $C_9H_9(OCH_3)NH$, and

Kairine, $C_9H_9(OH)N—C_2H_5$, are quinoline derivatives that have been used as antipyretics.

Analgen (quinalgen) is a more recent antipyretic, $C_9H_5(OC_2H_5)NH(COC_6H_5)N$.

Kynurenic acid, occurring in the urine of dogs, is a quinoline derivative,
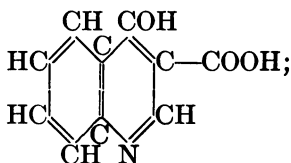
it is supposed to be derived from tryptophan.

Atophan is one of the newer remedies that is of importance. It is phenyl-quinoline-carboxylic acid,
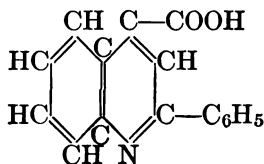
Novatophan is the ethyl ester of methyl atophan.

Isoquinoline, C_9H_7N, is an isomer of quinoline:

$$
\begin{array}{c}
\text{CH CH} \\
\text{HC} \diagup \overset{\text{C}}{\diagup} \diagdown \text{CH} \\
\text{HC} \diagdown \underset{\text{C}}{\diagdown} \diagup \text{N} \\
\text{CH CH}
\end{array}
$$
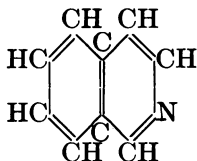
It is of importance because of the derivation of many alkaloids from it. The formula may be written with N at any one of the four positions at the sides of the rings.

SYNOPSIS

Aromatic Compounds

A. BENZENE HYDROCARBONS.

Benzene derivatives.

    1. *Halogen derivatives.*

    2. *Hydroxy derivatives.*

        a. Phenols $\left\{ \begin{array}{l} \text{Ethers.} \\ \text{Ethereal salts.} \end{array} \right.$

            (1) Monacid phenols $\left\{ \begin{array}{l} \text{Substitution} \\ \text{ products.} \end{array} \right.$

            (2) Diacid phenols.

            (3) Triacid phenols.

        b. Fatty alcohol side-chain compounds and deriva-

            tives $\left\{ \begin{array}{l} \text{Alcohols.} \\ \text{Aldehydes.} \\ \text{Ketones.} \\ \text{Monobasic acids} \left\{ \begin{array}{l} \text{Salts.} \\ \text{Ethereal salts.} \end{array} \right. \end{array} \right.$

        c. Phenolic monobasic acids.

    3. *Dibasic acids.*

    4. *Nitrogen derivatives.*

        (*a*) Nitro compounds.

        (*b*) Amino compounds.

        (*c*) Diazo compounds.

CHAPTER XXXIII

ALKALOIDS AND DRUG PRINCIPLES

ALKALOIDS

In its broadest application the term alkaloid includes all nitrogenous organic substances that are basic in character (*alkaloid = alkali-like*). Caffeine and theobromine, purin bases and other leucomaines, choline, muscarine, and ptomaines have all been called alkaloids.

The most recent definition which seems acceptable is that alkaloids include all nitrogenous plant products which have N in a closed chain of atoms. Many of them contain more than one N atom in the molecule. Most alkaloids are tertiary ammonia bases. Those the structure of which is known are derivatives of pyridine, pyrrolidine, quinoline, isoquinoline, phenanthrene, or purin.

The empirical formulæ of the chief alkaloids are as follows:

Coniine. . . . . $C_8H_{17}N$.
Nicotine. . . . . $C_{10}H_{14}N_2$.
Sparteine. . . . . $C_{15}H_{26}N_2$.
Theobromine. . . . . . $C_7H_8N_4O_2$.
Theophylline. . . . . . $C_7H_8N_4O_2$.
Caffeine. . . . . $C_8H_{10}N_4O_2$.
Pelletierine. . . . . . . $C_8H_{15}NO$.

Pilocarpidine...... $C_{10}H_{14}N_2O_2$.
Hydrastinine...... $C_{11}H_{13}NO_3$.
Pilocarpine....... $C_{11}H_{16}N_2O_2$.
Physostigmine..... $C_{15}H_{21}N_3O_2$ (Eserine).
Eseridine......... $C_{15}H_{23}N_3O_3$.
Homatropine...... $C_{16}H_{21}NO_3$.
Sinipine.......... $C_{16}H_{25}NO_6$.
Apomorphine..... $C_{17}H_{17}NO_2$.
Piperine.......... $C_{17}H_{19}NO_3$.
Morphine......... $C_{17}H_{19}NO_3$.
Cocaine.......... $C_{17}H_{21}NO_4$.
Hyoscine......... $C_{17}H_{21}NO_4$. (Scopolamine).
Atropine.......... $C_{17}H_{23}NO_3$ ⎫
                                      ⎬ Isomers.
Hyoscyamine..... $C_{17}H_{23}NO_3$ ⎭
Codeine.......... $C_{18}H_{21}NO_3$.
Lobeline.......... $C_{18}H_{23}NO_2$.
Thebaine......... $C_{19}H_{21}NO_3$.
Cinchonine....... $C_{19}H_{22}N_2O$ ⎫
                                      ⎬ Isomers.
Cinchonidine...... $C_{19}H_{22}N_2O$ ⎭
Curarine.......... $C_{19}H_{26}N_2O$.
Sanguinarine...... $C_{20}H_{15}NO_4$.
Berberine......... $C_{20}H_{17}NO_4$.
Papaverine....... $C_{20}H_{21}NO_4$.
Quinine.......... $C_{20}H_{24}N_2O_2$ (Isomer, Quinidine)
Hydrastine....... $C_{21}H_{21}NO_6$.
Strychnine........ $C_{21}H_{22}N_2O_2$.
Narcotine......... $C_{22}H_{23}NO_7$.
Colchicine........ $C_{22}H_{25}NO_6$.
Gelseminine....... $C_{22}H_{26}N_2O_3$.
Yohimbine........ $C_{22}H_{28}N_2O_3$.
Brucine.......... $C_{23}H_{26}N_2O_4$.
Narceine......... $C_{23}H_{27}NO_8$.

Jervine...........$C_{26}H_{37}NO_3$.
Veratrine.........$C_{32}H_{49}NO_9$.
Aconitine.........$C_{34}H_{47}NO_{11}$.
Ergotinine........$C_{35}H_{39}N_5O_5$.
Ergotoxine........$C_{35}H_{41}N_5O_6$.

