Azadirachtæ Cortex et Folia, P. I., from *Azadirachta indica*, Nim or Margosa. (A resin; $C_{36}H_{50}O_{11}$. Broughton.)

Bonducella semina, P. I., from *Cæsalpinia (guilandina) bonducella*. Bonduc-seeds or nickar-nuts.

Buchu folia.

Calendula officinalis. Marigold. (Calendulin, Stoltze.)

Calotropis Cortex, P. I., from *Calotropis procera* and *C. gigantea*. Mudar.

Canellæ cortex (Cascarillin, $C_{12}H_{11}O_4$).

Caulophyllum thalictroides. Blue cohosh. Alkaloid ?

Cimicifuga (Actæa) racemosa (Cimicifugin; said by Conard to be neutral, and by Falck alkaloidal). Black snake-root (*Cimicifugæ Rhizoma*, B. P.).

Cypripedium pubescens (Cypripedin ?). Ladies' Slipper.

Euonymus atropurpureus. Wahoo-bark (Euonymin ?).

Eupatorium perfoliatum. Thoroughwort or Boneset.

Gulancha (Tinosporæ Radix et Caules, P. I.).

Gynocardiæ semina, from *Gynocardia odorata* (Chaulmugra, P. I.).

Hamamelis virginica. Witchhazel.

Hydrocotyles folia, P. I., from *Hydrocotyle asiatica.* Indian pennywort.

Iris versicolor. Blue flag (Iridin or Irisin ?).

Lactuca (Lactucin, etc.). The milk-juice, dried, yields *Lactucarium*, U. S. P.

Lappa, U. S. P., *Arctium lappa*, *Lappa officinalis.* Burdock.

Lupulus.

Magnolia. Swamp Sassafras or Beaver Tree.

Marrubium. Horehound. Marrubein, a crystalline bitter substance (Mein).

Maticæ folia. Matico.

Melia Azedarach (Resin, Jacobs).

Pepo. The seed of *Cucurbita pepo.* A remedy for tape-worm.

Phytolacca Bacca et Radix. Pokeberry and root. Phytolaccin, a crystalline substance (Claassen).

Scutellaria. Skullcap.

Serpentaria. Virginia Snakeroot.

Soymidæ Cortex, P. I. Rohunbark, from *Soymida febrifuga.*

Taraxaci radix (Taraxacin).

Toddaliæ radix, P. I.

Triticum repens. Rhizome of couch-grass.

Veronica virginica, or *Leptandra virginica.* Culvers-root; *Leptandra*, U. S. P. (Leptandrin ?).

Viburnum. Black haw (*Viburnin*).

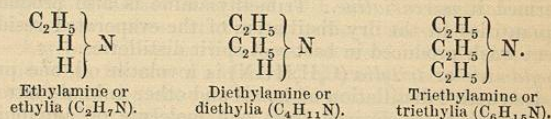# ALKALOIDS.

Constitution of Alkaloids or Organic Bases.

Natural Alkaloids.—The natural organic bases, alkaloids, or alkali-like bodies (εἶδος, *eidos*, likeness), have many analogies with ammonia. Their constitution, as a class, is not yet satisfactorily known; but some are probably direct derivatives of a single molecule of ammonia (NH_3) or of double, triple, or quadruple molecules (N_2H_6, N_3H_9, N_4H_{12}); others of ammonias in which the ammoniacal structure is largely merged in or conditioned by a benzenoid or aromatic structure, or, *vice versâ*, in which the ben-

zenoid character is conditioned by the ammoniacal; while others, again, certainly appear to be benzenoid, but of a more or less nitrogen-benzene (pyridinoid) rather than a completely carbon-benzene character—benzene (p. 634) in which CH''' is displaced by N'''.

Artificial Alkaloids.—Numerous artificial alkaloids or artificial organic bases having a simple ammoniacal constitution have already been formed. These are sometimes termed amines, and are primary, secondary, and tertiary according as one, two, or three atoms of hydrogen in ammonia have been displaced by radicals, as seen in the following general formulæ (R = any univalent radical):—

$$\left.\begin{array}{c}R\\H\\H\end{array}\right\}N \qquad \left.\begin{array}{c}R\\R\\H\end{array}\right\}N \qquad \left.\begin{array}{c}R\\R\\R\end{array}\right\}N\;;$$

or in the following examples:—

$$\left.\begin{array}{c}C_2H_5\\H\\H\end{array}\right\}N \qquad \left.\begin{array}{c}C_2H_5\\C_2H_5\\H\end{array}\right\}N \qquad \left.\begin{array}{c}C_2H_5\\C_2H_5\\C_2H_5\end{array}\right\}N.$$

Ethylamine or ethylia (C_2H_7N).   Diethylamine or diethylia ($C_4H_{11}N$).   Triethylamine or triethylia ($C_6H_{15}N$).

