

FUNDAMENTALS OF ORGANIC CHEMISTRY

A.N. NESMEYANOV, N.A. NESMEYANOV

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FUNDAMENTALS OF ORGANIC CHEMISTRY

Volume II



А. Н. Несмеянов, Н. А. Несмеянов

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ACYCLIC COMPOUNDS
(continued)

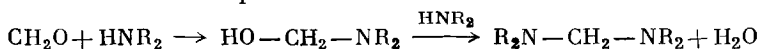
Heterofunctional Compounds

Heterofunctional compounds are compounds containing two or more different functional groups. The number of such combinations is evidently legion. We shall consider only the most important compounds, beginning with aminoalcohols and combinations of the carboxyl group with other groups (OH, C=O, NO₂, NH₂) and passing then over to combinations of the carbonyl group with other groups (chiefly, with OH). It is exactly these types that many important natural compounds belong to.

In studying the various combinations of functional groups we shall direct our attention to new properties arising in such combinations without resorting to the already familiar behaviour of individual functional groups. The closer are the functional groups to each other, the more sharply pronounced is their interaction and the more prominent are the new properties of the combination. This may be illustrated by the example of a combination of a hydroxyl and a carbonyl group which are joined together into a carboxyl group—a completely new function which differs sharply from the hydroxyl and carbonyl groups taken separately.

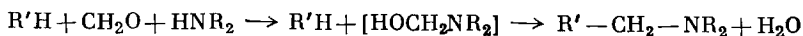
4.1. Aminoalcohols

When formaldehyde is allowed to react with secondary amines, methylol derivatives of the amines can be isolated in certain cases, which are converted into methylene bis-amines provided that an excess of the amine is present:



The hydroxyl group of the methylol derivatives of amines is easily eliminated in the form of water with the sufficiently mobile

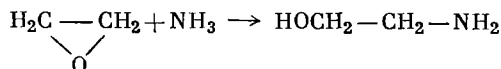
hydrogen atom of the second reagent. This happens, for example, in the Mannich reaction which proceeds by the following scheme:



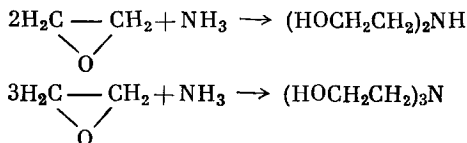
where $R'H$ is an aliphatic compound with an active hydrogen atom or an aromatic compound.

Methylol compounds do not, in principle, belong to aminoalcohols because they are functional derivatives of formaldehyde and their reactions are specifically different.

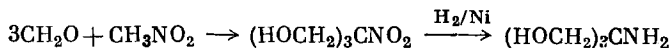
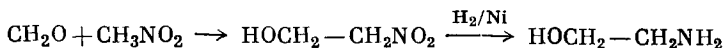
The simplest true aminoalcohol, 2-aminoethanol or ethanolamine (*colamine*), can be obtained by the interaction of ammonia with ethylene oxide:



Depending on the ratio of the reagents, the same easily proceeding reaction may lead to diethanolamine or triethanolamine:



Another route to the preparation of aminoalcohols with a primary amino group is based on the interaction of the nitro derivatives of aliphatic hydrocarbons with formaldehyde:



The properties of some aminoalcohols are given in Table 4.1.

The most widely used aminoalcohol is triethanolamine [TEA; tri-(2-hydroxyethyl)amine] which serves as an absorbent of CO_2 and other acid gases in gas-purifying processes (for example, in the purification of hydrogen). The triethanolamine that absorbed carbon dioxide loses it on heating and is thus regenerated. It also finds application as a harmless softening agent and plasticizer in the textile industry, for soap pastes, etc.

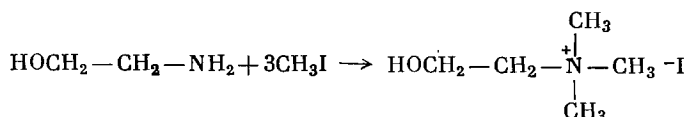
When the hydroxyl groups are replaced by chlorine (through the action of HCl or PCl_3), triethanolamine changes to tris-(β -chloroethyl)-amine, $(ClCH_2CH_2)_3N$, which is the analogue of yperite, $(ClCH_2CH_2)_2S$, by structure and vesicant action.

The grouping $(ClCH_2CH_2)_2N-$ is contained in the molecule of sarcolysine and other cancerolytic drugs.