Coniine and nicotine are the only important alkaloids that contain no oxygen and that are volatile liquids. Sparteine, pelletierine, and pilocarpidine are liquids, but non-volatile. All of the alkaloids form salts with acids (see p. 258); these salts are very much more soluble in water and alcohol than the free alkaloids. The free alkaloids, on the other hand, are more soluble than their salts in the immiscible solvents—ether, chloroform, benzene, and amyl alcohol. In solution some of the alkaloids are distinctly alkaline. Most of the alkaloids are optically active, and generally lævorotatory.

All alkaloids are precipitated by phosphomolybdic and phosphotungstic acids, most of them by potassium mercuric iodide and many of them by tannic acid.

Many of the alkaloids are extremely poisonous, but in minute doses they are very valuable remedies.

The alkaloids here considered are of vegetable origin. They are present in plants as salts of various organic acids (e.g., citric, malic, and tannic acids).

Methods of determining the constitution of alkaloids. By violent reactions (e.g., fusing with alkali, heating with bromine or phosphoric acid, or distilling with zinc dust) the molecule may be shattered, so that as a result of the reaction a

stable nucleus is found, such as pyridine, quinoline or isoquinoline. Methyl ether linkings of alkaloids may be broken up by heating with hydriodic acid, and from the methyl iodide formed the number of methoxy groups (OCH_3) can be ascertained.

Alkaloids that are esters can be hydrolyzed, and the products of hydrolysis can be examined. Hydroxyl, carboxyl and carbonyl groups are readily determined. In the case of a few alkaloids the structure of the molecule has been proved by synthesis.

We shall consider now some of the facts that are known in regard to the structure of alkaloids.

PYRIDINE DERIVATIVES

It is necessary to designate the positions of groups in the pyridine ring thus:

$$
\begin{array}{c}
CH(\gamma) \\
(\beta')HC \quad CH(\beta) \\
(\alpha')HC \quad CH(\alpha) \\
N
\end{array}
$$
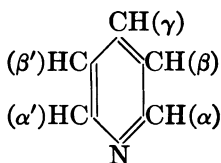
Piperidine is the simplest derivative,

$$
\begin{array}{c}
CH_2 \\
H_2C \quad CH_2 \\
H_2C \quad CH_2 \\
NH
\end{array}
$$
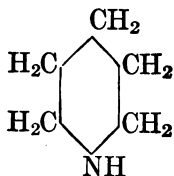
Piperine is contained in pepper. It is a combination of piperidine and piperic acid, $C_{12}H_{10}O_4$.

Coniine is dextro-α-propyl piperidine,

$$
\begin{array}{c}
CH_2 \\
H_2C \diagup \diagdown CH_2 \\
H_2C \diagdown \diagup CH\text{---}CH_2 \cdot CH_2 \cdot CH_3 \\
NH
\end{array}
$$
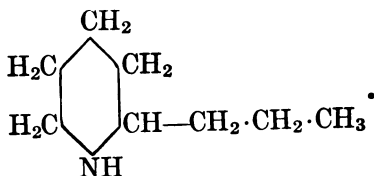
Nicotine is a pyrrol derivative (see p. 414) of pyridine the attachment of methyl pyrrolidine to pyridine being in the β position of the latter and position 2 of the former:

$$
\begin{array}{cc}
CH \qquad H_2C\text{---}CH_2 \\
HC \diagup \diagdown C \text{------} \quad \diagdown CH_2 \\
\quad \qquad HC \qquad N \\
HC \diagdown \diagup CH \qquad | \\
N \qquad \quad CH_3
\end{array}
$$
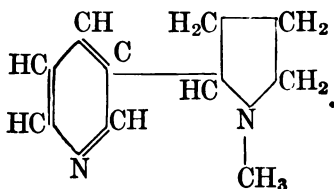
Coniine and nicotine have marked similarities; both are volatile liquids having a strong odor, and both are very poisonous. Coniine is obtained from hemlock-seed, and nicotine from tobacco. Both are strongly alkaline to litmus. In tobacco the nicotine is combined with malic acid and citric acid. Synthetic α-propyl piperidine is identical with coniine, except that it is optically inactive. Optically active coniine can be obtained from this by securing crystals of the tartrate of coniine, the first crop of crystals containing only dextroconiine. This was the first synthesis (1886) of a natural alkaloid.

Nicotine is lævorotatory. *d l*-Nicotine has been synthesized; from this the *l* variety is separated by

crystallization of the tartrate.   *d*-Nicotine is much less toxic than *l*-nicotine.

Sparteine is thought to be a piperidine derivative, but its chemical structure has not been fully determined.   It is dextrorotatory.

The artificial alkaloids α- and β-**eucaine** are complex piperidine bodies.
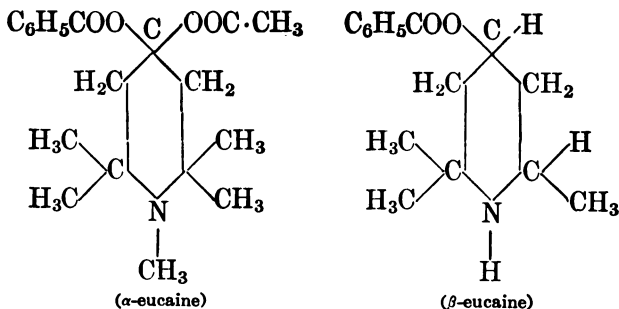
(α-eucaine)   (β-eucaine)

The eucaines are local anæsthetics, and differ from cocaine in action in that they do not affect the pupil.

Euphthalmine is related to β-eucaine, having a CH_3 group in place of the H attached to N and having the mandelic acid radicle, $C_6H_5 \cdot CHOH \cdot COO$ instead of the benzoic acid radicle.   It dilates the pupil more quickly and less persistently than atropin. It is not an anæsthetic.

PYRROLIDINE DERIVATIVES

The alkaloids of the cocaine and atropine group are all pyrrolidine derivatives.   This class of alkaloids is of great pharmacological importance.   Cocaine is an invaluable local anæsthetic, while members of the atropine group are used to dilate the pupil. The basal substance for all of these compounds is

tropine. This has, as will be noticed, a secondary closed carbon chain:

This double ring nucleus is called the tropan nucleus. It may be looked upon as a condensation of the pyrrol with the pyridine ring, having N and the two neighboring C atoms in common to the two rings.