The three classes have also been termed amidogen-bases (NH_2), imidogen-bases (NH), and nitrile-bases (N).

Mode of Formation of Artificial Ammoniacal Alkaloids.—A few illustrations will suffice. Just as the addition of iodide of hydrogen (HI) to ammonia (that is, the common trihydrogen ammonia, NH_3) gives iodide of common ammonium (NHHHHI or NH_4I), so the addition of iodide of ethyl (C_2H_5I or EtI) (see page 401) to *ammonia* (NH_3) gives the iodide of ethyl-ammonium (NHHHEtI, or NH_3EtI or $NH_3C_2H_5I$). A fixed alkali turns out common *ammonia* (NHHH) from the iodide (or any other salt) of common ammonium; it turns out ethyl-ammonia (NHHEt) from the iodide (or any other salt) of ethyl-ammonium. Ethyl-ammonia (or *ethylia* or ethylamine), NHHEt, with iodide of ethyl, EtI, gives iodide of diethyl-ammonium [NHHEtEtI, or NH_2Et_2I, or $NH_2(C_2H_5)_2I$]. From the latter, potash turns out diethyl-ammonia ($NHEt_2$). Diethyl-ammonia (*diethylia* or diethylamine) with iodide of ethyl gives iodide of triethyl-ammonium ($NHEt_3I$). The latter with alkali gives triethyl-ammonia or *triethylia* or triethylamine (NEt_3), and this with iodide of ethyl gives iodide of tetrethyl-ammonium, NEt_4I.

What has just been stated respecting iodide of ethyl is true of other salts of ethyl; and what is true of salts of ethyl is true of salts of an immense number of other radicals—univalent, bivalent, etc.; so that a vast number of artificial ammoniacal alkaloids and their salts can be produced. The reactions are not always so sharp as those just given. Mixtures of primary, secondary, and tertiary compounds rather than either alone often result in an experiment; but the reactions are typically true.

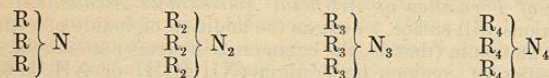Some of these artificial ammoniacal alkaloids not only resemble

natural alkaloids, but are strong caustic liquids, like solution of ammonia.

Then, the displacing radical in an artificial alkaloid or its salt may not only be of one kind, as indicated in the preceding paragraphs, but of different kinds; and while the radical displacing one atom of hydrogen is keeping its place, any of the many known radicals may occupy the position of one or all of the other atoms of hydrogen. Thus, for example, we have methyl-ethyl-amylamine ($C_8H_{19}N$, or $NCH_3C_2H_5C_5H_{11}$, or NMeEtAy), a colorless, oily body of agreeable aromatic odor. The empirical formulæ of the vegeto-alkaloids morphine, quinine, etc. may some day be similarly resolvable into rational formulæ, either simply ammoniacal, benzenoid, or pyridinoid. Their artificial production will then quickly follow.

Methylamine, (CH_3HHN), and *trimethylamine*, ($CH_3)_3N$, are artificial ammoniacal alkaloids. The former was found, by Schmidt, in *Mercurialis annua* and *M. perennis*, and previously by Reichardt, who termed it *mercurialine*. Trimethylamine is also produced in large quantities in the dry distillation of the evaporated residue of the spent wash produced in beet-root spirit distilleries.

Propylamine or *tritylia* (C_3H_7HHN) is a volatile oil, one product of the destructive distillation of bones and other animal matters.

The organic bases derived from one molecule of ammonia are termed *monamines*; from two molecules, *diamines*; from three, *triamines*; and from four, *tetramines*:—

$$\left.\begin{array}{c}R\\R\\R\end{array}\right\}N \quad \left.\begin{array}{c}R_2\\R_2\\R_2\end{array}\right\}N_2 \quad \left.\begin{array}{c}R_3\\R_3\\R_3\end{array}\right\}N_3 \quad \left.\begin{array}{c}R_4\\R_4\\R_4\end{array}\right\}N_4$$

In these amines any bivalent, trivalent, or quadrivalent radical may occupy the place of two, three, or four univalent radicals.

Wurtz first obtained methylamine and ethylamine in 1849: Hofmann, in 1850 and subsequently, added enormously to our knowledge of the secondary, tertiary, and other amines, and to the directly ammoniacal type of bodies generally. Kekulé linked on the aromatic or benzenoid type in 1865. Dewar and Körner, almost simultaneously in 1870, demonstrated the benzenoid character of pyridine and quinoline (see next paragraph), while no one has since been so active in alkaloidal research as Ladenburg.

Vegetal Alkaloids.—These are of great importance to the medical and pharmaceutical student. They are treated in considerable detail in the succeeding pages.