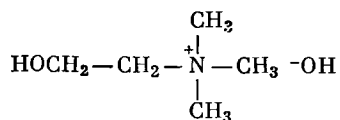
TABLE 4.1. Aminoalcohols

Formula	Name	m.p., °C	b.p., °C	Density, d_4^{20}	K_b (at 25 °C)
$\text{HOCH}_2-\text{CH}_2-\text{NH}_2$	Ethanolamine or colamine	10.5	172.2	1.0180	3.63×10^{-10}
$\text{HOCH}_2-\text{CH}_2-\text{N}(\text{CH}_3)_2$	2-Dimethyl- aminoethanol	—	135	0.8866	—
$[\text{HOCH}_2-\text{CH}_2-\overset{+}{\text{N}}(\text{CH}_3)_3]\text{OH}^-$	Choline or tri- methyl- β -hydroxyethylammonium hydroxide	Viscous liquid	—	—	8.77×10^{-6}
$(\text{HOCH}_2-\text{CH}_2)_2\text{NH}$	Diethanolamine or di-(2-hydroxyethyl)- amine	28	268	1.0966	1.32×10^{-9}
$(\text{HOCH}_2-\text{CH}_2)_3\text{N}$	Triethanolamine or tri-(2-hydroxyethyl)amine	21.2	279 (at 50 mm Hg)	1.1242	1.70×10^{-8}

The methylation of ethanolamine via the stages of monomethylaminoethanol and dimethylaminoethanol yields a trimethylethanolammonium salt:

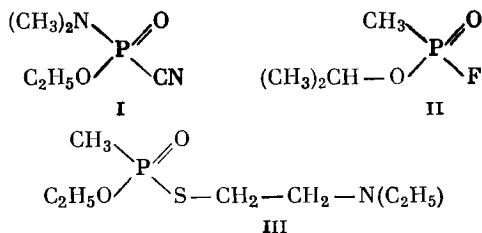


The action of moist silver oxide on this salt is used to synthesize **choline** (trimethylethanolammonium hydroxide):



Choline plays an important part in the regulation of metabolism in the animal organism and is comparable to vitamins in its effect. Its acetate ester, choline acetate, which is commonly known as **acetylcholine** and serves as a mediator (a chemical transmitter) in the functioning of the nervous system, is liberated at nerve endings

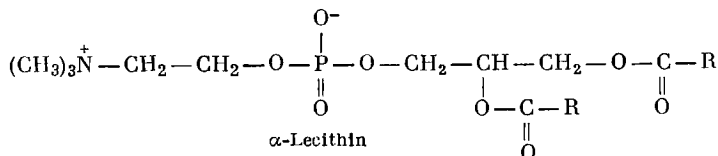
in the transmission of nerve-to-muscle impulses. Acetylcholine exerts an exceptionally strong physiological effect. When administered into the body acetylcholine causes the contraction of the muscles, convulsions, the intensive peristalsis of the intestines, and, in contrast to choline itself, causes a rapid fall in blood pressure. Acetylcholine released at nerve endings and having played its part in the transmission of nervous impulses is instantly hydrolysed by the action of the enzyme acetylcholinesterase (or cholinesterase) to choline which has a relatively weak (and opposite in many respects) physiological effect. The inactivation of cholinesterase is tantamount in its effect to the administration of acetylcholine itself. Such deactivation is accomplished by so-called **nerve gases**, such as Tabun I, Sarin II and the even more toxic substance (III) discovered by the Swedish scientist Tammelin:



or by insecticides (in insects) like Thiophos, mercaptophos, M-81, and others (see Volume IV, "Organoelement Compounds").

The dehydration of choline leads to the formation of **neurine**, $\text{CH}_2=\text{CH}-\text{N}^+(\text{CH}_3)_3\text{OH}^-$ (trimethylvinylammonium hydroxide; a toxic substance).

Choline occurs in a combined form (choline phosphate) in a variety of substances belonging to a class of lipids, known as **phosphatides** or **phospholipids**. Typical phospholipids are the compounds known as **lecithins** (see Volume I, page 416). Lecithins are built just as the mixed glycerides of fatty acids and choline phosphate, i.e., one of their possible formulas is a formula of the following type:



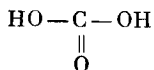
There are also **cephalins** (*kephalins*) which have a structure of the same type based on monoethanolamine. Lecithins are in most cases found associated with fats and are a constituent of food in which they serve as one of the sources of phosphoric acid necessary to life.

4.2. Hydroxy Acids

Hydroxy acids are carboxylic acids that have a second function—a hydroxyl group.

The hydroxy acids are derived from the fatty acids by replacing a hydrogen atom of the hydrocarbon radical by a hydroxyl group.