Tropic acid has the formula

$$C_6H_5\text{---}CH\text{<}^{CH_2OH}_{COOH} \; .$$
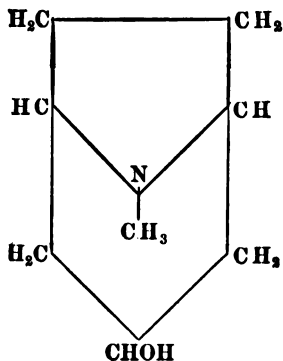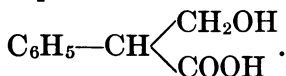
Atropine is the tropine ester (tropine being an alcohol) of tropic acid, its formula being,
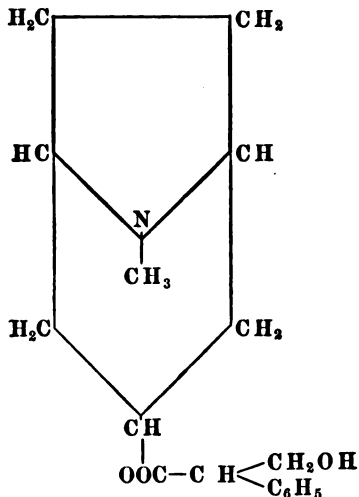
Atropine is optically inactive. Its physiological action is what would be expected of *d l*-hyoscyamine.

Hyoscyamine is lævorotatory. *d*-Hyoscyamine has a different degree of physiological action. Like other esters, atropine and hyoscyamine can be saponified. Atropine has been synthesized.

Atropine and its isomers have a marked pharmacological action.

Eumydrine is the nitrate of methyl atropine, CH_3 and NO_3 attaching to the N atom of atropine, the latter changing its valence to five. It is used for the same purposes as atropine, but is much less toxic.

Homatropine is an artificial alkaloid prepared by the condensation of tropine and mandelic acid in ester combination. It dilates the pupil more promptly and less persistently than atropine.

Scopolamine, also called *hyoscine*, is an ester, consisting of tropic acid combined with scopolin, $C_8H_{13}NO_2$, an alcohol derived from pyrrolidine. It is lævorotatory. It is used to cause analgesia.

If in tropine an H atom of a CH_2 group of the secondary ring be replaced by COOH, ecgonine is obtained:

$$H_2C \quad\quad CH_2$$
$$HC \quad\quad CH$$
$$N$$
$$CH_3$$
$$H_2C \quad\quad C{<}^{H}_{COOH}$$
$$CHOH$$
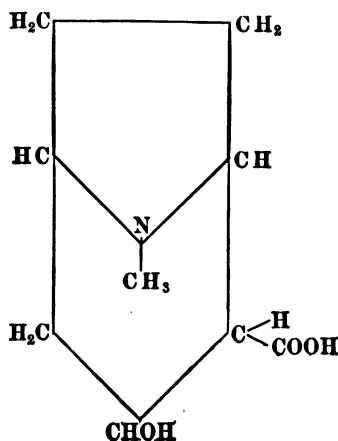
From this is derived **cocaine,** which is the methyl ester of benzoyl ecgonine:
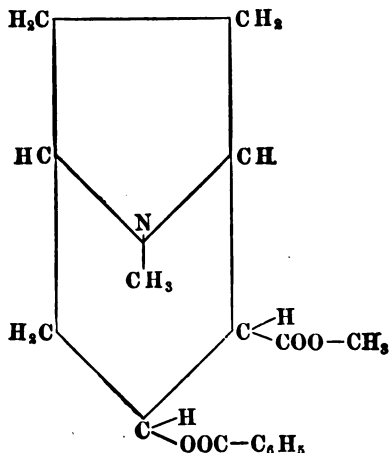
Cocaine exists both as d and as l, the latter having a more marked action. Cocaine is a very valuable local anæsthetic. Its solution cannot be sterilized by heat, because it hydrolyzes readily, yielding methyl alcohol and benzoylecgonine.

Besides this similarity of cocaine to atropine in chemical structure, there are some resemblances in pharmacological action.

Tropacocaine has a formula similar to cocaine, but has CH_2 instead of $CH \cdot COOCH_3$. It is less toxic than cocaine and as strongly anæsthetic. It has little effect on the pupil.

Other substitutes for cocaine, namely, novocaine, stovaine, and alypin (see p. 360) have been previously mentioned.

Nicotine is a pyrrolidine derivative as well as a pyridine derivative (see p. 429).

QUINOLINE DERIVATIVES

The chief alkaloids of this class are the cinchona alkaloids. The following formula has been suggested for **cinchonine**:

$$CH_2=CH-CH-CH-CH_2$$

(X)
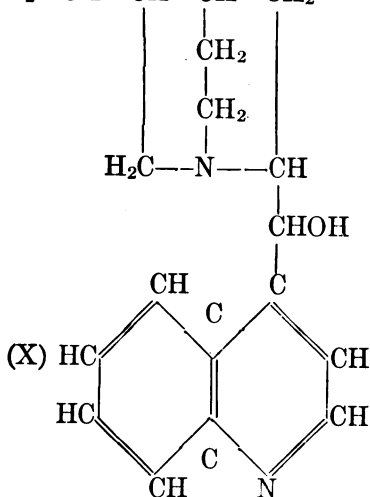
Quinine probably has the same formula, except that an H atom at the position marked (X) is replaced by the methoxy group (OCH_3).

Cinchonine is dextrorotatory, quinine lævorotatory. **Cinchonidine** is the lævorotatory isomer of cinchonine. **Quinidine** is the dextrorotatory isomer of quinine. Quinine is important as a medicine. It is very bitter.

Euquinine, an ester, quinine ethyl carbonate, is tasteless. It gives full quinine action.

Aristoquin is similar to euquinine. It is diquinine carbonic ester. Its action is the same as that of quinine, but it has none of the disadvantages of the latter.

Quinine and urea hydrochloride, a crystalline double salt, is very soluble and is suitable for subcutaneous injection, being non-irritating and even anæsthetic locally.

Strychnine and brucine are believed to be quinoline derivatives, but their structure has not been fully worked out.

Both strychnine and brucine are lævorotatory. Strychnine is much used as a medicine, brucine not at all.