Animal Alkaloids.—Many well-known alkaloids occur in the juice of the flesh and in other parts of animals. Ordinary extract of meat contains abundance of crystals of *creatine*, $C_4H_9N_3O_2$, and some *creatinine*, $C_4H_7N_3O$. Creatine easily parts with the elements of water and yields creatinine; it takes up the elements of water and yields *sarkosine*, $C_3H_7NO_2$, and *urea*, CH_4N_2O. Sarkosine is methyl-glycocoll. *Taurine*, $C_2H_7NSO_3$, may be obtained from bile, and it can

be constructed artificially from its elements. Glandular tissue, as of the spleen, brain, and pancreas, yield, as a product of work, *leucine*, $C_6H_{13}NO_2$, which occurs in white, pearly crystals. Gautier recently obtained several new alkaloids from albuminoids, and hence termed them *leucomaïnes* (λευκωμα, *leucoma*, white of egg)—namely, *xanthocreatinine*, $C_5H_{10}N_4O$; *crusocreatinine*, $C_5H_8N_4O$; *amphicreatine*, $C_9H_{19}N_7O_4$; and *pseudoxanthine*, $C_4H_5N_5O$. The leucomaïnes and the animal alkaloids generally are of great physiological interest. Some of the leucomaïnes are toxic, and indistinguishable from ptomaïnes; in fact, the three classes merge into one another.

Ptomaïnes.—A series of diamines, many of them toxic, have been isolated by Brieger from decaying nitrogenous animal principles, including the putrid proteids or albuminoids of the human body itself; hence the name *ptomaïnes* (πτωμα, *ptoma*, a corpse). These have some medico-legal importance, but, inasmuch as they may occur in life, poisoning the blood during the progress of disease—especially disease associated with the development of micro-organisms or microbes; that is, zymotic disease (ζύμη, *zume*, ferment)—they have great pathological interest; indeed, physiological importance also, for one of a curaroid character seems to play a part in the process of digestion. The names of some of these bases are *neurine* ($C_5H_{13}NO$) and *neuridine* ($C_5H_{14}N_2$), from putrid flesh; *muscarine* ($C_5H_{13}NO_2$) and *gadinine* ($C_7H_{16}NO_2$), from putrid fish; *cadaverine* ($C_5H_{16}N_2$), *saprine*, and *putrescine* ($C_4H_{12}N_2$), from putrid human remains, *choline* being met with in the earlier stages of decay; and *tetanine*, $C_{13}H_{30}N_2O_4$, the administration of which to animals produced symptoms resembling those of tetanus in man from beef putrefied by the agency of the microbe, which is associated with the cause of traumatic tetanus so distressing to the human subject. *Tyrotoxicon* was the name given by Vaughan to a toxic ptomaïne he isolated from poisonous cheese (τυρὸς, *turos*, cheese; τοξικον, *toxicon*, poison), afterward from poisonous milk and cream, which, taken as food, had caused more or less vomiting, headache, and diarrhœa. He afterward recognized it as *diasobenzene*, $C_6H_5.N : N.OH$. Brieger states that when shellfish is poisonous it is due to the presence of a ptomaïne, *mytiloxine*, $C_6H_{15}NO_2$. Para- and meta-phenylene diamine appear to have all the characters of leucomaïnes or ptomaïnes, the latter causing intense influenza.

Evidence of Constitution of the Natural Alkaloids.—Attempts to form artificially the natural organic bases commonly used in medicine have hitherto failed. Many artificial colorific alkaloids of the type of amido-benzene (aniline or phenylamine) and of a curious double nitrogen (azo- or diazo-) type (see the non-colorific diazobenzene above) have been obtained. But the type of the natural medicinal alkaloids seems rather to be found in *pyridine*, C_5H_5N. Pyridine is producible in various ways, but was originally obtained from bone-oil (a product of the destructive distillation of bones), together with the homologues *picoline*, C_6H_7N (or methyl-pyridine, ortho-, meta-, or para-); *lutidine*, C_7H_9N; and *collidine*, $C_8H_{11}N$, forming an homologous series of *pyridine bases*, $C_nH_{2n-5}N$.

Phenylamine or Amidobenzene. Pyridine.
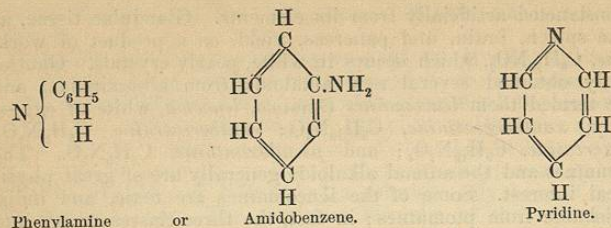
From quinine, cinchonine, and strychnine, by the disruptive action of caustic alkalies, not only pyridine and homologues, but *quinoline* or *chinoline*, C_9H_7N, have been obtained; hence pyridine and quinoline would seem to contribute to the construction of those and similar alkaloids. Quinoline can be made in various other ways, especially (Skraup) from nitrobenzene, aniline, and glycerin. Quinoline is closely related both to benzene and to pyridine, as will be seen by a glance at the following formula. Its relation to naphthalene (two carbon-conjoined benzene residues) is just the relation of pyridine to benzene:—