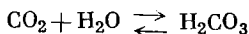
The first and specific member of a series of hydroxy acids is hydroxyformic acid, i.e., carbonic acid



A. Carbonic Acid and Its Derivatives

In distinction to other hydroxy acids in which the hydroxyl group, being more remote from the carboxyl group, has an alcoholic character, the hydroxyls of carbonic acid are united with the carbonyl group, no differences being observed between them: they are carboxyl-hydroxyl groups. Therefore, carbonic acid, which formally belongs to the class of hydroxy acids, is in fact closer to (though also considerably different from) the dicarboxylic acids. In essence, carbonic acid is an exceptional compound because of its properties and also because it has no homologues since any substitution reaction in it leads to the formation of a functional derivative. For this reason we shall consider carbonic acid separately from other hydroxy acids.

Carbonic acid exists only in weak aqueous solutions (solutions of carbon dioxide in water), the equilibrium in such solutions



being strongly displaced to the left, which is what gives an impression of the weakly acidic character of carbonic acid. The measured concentration of hydrogen ions is referred to the entire concentration of carbon dioxide, whereas in actual fact only a small portion of CO_2 is hydrated in H_2CO_3 .

(a) Functional Derivatives of Carbonic Acid

The formulas, names and physical properties of a number of derivatives of carbonic acid are presented in Table 4.2.

The salts of carbonic acid are not discussed in this book since they are studied in a course of general chemistry.

The acid chloride of carbonic acid, **carbonyl chloride** or **phosgene**, COCl_2 , is produced by direct combination of carbon monoxide and chlorine (either by exposing the mixture to the direct rays of the sun or in the presence of activated charcoal) and is an important

TABLE 4.2. Derivatives of Carbonic Acid

Formula	Name	m.p., °C	b.p., °C	Density, d_4^{20}
$\begin{array}{c} \text{HO}-\text{C}-\text{OH} \\ \\ \text{O} \end{array}$	Carbonic acid	-58.6 (at 5.2 kg/cm ²)	-78.5 (subl.)	1.56 (at -79°C, solid) 1.101 (at -37°C, liquid)
$\begin{array}{c} \text{Cl}-\text{C}-\text{Cl} \\ \\ \text{O} \end{array}$	Phosgene or carbonyl chloride	-118	+8.3	1.392 (d_4^{20})
$\begin{array}{c} \text{Cl}-\text{C}-\text{OCH}_3 \\ \\ \text{O} \end{array}$	Methyl chlorocarbonate or methyl chloroformate	—	71.4	1.236 (at 15°C)
$\begin{array}{c} \text{Cl}-\text{C}-\text{OC}_2\text{H}_5 \\ \\ \text{O} \end{array}$	Ethyl chlorocarbonate or ethyl chloroformate	-80.6	94	1.138
$\begin{array}{c} \text{CH}_3\text{O}-\text{C}-\text{OCH}_3 \\ \\ \text{O} \end{array}$	Dimethyl carbonate	+0.5	91	1.0694
$\begin{array}{c} \text{C}_2\text{H}_5\text{O}-\text{C}-\text{OC}_2\text{H}_5 \\ \\ \text{O} \end{array}$	Diethyl carbonate	-43	126.8	0.9751
$\text{C}(\text{OCH}_3)_4$	Tetramethyl orthocarbonate	—	—	—
$\text{C}(\text{OC}_2\text{H}_5)_4$	Tetraethyl orthocarbonate	—	159	0.9186
$\begin{array}{c} \text{NH}_2-\text{C}-\text{OCH}_3 \\ \\ \text{O} \end{array}$	Methyl carbamate	+52	177	1.136 (d_4^{20})
$\begin{array}{c} \text{NH}_2-\text{C}-\text{OC}_2\text{H}_5 \\ \\ \text{O} \end{array}$	Ethyl carbamate or urethane	50	180	0.9862 (d_4^{21})
$\begin{array}{c} \text{NH}_2-\text{C}-\text{NH}_2 \\ \\ \text{O} \end{array}$	Carbamide or urea	132.7	Dec.	1.335
$\begin{array}{c} \text{Cl}-\text{C}-\text{NH}_2 \\ \\ \text{O} \end{array}$	Carbamoyl chloride	-50	61-62	—
$\begin{array}{c} \text{NH}_2-\text{C}-\text{NHCH}_3 \\ \\ \text{O} \end{array}$	Methylurea	+101	Dec.	1.204
$\begin{array}{c} \text{NH}_2-\text{C}-\text{NH}_2 \\ \\ \text{NH} \end{array}$	Guanidine	50	—	—