ISOQUINOLINE DERIVATIVES

The *minor opium alkaloids*, papaverine, narcotine, and narceine, also *hydrastine* and *berberine*, belong to this group. These alkaloids are therapeutically of very little importance (except hydrastine). **Papaverine** has the simplest structure; it is tetramethoxy-benzylisoquinoline; its formula is
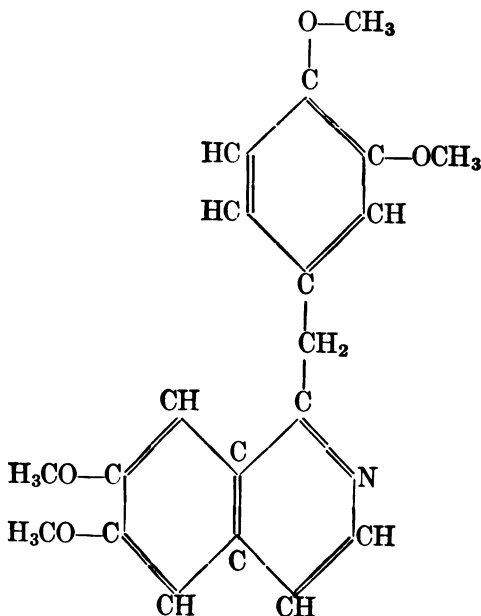
Papaverine has been synthesized.

Hydrastine probably has the similar but more complicated formula:
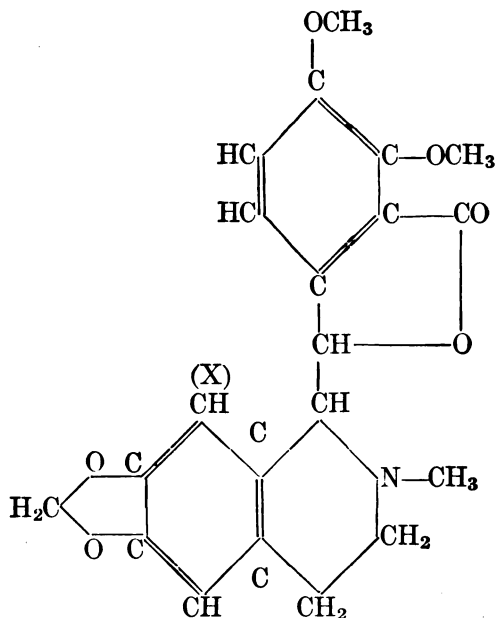
Narcotine is believed to be methoxyhydrastine, the OCH_3 group taking the place of H at (X).

Hydrastinine is an alkaloid prepared by oxidation of hydrastine with nitric acid. It has a much stronger physiological action than hydrastine. Its
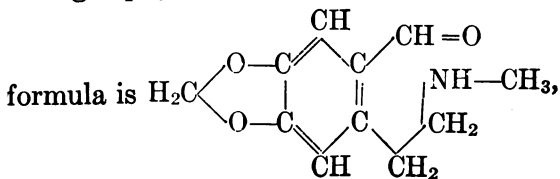
formula is

the side chain being bent so as to point out its derivation from hydrastine.

Narceine has a somewhat similar formula, but it has in addition a benzoic acid group and several methoxy groups.

Berberine has a still more complex formula.

Cotarnine, $C_{12}H_{15}NO_4$, is an oxidation product of narcotine, as hydrastinine is of hydrastine. Its formula corresponds to the isoquinoline half of the narcotine formula. It is methoxyhydrastinine. Its hydrochloride is called stypticin, and the phthalate is called styptol.

Cotarnine and hydrastinine have very similar physiological action; both affect the circulatory system in such a way as to lessen hæmorrhage. Cotarnine is much less expensive.

PHENANTHRENE DERIVATIVES

These are *morphine, codeine,* and *thebaine,* all of them being alkaloids present in opium. Derivatives of morphine artificially produced are apomorphine, dionine, heroine and peronine.

Morphine is the most valuable alkaloid for therapeutic purposes that we have. Opium contains about 10% of morphine. Its derivatives are much weaker in physiological action.

Its constitutional formula is supposed by some to be:
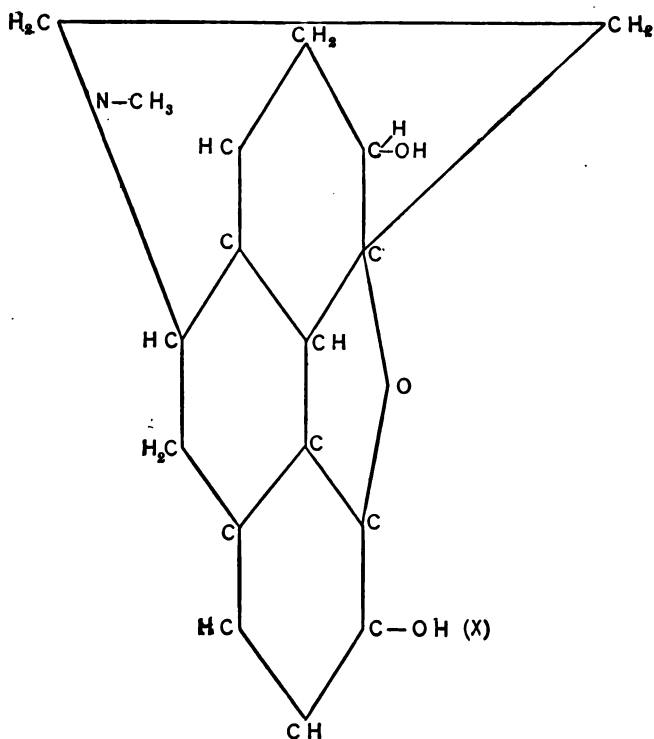
Codeine is supposed to have the above formula, with CH_3 substituted for the H of the OH group at X. Thus codeine is the monomethyl ether of morphine. Codeine has been prepared from morphine by treating the latter with methyl iodode in the presence of caustic potash:

$$C_{17}H_{17}NO(OH)_2 + CH_3I + KOH =$$
(Morphine)
$$= C_{17}H_{17}NO(OH)(OCH_3) + KI + H_2O.$$
(Codeine)
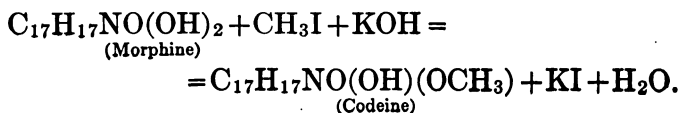
It is prepared by heating a mixture of morphine and potassium methyl sulphate ($K(CH_3)SO_4$) with alcoholic KOH (see exp.).