Naphthalene. Quinoline.
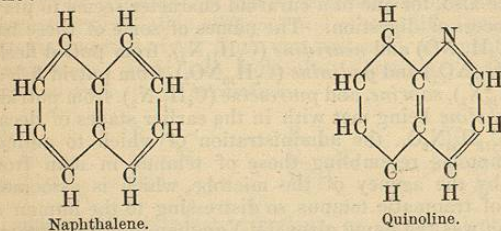
Both pyridine and quinoline form additive compounds with hydrogen. (See "Piperidine" in Index.) Chemists, in the hope, doubtless, of discovering how to produce the medicinal alkaloids artificially, have obtained several alkaloidal derivatives of quinoline. One, *kairine*, somewhat resembles quinine. Again, alkaloids yield organic acids, and organic acids, notably those occurring in nicotine-yielding and morphine-yielding plants, may be converted into pyridine compounds when the constituents of their molecules are interwoven with those of ammonia.

A careful consideration of the above and allied facts irresistibly leads to the inference that we are at last almost "within measurable distance" of the artificial production of most of the natural alkaloids—a subject still of financial and general commercial weight, of considerable technological (including pharmaceutical) importance, of very great medical consequence, especially taken in connection with its ramifications, and of transcendent interest as illustrating the working of the forces of nature within the molecules of matter.

Animal and Vegeto-animal Alkaloids.—Choline, $C_5H_{15}NO_2$, occurs in the bile and the brain, also in ergot and ipecacuanha, etc. *Guanine*, $C_5H_5N_5O$, and *Sarkine*, $C_5H_4N_4O$, are found in flesh and in

young plane-leaves. Fresh meat furnishes *Carnine*, $C_7H_8N_4O_3$, *Cruso-creatinine*, $C_5H_8N_4O$, and *Xantho-creatinine*, $C_5H_{10}N_4O$. Urine yields *Creatinine*, $C_4H_7N_3O$. *Betaine*, $C_5H_{11}NO_2$, is met with in beet-root and in urine.

Hydroxylamine.—Besides the amide, imide, and nitrile bases already mentioned, ammonia may have one atom of its hydrogen displaced by hydroxyl, hydroxylamine (NH_2OH) resulting. It is often formed when nascent hydrogen acts on an oxide of nitrogen, as when zinc, diluted sulphuric acid, and a little nitric acid are brought together. It yields substitution-products, as ethyl-hydroxylamine (NHC_2H_5OH), and additive compounds, as hydrochlorate of hydroxylamine (NH_2OH,HCl):—

Ammonia. Hydroxylamine. Ethyl hydroxylamine. Hydrochlorate of hydroxylamine.
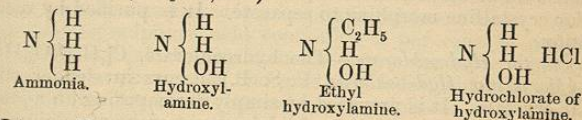
Note on Nomenclature of Natural Alkaloids.—The first syllables of the names of the natural alkaloids recall the name of the plant whence they were obtained or some characteristic property. It is to be regretted that the last syllable is not either *ine* or *ia*, instead of sometimes one and sometimes the other. The termination in *ia* distinguishes the alkaloids from some other substances the names of which end in *ine*, as chlorine, bromine, iodine, fluorine, etc., but traders generally, and the compilers of the American, British, French, and German Pharmacopœias, adopt the termination in *ine*. The names of the salts of the alkaloids are given on the assumption that the acid unites with the alkaloid without decomposition. Thus, hydrochlorate (sometimes termed "hydrochloride") of morphine is regarded as morphine with added hydrochloric acid, as we might assume sal-ammoniac to be ammonia (NH_3) with hydrochloric acid (HCl), and name it hydrochlorate of ammonia (NH_3HCl), instead of chloride of ammonium (NH_4Cl). All acids, even sulphydric, unite with alkaloids and form salts having similar names.

Antidotes.—In cases of poisoning by alkaloids, emetics and the stomach-pump must be relied on rather than chemical agents. But astringent liquids may be administered, for tannic acid precipitates many of the alkaloids from their aqueous solution, absorption of the poison being thus possibly retarded.

MORPHINE, OR MORPHIA.

Formula $C_{17}H_{19}NO_3,H_2O$. Molecular weight 303.