Both morphine and codeine are lævorotatory.

Thebaine is supposed to have two less hydrogen atoms attached to the phenanthrene nucleus, and two OCH_3 groups in place of the two hydroxyls of morphine.

By the action of concentrated. mineral acids, a molecule of water can be removed from morphine, producing **apomorphine**:

$$\underset{\text{(Morphine)}}{C_{17}H_{19}NO_3} - H_2O = \underset{\text{(Apomorphine)}}{C_{17}H_{17}NO_2}.$$
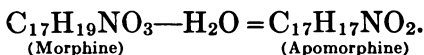
It is supposed that in apomorphine the phenanthrene nucleus is condensed with methyl piperidine. It turns green after long standing.

Other derivatives of morphine have been recently put forward as therapeutic agents.

Dionine is the hydrochloride of the ethyl ether of morphine, $C_{17}H_{17}NO(OH)(OC_2H_5) \cdot HCl$.

Heroine is an ester, diacetyl morphine,

$$C_{17}H_{17}NO\!\!\begin{array}{c}\diagup OOCCH_3 \\ \diagdown OOCCH_3\end{array}.$$
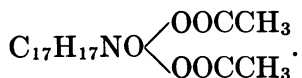
Peronine is the hydrochloride of the benzyl ether of morphine

$$C_{17}H_{17}NO(OH)(OCH_2C_6H_5) \cdot HCl.$$
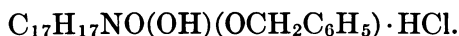
Experiments. (1) Test solutions of morphine sulphate and quinine sulphate with alkaloidal reagents, such as phosphomolybdic acid, picric acid,

iodine potassium iodide solution, mercuric potassium iodide, and tannic acid solutions.

(2) Dissolve quinine in dilute H_2SO_4, and notice the fluorescence of the quinine bisulphate solution.

(3) *Extraction of an alkaloid.* To 10 grams of tea add 500 c.c. of water, and heat, keeping the liquid barely at boiling temperature for 15 minutes. Precipitate tannin from the filtrate of this by adding 10% lead acetate, a drop at a time, until no more precipitate forms. Filter, and evaporate to about 75 c.c. Cool the solution, and if it is turbid filter again. Extract it twice by shaking with two portions of 15 c.c. of chloroform. Dry the chloroform with anhydrous Na_2SO_4. Filter through a small filter into an evaporating dish. Let the chloroform evaporate spontaneously, then examine the crystalline character of the caffeine residue. Remove a little of it, and taste it. Dissolve part of the residue in a few c.c. of hot water and test the solution with alkaloidal reagents (exp. 1).

(4) *Produce codeine.* Dissolve 1 gm. of morphine (pure alkaloid) and 0.6 gm. potassium methyl sulphate in 50 c.c. of pure methyl alcohol, warming and shaking. Then add an excess of powdered KOH until strongly alkaline, attach a reflux condenser and heat in a water-bath for two hours. Add 20 c.c. of water, neutralize with HCl and distill off all volatile materials on a boiling water-bath. Cool, make slightly alkaline with ammonia and filter; transfer to a separating funnel, and shake with several portions of benzene. Dry the combined ben-

zene extracts with calcium chloride, filter into an evaporating dish, and evaporate to dryness on a water-bath. Dissolve part of the residue with 2% HCl, warming gently.

Test a drop of the solution with potassium mercuric iodide solution. Also make the following test: (*a*) make a paste of some ammonium molybdate with a few drops of C.P. H_2SO_4; on adding a drop of the alkaloid solution a blue color is obtained, warm if necessary to develop the color; (*b*) to a few drops of the solution add 2 c.c. of H_2SO_4 containing 1 drop of formaline, and a reddish-violet color appears. These two tests are given also by morphine, but morphine cannot be extracted by means of benzene. A test given by codeine, but not by morphine, is this: to the residue in the evaporating dish add about 1 c.c. of 20% H_2SO_4 and warm, a faint pink color appears.

This method of synthesis should yield considerable impure codeine. Crystals can be obtained by dissolving a little in chloroform, and allowing a drop of the solution to evaporate on a slide.

PURIN DERIVATIVES

The methyl xanthins, caffeine and theobromine, have been discussed elsewhere (p. 293).

Theophylline is 1, 3- dimethyl- 2, 6- dioxypurin, an isomer, therefore, of theobromine. These three alkaloids can be prepared synthetically. All are used as remedies.

Pilocarpine does not have the full purin nucleus, but has the heterocyclic ring imidazol (see p. 414).

$$C_2H_5-CH-CH--CH_2$$

with structure showing OC, CH_2, $C-N-CH_3$, O, $HC-N$, CH
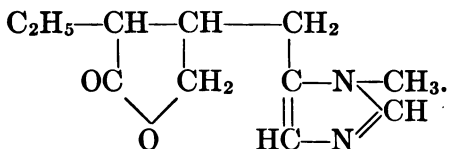
It is dextrorotatory. It has a marked pharmacological action.

CERTAIN ALKALOIDS THAT HAVE NOT BEEN CLASSIFIED

The following indicates what is known about the structure of **aconitine**:

$$C_{21}H_{27}(OCH_3)_4(NO_5){\Big\langle}{{OC \cdot CH_3}\atop{OC \cdot C_6H_5}}.$$
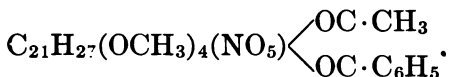
Colchicine is given the formula:

$$C_{15}H_9(OCH_3)_3{\Big\langle}{{COOCH_3}\atop{NH \cdot OC \cdot CH_3}}.$$
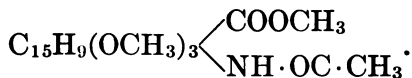
DRUG PRINCIPLES OF UNKNOWN STRUCTURE

Cantharidin, $C_{10}H_{12}O_4$, is an acid lactone, derived from either benzene or cyclohexane.

Picrotoxin, $C_{15}H_{16}O_6$.

Picropodophyllin, $C_{23}H_{24}O_9 \cdot 2H_2O$.