Occurrence.—Morphine occurs in opium (the inspissated juice of the fruit *Papaveris capsulæ*, of the White Poppy, *Papaver somniferum*) as meconate of morphine [$(C_{17}H_{19}NO_3)_2$, $C_7H_4O_7$, $5H_2O$, Dott, and as sulphate]. The dried poppy-capsule of pharmacy contains opium principles, but varying much in nature and proportion. The presence in the capsule of morphine, narcotine, and meconic acid

22

has been demonstrated, and, by Groves, of narceine and codeine. Ordinary Asia Minor opium (*Opium*, U. S. P.) (Turkey, Smyrna, or Constantinople opium) should contain "not less than 9 per cent. of morphine," and when dried at 85° C. and powdered (*Opii Pulvis*, U. S. P.), from 12 to 16 per cent. of morphine.

Denarcotized Opium (*Opium Denarcotisatum*, U. S. P.) is dried and powdered opium from which narcotine has been washed out by ten times its weight of stronger ether, the product being redried at 85° C., and made up to its original weight with powdered sugar of milk.

Morphina, U. S. P., may be made by adding to infusion of opium an equal bulk of alcohol, then slight excess of ammonia, and setting aside for crystalline morphine to separate. It is purified by recrystallization.

Process for Hydrochlorate.—The hydrochlorate, $C_{17}H_{19}NO_3,HCl,3H_2O$ (*Morphinæ Hydrochloras*, U. S. P.), occurs in slender white acicular crystals. It is prepared by simply decomposing an aqueous infusion of opium with chloride of calcium, meconate of calcium and hydrochlorate of morphine being produced. (If the infusion, which is always acid, be first nearly neutralized by the cautious addition of small quantities of very dilute solution of ammonia, the chloride of calcium then at once causes a precipitate of meconate of calcium, which can be filtered off, leaving a colored solution of hydrochlorate of morphine. On the large scale (*vide* B. P.) the details are somewhat different.) The salt is partially purified by crystallization from the evaporated liquid, then by treatment of the solution of the impure hydrochlorate by animal charcoal, and lastly, by precipitation of the morphine from the still colored liquid by ammonia and re-solution of the morphine in hot dilute hydrochloric acid; hydrochlorate of morphine separates out on cooling.

Hydrochlorate of morphine deposited from a hot solution in about twenty times its weight of alcohol is anhydrous.

Morphine may also, of course, be prepared by the methods given for its quantitative separation from opium (see Index).

Morphinæ Sulphas, U. S. P. ($2C_{17}H_{19}NO_3,H_2SO_4,5H_2O$) may be made by neutralizing morphine with sulphuric acid. It is a constituent of *Pulvis Morphinæ Compositus*.

Process for Acetate.—Acetate of morphine ($C_{17}H_{19}NO_3,C_2H_4O_2$) (*Morphinæ Acetas*, U. S. P.) is a white pulverulent salt prepared by dissolving pure morphine in acetic acid. One grain of acetate, so made, in twelve minims of water, forms the *Injectio Morphiæ Hypodermica*, B. P.

Both the hydrochlorate and acetate of morphine are soluble in water, but the solution is not stable unless acidulated and containing alcohol; hence the official solutions, 4 grains in one ounce, 1 in 110 (*Liquor Morphiæ Hydrochloratis*, B. P., and *Liquor Morphiæ Acetatis*, B. P.), consist of three parts water and one part rectified spirit, a few minims per ounce of hydrochloric or acetic acid being added. Even solid acetate of morphine is unstable, slowly dissociating into acetic acid and morphine; hence the acid odor of acetate of morphine.

Solubility of morphine salts in water at 60° F.—According to Dott, 1 part of the respective salts is soluble in the annexed number of parts of water: Acetate, $2\frac{1}{2}$; Tartrate, $9\frac{3}{4}$; Sulphate, 23; Hydrochlorate, 24; Meconate, 34.

Tartrate of Morphia has the formula $(C_{17}H_{19}NO_3)_2, C_4H_6O_6,3H_2O$.

Other alkaloids exist in opium. In the above process a considerable quantity of an alkaloid of very weak basic properties, *narcotine* ($C_{22}H_{23}NO_7$) (*Narcotina*, P. I.), remains in the exhausted opium, and may be extracted by digesting in acetic acid, filtering, precipitating by ammonia. It crystallizes in brilliant needles from alcohol or ether. By oxidation it yields *cotarnine* and an acid termed *opianic*.