APPENDIX

Note to the Instructor.[1]   If it is desired to shorten the time given to the experiments, we should advise omitting the following: preparation of phenol from potassium benzene sulphonate (see p. 392), the diazonium experiments (see p. 386), preparation of sulphanilic acid (see p. 395), of quinoline (see p. 421), and of codeine (see p. 440).

Diazonium salt may be prepared as a demonstration by the instructor.

To permit of using one apparatus (as a Beckmann apparatus or a combustion furnace) with the entire class, we should suggest dividing the class or a section of it into five groups of three or four men each, the men of each group working together on a particular experiment, but the various groups performing different experiments on the same day.   Thus, one group may do crystallization and melting-point experiments (see pp. 9, 10), a second may carry out fractional distillation (see p. 14) and boiling-point determination (see p. 18), a third may make

[1] We can recommend as valuable books for reference the textbooks of organic chemistry by Holleman, W. A. Noyes, Bernthsen, and Meyer and Jacobson, the laboratory manuals by Gattermann (translated by Schober), W. A. Noyes, and Cohen, and " Introduction to Physical Chemistry," by Walker.

specific gravity determinations (see p. 25), a fourth may do a combustion analysis (see p. 32), and a fifth may use the Beckmann apparatus (see p. 62). Each group will, of course, have to take the experiments in a different order, thus:

> Group   I, Lessons 1, 2, 3, 4, 5.
> Group II, Lessons 2, 3, 4, 5, 1.
> Group III, Lessons 3, 4, 5, 1, 2.
> Group IV, Lessons 4, 5, 1, 2, 3.
> Group V, Lessons 5, 1, 2, 3, 4.

Spellings. We have retained the ending " ine " in the case of amines and alkaloids, with the idea of indicating by this means the organic substances that are *distinctly basic* in character.

Formulæ. We strongly advise that the learning of empirical formulæ by the student be discouraged, but that, on the other hand, the student be thoroughly drilled in giving structural formulæ.

The Student. Many students need advice as to the proper method of studying chemistry, since some try to learn it by rote. Medical students should be urged to retain this textbook for use as a reference book while studying biochemistry, physiology, pathology, and pharmacology.

REFERENCE TABLES

TABLE I

Specific Gravity and Percentage of Alcohol

[According to Squibb.]

Per Cent Alcohol by Volume.	Per Cent Alcohol by Weight.	Specific Gravity.		Per Cent Alcohol by Volume.	Per Cent Alcohol by Weight.	Specific Gravity.	
		At $\frac{15.56°}{15.56}$C.	At $\frac{25°}{15.56}$C.			At $\frac{15.56°}{15.56}$C.	At $\frac{25°}{15.56}$C.
1	0.79	0.9985	0.9970	31	25.51	0.9643	0.9594
2	1.59	.9970	.9953	32	26.37	.9631	.9582
3	2.39	.9956	.9938	33	27.23	.9618	.9567
4	3.20	.9942	.9922	34	28.09	.9609	.9556
5	4.00	.9930	.9909	35	28.96	.9593	.9538
6	4.80	.9914	.9893	36	29.83	.9578	.9521
7	5.61	.9898	.9876	37	30.70	.9565	.9507
8	6.42	.9890	.9868	38	31.58	.9550	.9489
9	7.23	.9878	.9855	39	32.46	.9535	.9473
10	8.04	.9869	.9846	40	33.35	.9519	.9456
11	8.86	.9855	.9831	41	34.24	.9503	.9438
12	9.67	.9841	.9816	42	35.13	.9490	.9424
13	10.49	.9828	.9801	43	36.03	.9470	.9402
14	11.31	.9821	.9793	44	36.93	.9452	.9382
15	12.13	.9815	.9787	45	37.84	.9434	.9363
16	12.95	.9802	.9773	46	38.75	.9416	.9343
17	13.78	.9789	.9759	47	39.67	.9396	.9323
18	14.60	.9778	.9746	48	40.60	.9381	.9307
19	15.43	.9766	.9733	49	41.52	.9362	.9288
20	16.26	.9760	.9726	50	42.52	.9343	.9267
21	17.09	.9753	.9719	51	43.47	.9323	.9246
22	17.92	.9741	.9706	52	44.42	.9303	.9226
23	18.76	.9728	.9692	53	45.36	.9283	.9205
24	19.59	.9716	.9678	54	46.32	.9262	.9184
25	20.43	.9709	.9668	55	47.29	.9242	.9164
26	21.27	.9698	.9655	56	48.26	.9221	.9143
27	22.11	.9691	.9646	57	49.23	.9200	.9122
28	22.96	.9678	.9631	58	50.21	.9178	.9100
29	23.81	.9665	.9617	59	51.20	.9160	.9081
30	24.66	.9652	.9603	60	52.20	.9135	.9056

TABLE I—*Continued*

[According to Squibb.]

Per Cent Alcohol by Volume.	Per Cent Alcohol by Weight.	SPECIFIC GRAVITY.		Per Cent Alcohol by Volume.	Per Cent Alcohol by Weight.	SPECIFIC GRAVITY.	
		At $\dfrac{15.56°}{15.56}$C.	At $\dfrac{25°}{15.56}$C.			At $\dfrac{15.56°}{15.56}$C.	At $\dfrac{25°}{15.56}$C.
61	53.20	0.9113	0.9034	81	74.74	0.8611	0.8530
62	54.21	.9090	.9011	82	75.91	.8581	.8500
63	55.21	.9069	.8989	83	77.09	.8557	.8476
64	56.22	.9047	.8969	84	78.29	.8526	.8444
65	57.20	.9025	.8947	85	79.50	.8496	.8414
66	58.27	.9001	.8923	86	80.71	.8466	.8384
67	59.32	.8973	.8895	87	81.94	.8434	.8352
68	60.38	.8949	.8870	88	83.19	.8408	.8326
69	61.42	.8925	.8846	89	84.46	.8373	.8291
70	62.50	.8900	.8821	90	85.75	.8340	.8258
71	63.58	.8875	.8796	91	87.00	.8305	.8223
72	64.66	.8850	.8771	92	88.37	.8272	.8191
73	65.74	.8825	.8746	93	89.71	.8237	.8156
74	66.83	.8799	.8719	94	91.07	.8199	.8118
75	67.93	.8769	.8689	95	92.46	.8164	.8083
76	69.05	.8745	.8665	96	93.89	.8125	.8044
77	70.18	.8721	.8641	97	95.34	.8084	.8003
78	71.31	.8696	.8616	98	96.84	.8041	.7960
79	72.45	.8664	.8583	99	98.39	.7995	.7914
80	73.59	.8639	.8558	100	100.00	.7946	.7865

The table of the U. S. Bureau of Standards gives specific gravities for a number of concentrations of alcohol differing from those in this table by 0.0002 to 0.0005; for instance, the figures for 95–100% alcohol are lower by 0.0004–0.0006.

TABLE II

MILLIGRAMS OF PURE NITROGEN IN 1 C.C. OF THE MOIST GAS AT VARIOUS TEMPERATURES AND UNDER VARIOUS PRESSURES (MILLIMETERS OF MERCURY)

Temperature.	721	724	727	730	733	736	739	742
10°	1.130	1.135	1.139	1.144	1.149	1.154	1.158	1.163
11	1.125	1.129	1.134	1.139	1.144	1.148	1.153	1.158
12	1.120	1.124	1.129	1.134	1.139	1.143	1.148	1.153
13	1.115	1.119	1.124	1.129	1.134	1.138	1.143	1.148
14	1.110	1.114	1.119	1.124	1.129	1.133	1.138	1.143
15	1.105	1.109	1.114	1.119	1.124	1.128	1.133	1.138
16	1.099	1.103	1.108	1.113	1.118	1.123	1.127	1.132
17	1.094	1.098	1.103	1.108	1.113	1.118	1.122	1.127
18	1.089	1.093	1.098	1.102	1.107	1.112	1.116	1.121
19	1.084	1.088	1.093	1.097	1.102	1.107	1.111	1.116
20	1.079	1.083	1.088	1.092	1.097	1.102	1.106	1.111
21	1.074	1.078	1.082	1.087	1.091	1.096	1.101	1.106
22	1.068	1.072	1.076	1.081	1.086	1.091	1.095	1.100
23	1.062	1.067	1.071	1.076	1.080	1.085	1.090	1.094
24	1.057	1.061	1.066	1.071	1.075	1.080	1.084	1.089
25	1.051	1.056	1.060	1.065	1.069	1.074	1.078	1.083
26	1.046	1.050	1.054	1.059	1.064	1.068	1.072	1.077
27	1.040	1.044	1.048	1.053	1.058	1.062	1.066	1.071
28	1.034	1.038	1.042	1.047	1.052	1.056	1.060	1.065
29	1.028	1.032	1.036	1.041	1.046	1.050	1.054	1.059
30	1.022	1.026	1.031	1.035	1.040	1.044	1.048	1.053

Temperature.	745	748	751	754	757	760	763	766
10°	1.168	1.173	1.177	1.182	1.187	1.192	1.197	1.202
11	1.162	1.167	1.172	1.176	1.181	1.186	1.191	1.196
12	1.157	1.162	1.167	1.171	1.176	1.181	1.186	1.190
13	1.152	1.157	1.162	1.166	1.171	1.176	1.181	1.185
14	1.147	1.152	1.157	1.161	1.166	1.171	1.176	1.180
15	1.142	1.147	1.152	1.156	1.161	1.166	1.170	1.175
16	1.137	1.141	1.146	1.150	1.155	1.160	1.164	1.169
17	1.131	1.136	1.140	1.144	1.149	1.154	1.158	1.163
18	1.125	1.130	1.135	1.139	1.144	1.149	1.153	1.158
19	1.120	1.125	1.130	1.134	1.139	1.144	1.148	1.153
20	1.115	1.120	1.125	1.129	1.134	1.138	1.143	1.148
21	1.110	1.114	1.119	1.123	1.128	1.133	1.138	1.142
22	1.104	1.108	1.113	1.117	1.122	1.127	1.132	1.136
23	1.098	1.103	1.107	1.111	1.116	1.121	1.126	1.131
24	1.093	1.097	1.101	1.106	1.111	1.116	1.121	1.125
25	1.087	1.092	1.096	1.101	1.105	1.110	1.115	1.119
26	1.082	1.086	1.090	1.095	1.099	1.104	1.108	1.113
27	1.076	1.080	1.084	1.089	1.093	1.098	1.102	1.107
28	1.070	1.074	1.078	1.083	1.087	1.092	1.096	1.101
29	1.063	1.068	1.072	1.077	1.081	1.086	1.090	1.095
30	1.057	1.062	1.066	1.071	1.075	1.080	1.084	1.089

TABLE III

Specific Gravity and Percentage of NaOH in Aqueous Solution

Specific Gravity at 15°.	Per Cent NaOH.	Gm. NaOH in 100 c.c.	Specific Gravity at 15°.	Per Cent NaOH.	Gm. NaOH in 100 c.c.
1.007	0.61	0.6	1.220	19.58	23.9
1.014	1.20	1.2	1.231	20.59	25.3
1.022	2.00	2.1	1.241	21.42	26.6
1.029	2.71	2.8	1.252	22.64	28.3
1.036	3.35	3.5	1.263	23.67	29.9
1.045	4.00	4.2	1.274	24.81	31.6
1.052	4.64	4.9	1.285	25.80	33.2
1.060	5.29	5.6	1.297	26.83	34.8
1.067	5.87	6.3	1.308	27.80	36.4
1.075	6.55	7.0	1.320	28.83	38.1
1.083	7.31	7.9	1.332	29.93	39.9
1.091	8.00	8.7	1.345	31.22	42.0
1.100	8.68	9.5	1.357	32.47	44.1
1.108	9.42	10.4	1.370	33.69	46.2
1.116	10.06	11.2	1.384	34.96	48.3
1.125	10.97	12.3	1.397	36.25	50.6
1.134	11.84	13.4	1.410	37.47	52.8
1.142	12.64	14.4	1.424	38.80	55.3
1.152	13.55	15.6	1.438	39.99	57.5
1.162	14.37	16.7	1.453	41.41	60.2
1.171	15.13	17.7	1.468	42.83	62.9
1.180	15.91	18.8	1.483	44.38	65.8
1.190	16.77	20.0	1.498	46.15	69.1
1.200	17.67	21.2	1.514	47.60	72.1
1.210	18.58	22.5	1.530	49.02	75.0