Codeine ($C_{18}H_{21}NO_3,H_2O$) (*Codeina*, U. S. P.) is soluble in the slight excess of ammonia employed in precipitating the morphine. "Codeine is dissolved by sulphuric acid containing 1 per cent. of molybdate of sodium to a liquid having, at first, a dirty-green color, which, after a while, becomes pure blue, and gradually fades, within a few hours, to pale yellow. On dissolving codeine in sulphuric acid a colorless liquid results, which, on the addition of a trace of ferric chloride and gentle warming, becomes deep blue. An aqueous solution of codeine, added to test-solution of mercuric chloride, should produce no precipitate; and if codeine be added to nitric acid of sp. gr. 1.200, it will dissolve to a yellow liquid which should not become red (difference from and abs. of morphine)."—U. S. P. It reduces a solution of 1 part of selenite of ammonium in 20 of strong sulphuric acid, yielding a green color (Lafon). From the mother-liquors there have also been obtained *thebaine* ($C_{19}H_{21}NO_3$), *papaverine* ($C_{21}H_{21}NO_4$, Hesse; $C_{20}H_{21}NO_4$, Merck), *opianine* ($C_{21}H_{23}NO_7$?), *narceine* ($C_{23}H_{29}NO_9$), *cryptopine* ($C_{21}H_{23}NO_5$), *meconine* ($C_{10}H_{10}O$), *meconoisine* ($C_8H_{10}O_2$), *laudanine* ($C_{20}H_{23}NO_4$), *codamine* ($C_{20}H_{25}NO_4$), *gnoscopine* ($C_{34}H_{36}N_2O_{11}$), *pseudomorphine* ($C_{17}H_{18}NO_3$), *protopine* ($C_{20}H_{19}NO_5$), *laudanosine* ($C_{21}H_{27}NO_4$), *hydrocotarnine* ($C_{12}H_{15}NO_3$), *rhœadine* ($C_{20}H_{21}NO_6$), *meconidine* ($C_{21}H_{23}NO_4$), *lanthopine* ($C_{23}H_{25}NO_4$). A little acetic acid also exists in all opium (D. Brown).

Analytical Reactions.

First Analytical Reaction.—To a minute fragment of a salt of morphine add one drop of water, and warm the mixture until the salt dissolves, then stir the liquid with a glass rod moistened by a strong *neutral* solution of perchloride of iron; a dirty-blue color is produced. This effect is not observed in dilute solutions. The reaction is accompanied by a reduction of the ferric salt to ferrous. The occurrence of the latter may be shown by ferricyanide of potassium giving Turnbull's blue.

Second Analytical Reaction.—To a drop or two of a strong solution of a morphine salt in a test-tube add a minute fragment of iodic acid (HIO_3; page 295); iodine is set free. Into the upper part of the tube insert a glass rod covered with mucilage of starch, and warm the solution; dark-blue starch iodide is

produced. If the mixture of morphine and iodic acid be shaken up with chloroform or bisulphide of carbon, a violet solution is obtained.

This reaction is only confirmatory of others, as albuminous matters also reduce iodic acid.

Third Analytical Reaction.—To a few drops of an aqueous infusion of opium add a drop of *neutral* solution of perchloride of iron; a red solution of meconate of iron is produced. Add solution of corrosive sublimate; the color is not destroyed (as it is in the case of sulphocyanate of iron, a salt of similar tint).

In cases of poisoning by a preparation of opium this test is almost as conclusive as a direct reaction of morphine (the poison itself), meconic acid being obtainable from opium only.

Other Reactions.—Add carbonate of sodium to a solution of a salt of morphine; a white precipitate of morphine falls, slowly, and of a crystalline character if the solution is dilute. Collect this precipitate, and moisten it with neutral solution of perchloride of iron; the bluish tint above referred to is produced.——Add an alkali to a solution of hydrochlorate or acetate of the alkaloid; morphine is precipitated, soluble in excess of the fixed alkali; far less readily so in ammonia.——Moisten a particle of a morphine salt with nitric acid; an orange-red coloration is produced.——Warm a little morphia with strong sulphuric acid and arseniate of sodium; blue-green tinges result. ——To morphine add strong sulphuric acid, mix, and strew nitrate of bismuth on the fluid; the mixture turns dark brown or black.——Heat morphine on platinum foil; it burns entirely away.

### *Apomorphine* ($C_{17}H_{17}NO_2$).

Apomorphine (ἀπὸ, *apo*, from, and *morphine*) is an alkaloid obtained from morphine by Matthiessen and Wright. It possesses remarkable physiological effects: one-tenth of a grain (in aqueous solution) injected under the skin, or one-quarter of a grain taken into the stomach, is said to produce vomiting in from four to ten minutes.

Process.—Hydrochlorate of morphine is hermetically sealed in a thick tube with considerable excess of hydrochloric acid, and heated to nearly 300° F. for two or three hours. The product is purified by diluting the contents of the tube with water, precipitating with bicarbonate of sodium, and treating the precipitate with ether or chloroform. On shaking up the ethereal or chloroform solution with a very small quantity of strong hydrochloric acid, the sides of the vessel become covered with crystals of the hydrochlorate of the new base. These may be drained from the mother-liquor, washed

with a little cold water, in which the salt is sparingly soluble, recrystallized from hot water, and dried on bibulous paper or over sulphuric acid. The formula ($C_{17}H_{17}NO_2$,HCl) indicates that the new alkaloid is derived from morphine by abstraction of the elements of water.

Hydrochlorate of Apomorphine (*Apomorphinæ Hydrochlorus*, U. S. P.) occurs in "colorless or grayish-white, shining crystals, turning greenish on exposure to light and air, odorless, having a bitter taste and a neutral or faintly acid reaction. Soluble in 6.8 parts of water and in 50 parts of alcohol at 15° C. (59° F.); slowly decomposed by boiling water or boiling alcohol; almost insoluble in ether or chloroform; should it impart color to either of these liquids it should be rejected, or it may be purified by thoroughly agitating it with either liquid, filtering, and then rapidly drying the salt on bibulous paper in a dark place. The aqueous solution, on gentle warming, rapidly turns green, but retains a neutral reaction. Solution of bicarbonate of sodium, added to an aqueous solution of the salt, throws down the white, amorphous alkaloid, which soon turns green on exposure to air, and forms a bluish-green solution with alcohol, a purple one with ether or pure benzol, and a violet or blue one with chloroform."

Codeine also, according to the same chemists, yields apomorphine by similar treatment, a reaction that would seem to indicate that codeine is a methyl-morphine; indeed, Grimaux (Hesse also) has since obtained codeine—or, possibly, an isomer of codeine, methylmorphine—from morphine.

$$C_{17}H_{17}CH_3HNO_3 + HCl = CH_3Cl + H_2O + C_{17}H_{17}NO_2$$
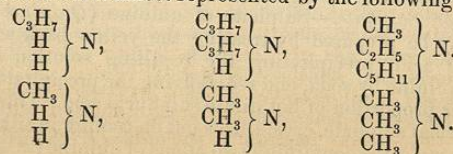Codeine   Chl. of methyl.   Apomorphine.
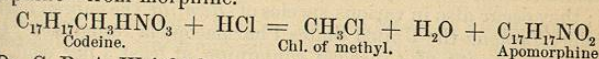
Dr. C. R. A. Wright has recently obtained several new derivatives of codeine.

Codeine neither gives a blue odor with ferric chloride nor a red with nitric acid. Both codeine and morphine, when heated with a mixture of strong sulphuric acid and arseniate of sodium, give a blue color, the morphine yielding a greenish-blue and the codeine a violet-blue.

Constitution of the Opium Alkaloids.—The opium alkaloids, like the cinchona alkaloids, have been attacked by many highly skilled chemists in the hope that analytical, or, in a sense, destructive, investigation would lead to synthetical or constructive knowledge; and many interesting and promising results have been obtained. But the subject is not yet sufficiently advanced for presentation before the younger students of medicine or pharmacy.

QUESTIONS AND EXERCISES.

817. Write some general formulæ of artificial alkaloids.

818. Name the substances represented by the following formulæ:—

$$\left.\begin{array}{c}C_3H_7 \\ H \\ H\end{array}\right\}N, \qquad \left.\begin{array}{c}C_3H_7 \\ C_3H_7 \\ H\end{array}\right\}N, \qquad \left.\begin{array}{c}CH_3 \\ C_2H_5 \\ C_5H_{11}\end{array}\right\}N.$$

$$\left.\begin{array}{c}CH_3 \\ H \\ H\end{array}\right\}N, \qquad \left.\begin{array}{c}CH_3 \\ CH_3 \\ H\end{array}\right\}N, \qquad \left.\begin{array}{c}CH_3 \\ CH_3 \\ CH_3\end{array}\right\}N.$$

819. What is the assumed constitution of the salts of the alkaloids?

820. Describe the treatment in cases of poisoning by alkaloids.

821. Give the process for the preparation of Hydrochlorate of Morphine. In what form does morphine occur in opium?

822. How is Acetate of Morphine prepared?

823. What plan is adopted for preventing the decomposition of the official solutions of morphine?

824. Mention the analytical reactions of morphine.

825. In addition to the reactions of morphine, what test may be employed in searching for opium in a liquid or semifluid material?

826. How is Apomorphine prepared, and what are its properties?

827. Describe the relation of morphine to codeine.

QUININE, OR QUINIA.

Formula $C_{20}H_{24}N_2O_2,3H_2O$. Molecular weight 378.

Source.—Quinine (*Quinina*, U. S. P.) and other similar alkaloids exist in cinchona-bark as kinates. In the yellow bark (*Cinchona Flava*, U. S. P., from *Cinchona calisaya*) chiefly quinine is present; in the pale bark (*Cinchonæ Pallidæ Cortex*, B. P., chiefly from *C. officinalis*) other alkaloids are more frequently found; in the red bark (*Cinchona Rubra*, U. S. P.) these alkaloids occur in irregular proportions; they occur also in various species of *Remijia*, the cuprea barks.