TABLE IV

SPECIFIC GRAVITY AND PERCENTAGE OF KOH IN AQUEOUS
SOLUTION

Specific Gravity at 15°.	Per Cent KOH.	Gm. KOH in 100 c.c.	Specific Gravity at 15°.	Per Cent KOH.	Gm. KOH in 100 c.c.
1.007	0.9	0.9	1.252	27.0	33.8
1.014	1.7	1.7	1.263	28.0	35.3
1.022	2.6	2.6	1.274	28.9	36.8
1.029	3.5	3.6	1.285	29.8	38.5
1.037	4.5	4.6	1.297	30.7	39.8
1.045	5.6	5.8	1.308	31.8	41.6
1.052	6.4	6.7	1.320	32.7	43.2
1.060	7.4	7.8	1.332	33.7	44.9
1.067	8.2	8.8	1.345	34.9	46.9
1.075	9.2	9.9	1.357	35.9	48.7
1.083	10.1	10.9	1.370	36.9	50.6
1.091	10.9	11.9	1.383	37.8	52.2
1.100	12.0	13.2	1.397	38.9	54.3
1.108	12.9	14.3	1.410	39.9	56.3
1.116	13.8	15.3	1.424	40.9	58.2
1.125	14.8	16.7	1.438	42.1	60.5
1.134	15.7	17.8	1.453	43.4	63.1
1.142	16.5	18.8	1.468	44.6	65.5
1.152	17.6	20.3	1.483	45.8	67.9
1.162	18.6	21.6	1.498	47.1	70.6
1.171	19.5	22.8	1.514	48.3	73.1
1.180	20.5	24.2	1.530	49.4	75.6
1.190	21.4	25.5	1.546	50.6	77.9
1.200	22.4	26.9	1.563	51.9	81.1
1.210	23.3	28.2	1.580	53.2	84.0
1.220	24.2	29.5	1.597	54.5	87.0
1.231	25.1	30.9	1.615	55.9	90.2
1.241	26.1	32.4	1.634	57.5	94.0

TABLE V

ACETIC ACID

SPECIFIC GRAVITY AT 15° OF VARIOUS CONCENTRATIONS.				FREEZING-POINT, AS AFFECTED BY WATER-CONTENT.			
Per Cent of Acetic Acid.	Specific Gravity.	Per Cent of Acetic Acid.	Specific Gravity.	Per Cent of Water.	Freez- ing- point.	Per Cent of Water.	Freez- ing- point.
10.0	1.014	60.0	1.069	1.0	14.8°	5.6	8.2°
20.0	1.028	70.0	1.073	2.0	13.25	6.5	7.1
30.0	1.041	80.0	1.075	2.9	11.95	8.3	5.3
40.0	1.052	90.0	1.071	3.8	10.5	9.1	4.3
50.0	1.062	100.0	1.055	4.8	9.4	9.9	3.6

TABLE VI

VAPOR TENSION (AQUEOUS PRESSURE IN MILLIMETERS OF MERCURY) OF WATER AND OF 40% KOH AT VARIOUS TEMPERATURES.

Tem- pera- ture.	Pure H_2O.	40% KOH.	Tem- pera- ture.	Pure H_2O.	40% KOH.	Tem- pera- ture.	Pure H_2O.	40% KOH.
0	4.6	2.6	12	10.5	5.8	24	22.2	11.7
1	4.9	2.8	13	11.2	6.1	25	23.5	12.4
2	5.3	3.0	14	11.9	6.5	26	25.0	13.1
3	5.7	3.2	15	12.7	6.9	27	26.5	13.8
4	6.1	3.4	16	13.6	7.4	28	28.1	14.7
5	6.5	3.6	17	14.4	7.8	29	29.8	15.5
6	7.0	3.9	18	15.4	8.3	30	31.6	16.4
7	7.5	4.1	19	16.4	8.9	31	33.4	17.3
8	8.0	4.4	20	17.4	9.3	32	35.4	18.3
9	8.6	4.7	21	18.5	9.9	33	37.4	19.4
10	9.2	5.1	22	19.7	10.5	34	39.6	20.5
11	9.8	5.4	23	20.9	11.1	35	41.9	21.5

TABLE VII

THE DISSOCIATION CONSTANTS OF CERTAIN ORGANIC ACIDS

Substance.	100K.	Substance.	100K.
Formic..........	0.02140	β-Hydroxypropionic	0.00311
Acetic...........	0.00180	Lactic.............	0.0138
Propionic........	0.00145	Glyceric...........	0.0228
Butyric..........	0.00175	Malonic...........	0.163
Valerianic.......	0.00156	Succinic...........	0.00665
Caproic.........	0.00147	Glutaric...........	0.00475
Monochloracetic..	0.155	Tartaric...........	0.097
Dichloracetic....	5.144	Benzoic............	0.006
Trichloracetic....	120.00	o-Hydroxybenzoic,	
Monobromacetic	0.138	salicylic..........	0.102
Cyanacetic......	0.370	m-Hydroxybenzoic..	0.0087
Glycollic.........	0.0152	p-Hydroxybenzoic ..	0.0029
Oxalic...........	10.06	Phenol............	0.000000013

TABLE VIII

DISSOCIATION CONSTANTS OF CERTAIN BASES

Substance.	100K.	Substance.	100K.
Ammonia..........	0.0023	Diethylamine	0.126
Methylamine......	0.050	Trimethylamine....	0.0074
Ethylamine........	0.056	Triethylamine......	0.064
Dimethylamine....	0.074	Benzylamine.......	0.0024

TABLE IX

The Power of Certain Acids to Cause Hydrolysis

Acid.	Inversion Coefficients (Cane-sugar).	Velocity Coefficients (Methylacetate).	Velocity Coefficients (Acetamide).
Hydrochloric acid..............	1.000	1.000	1.000
Nitric acid...................	1.000	0.915	0.955
Hydrobromic................	1.114	0.983	0.972
Sulphuric acid...............	0.536	0.541	0.547
Formic acid.................	0.0153	0.0131	0.00532
Acetic acid..................	0.0040	0.00345	0.000747
Monochloracetic acid.........	0.0484	0.0430	0.0295
Dichloracetic acid............	0.271	0.2304	0.245
Trichloracetic acid...........	0.754	0.6820	0.670
Oxalic acid..................	0.1857	0.1746	0.169
Succinic acid................	0.00545	0.00496	0.00195.
Citric acid..................	0.0172	0.01635	0.00797

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