Under *Cinchona* the United States Pharmacopœia recognizes "the bark of any species of *Cinchona* containing at least 3 per cent. of its peculiar alkaloids."

Extraction of the Mixed Alkaloids.—Take 750 grains of finely powdered bark. Make it into a paste with milk of lime (slaked lime about 400 grains and water about 4 ounces). Dry the mixture over a water-bath. Powder the residue and place the whole in a cylindrical percolator. Pour in 3½ fluidounces of chloroform. When, after standing, packing is complete, allow percolation to commence and to proceed slowly. After a time pour 3½ fluidounces more chloroform into the percolator. When percolation has ceased transfer the percolate to a retort, and add nearly half an ounce of water and enough dilute sulphuric acid to make the mixture acid to test-paper. Recover the chloroform by distilling from a water-bath, and allow the residue to cool; filter. To the filtrate, which contains the alkaloids as acid sulphates, add ammonia in slight excess. Collect the precipitated alkaloids on a filter, wash, and dry in the air or over a dish of sulphuric acid covered by a bell-jar. (For the separation of alkaloids see Index, "Dr. Vrij's process," an operation which should not be attempted at this stage of study.)

Process for Sulphate.—Sulphate of quinine (*Quininæ Sulphas.* U. S. P.) may be prepared by treating the yellow bark with dilute hydrochloric acid, precipitating the resulting solution of hydrochlorate of quinine by soda, and redissolving the precipitated quinine in the proper proportion of hot dilute sulphuric acid. This, the common commercial sulphate, crystallizes out on cooling in silky acicular crystals, one molecule containing two atoms of quinine ($2C_{20}H_{24}N_2O_2$),

one of sulphuric acid (H_2SO_4) and seven of water of crystallization ($7H_2O$).

In the process of the former United States Pharmacopœia (1870) lime was used instead of soda, the precipitated quinine dissolved in boiling alcohol, the latter recovered by distillation, the residual quinine neutralized by diluted sulphuric acid, the solution treated with animal charcoal, filtered while hot, set aside to crystallize, and recrystallized if necessary.

Sulphate of quinine, the *common* or so-called *disulphate* ($(C_{20}H_{24}N_2O_2)_2,H_2SO_4,8H_2O$, is only slightly soluble in water; on the addition of dilute sulphuric acid the so-called *neutral sulphate*, or *soluble sulphate* (*Quininæ Bisulphas*, U. S. P.; $C_{20}H_{24}N_2O_2,H_2SO_4,7H_2O$), is formed, which is freely soluble. The latter salt may be obtained in large rectangular prisms.* An *acid sulphate* ($C_{20}H_{24}N_2O_2,2H_2SO_4,7H_2O$) also exists.

The ordinary disulphate of quinine is more soluble in alcohol or alcoholic liquids than in water. The citrate of iron and quinine (*Ferri et Quininæ Citras*, U. S. P.) is the well-known scale compound. It is made by dissolving ferric hydrate, prepared from ferric sulphate, and quinine, prepared from the sulphate, in solution of citric acid; the liquid, evaporated to a syrupy consistence and dried in thin layers on glass plates, yields the usual greenish-yellow scales (*vide* p. 152).

Quininæ Valerianas, U. S. P., may be made by dissolving precipitated quinine in warm aqueous solution of valerianic acid and setting aside to crystallize. Its formula is $C_{20}H_{24}N_2O_2,C_5H_{10}O_2,H_2O$.

Basic Citrate of Quinine has the formula $(C_{20}H_{24}N_2O_2)_2,H_3C_6H_5O_7,5H_2O$. Other citrates contain three molecules of quinine to two of citric acid, and one of quinine to one of citric acid.

Quininæ Hydrobromas, U. S. P., has the formula $C_{20}H_{24}N_2O_2,HBr,2H_2O$.

Quininæ Hydrochloras, U. S. P., has the formula $C_{20}H_{24}N_2O_2,HCl,2H_2O$.

REACTIONS.

First Analytical Reaction.—To a solution of quinine or its salts in acidulated water add fresh chlorine-water, shake, and then add solution of ammonia; a green coloration (thalleiochin, or dalleiochin) is produced. Bromine-water or bromine vapor may be used instead of chlorine, excess being avoided.

---

* We do not know whether or not these sulphates are ordinary sulphates, the hydrogen of the acid going over to the quinine molecule, nor whether or not the quinine molecule is univalent or bivalent; hence we cannot say whether the *common* sulphate or the *soluble* sulphate is, in constitution, the neutral sulphate. In the above paragraph the names *disulphate*, *neutral sulphate*, *acid sulphate*, indicate nothing more than that the first sulphate contains in one molecule two atoms (chemical atoms) of quinine to one of sulphuric acid, the second one of each, and the third two of acid to one of quinine.