pared by the condensation of the proper dialkylmalonic ester and guanidine hydrochloride, in the presence of sodium alcoholate.

In a preliminary investigation of their pharmacological properties, the compounds were found to produce death by respiratory failure. Sufficient evidence has not yet been obtained to definitely classify the dialkylmalonylguanidines as hypnotics.

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Condensation of Amino Acids with Terpenes

I. Aminoacetic Acid and Limonene Nitrosochloride*

By C. F. Krewson

This paper is presented as an introduction to a research project in which it is planned to prepare a variety of condensation products of amino acids and terpenes and to study their biological properties. These remarks will be confined to the condensation of aminoacetic acid and limonene nitrosochloride.

The behavior of nitrosochlorides of terpenes toward a variety of bases has been studied and three different types of reactions observed.

I. $C_{10}H_{16}\begin{cases}NO\\Cl\end{cases} + KOH \xrightarrow{-HCl}$

Terpene nitrosochloride (or heat)

$C_{10}H_{15}NO \rightarrow C_{10}H_{14}NOH$

Nitroso-terpene Isonitroso-terpene (oxime), (1)

II. $C_{10}H_{16}\begin{cases}NO\\Cl\end{cases} + 2HNHR' \text{ (or } HNR') \rightarrow$

Terpene nitrosochloride Primary or secondary base

$C_{10}H_{16}\begin{cases}NOH\\NHR'\end{cases} + HNH.HCl.R'$

Nitrolamine Hydrochloride of base

III. $C_{10}H_{16}\begin{cases}NO\\Cl\end{cases} \xrightarrow{-NOCl} C_{10}H_{16}$

Terpene nitrosochloride Regenerated terpene, (2)

Reactions of type II have long been used to characterize terpenes since nitrolamines of this type are well-defined crystalline compounds.

Several preliminary experiments with aminoacetic acid (2 moles) and limonene nitrosochloride (1 mole) indicated that these compounds do not combine quantitatively according to reaction II but that the former seems to behave like an inorganic base removing hydrogen chloride, a fact verified by the isolation of carvoxime and the recovery of much of the aminoacetic acid as a hydrochloride.

The reaction products obtained from several experiments where equimolecular quantities of reactants were used showed the presence of the compound desired, a new compound, limonene nitrolaminoacetic acid hydrochloride, [Glycine, *N*-(2-oxo-1-$\Delta^{8(9)}$-*p*-menthenyl)-, oxime hydrochloride], and the volatile oil obtained by steam distillation of the reaction products was found to contain, not only carvoxime, but also a relatively large amount of carvone apparently a result of the hydrolysis of carvoxime to carvone and hydroxylamine.

EXPERIMENTAL

In order to effect condensation 60 Gm. of aminoacetic acid and 158 Gm. of limonene nitrosochloride,

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dissolved in 600 cc. of 85 per cent alcohol, were warmed to 50° C. for several hours and the mixture distilled with steam to remove volatile products. The oil obtained by the extraction of the distillate with ether amounted to 80 Gm., 36.7 per cent of the original weight of the reacting materials. Spontaneous evaporation of the water distillate left no residue.

A quantitative estimation of the amount of aldehydes and ketones in the volatile oil by use of the Burgess modification (3) of Tiemann's sulfite method gave a value of 41.7 per cent by weight. Rough separation of the oil into two main fractions was secured by use of an eight-inch Vigreux column with reduced pressure. The fraction of lower boiling range amounted to 34 Gm., 42.5 per cent of the volatile oil by weight, a figure in close agreement with that reported for the per cent aldehydes and ketones. This fraction, after purification by two redistillations, one at atmospheric pressure using an ordinary distilling flask, and one under reduced pressure using a ten-plate Podbielniak column [see (4) for column specifications], gave a product having a constant index of refraction, n_D^{20} 1.4960, which was identified as carvone. The yield of carvone was 28.9 per cent of that theoretically possible.

The fraction of higher boiling range obtained from the Vigreux column distillation weighing 25.9 Gm. solidified, and the crystalline mass, which was filtered with the aid of suction, weighed 12.5 Gm., *i. e.*, 15.6 per cent of the volatile oil. These crystals, amounting to 9.7 per cent of the theoretical yield, were characterized as carvoxime and their oil-filtrate failed to show reactions characteristic of carvone, carvoxime or carvacrol, but gave positive qualitative tests for nitrogen and for chloride after fusion with sodium.

An attempt was made to fractionate this oil-filtrate by use of an 18-inch spinning-band column of the Lesesne and Lochte type (5) having a plate value of 19.7 (4). The variation of indices, n_D^{20} 1.4920–1.5210, shown by the thirteen fractions distilled is evidence of the complexity of the material examined. At least two compounds, n_D^{20} 1.5205, n_D^{20} 1.5066, were present in the first nine fractions, these having been obtained before any decomposition became apparent in the column. Each fraction was non-nitrogenous, gave no test for chloride and did not react with phenylhydrazine. Marked decomposition occurred between the take-off of the ninth and tenth fractions and four more fractions were taken after the column cleared but the indices of these fractions showed no sharp breaks, grading from n_D^{20} 1.5090–1.5192. These fractions were found to contain the nitrogenous and the chloride portion of the original oil-filtrate. The limited amount of material curtailed thorough examination of the oil-filtrate.

From the water portion in the flask after the steam distillation of the volatile oil, 39.9 per cent of the aminoacetic acid used was recovered as aminoacetic acid hydrochloride and 3.1 per cent accounted for as a new compound, Glycine, *N*-(2-oxo-1-$\Delta^{8(9)}$-*p*-menthenyl)-, oxime hydrochloride. The residual tarry matter obtained from the steam distillation indicated that considerable polymerization had taken place and it was discarded. The Glycine, *N*-(2-oxo-1-$\Delta^{8(9)}$-*p*-menthenyl)-, oxime hydrochloride, after several recrystallizations from water-alcohol, gave a melting point of 141.0–141.5° C. (uncorrected) and was found to be very soluble in water, less soluble in alcohol and only slightly soluble in ether. Upon analysis for nitrogen using the Kjeldahl method, a 202.5-mg. sample gave a value of 10.14 per cent and a 204.0-mg. sample gave a value of 10.39 per cent, values in close agreement with that of 10.14 per cent, the theoretical amount for the compound $C_{10}H_{15}\begin{cases}NOH\\(NH.HCl)CH_2COOH\end{cases}$. A 312.0-mg. sample of this compound gave 70.8 mg. of copper oxide equivalent to 18.12 per cent copper and a 344.6-mg. sample gave 76.2 mg. of copper oxide equivalent to 17.66 per cent copper, values in agreement with the theoretical 16.95 per cent in the compound, $Cu\left(C_{10}H_{15}\begin{cases}NOH\\NHCH_2COO\end{cases}\right)_2.CuCl_2.2H_2O$, a compound similar to $Cu(A')_2.Cu(NO_3)_2.2H_2O$ which has been reported in the literature (6).

CONCLUSIONS

The reaction between aminoacetic acid and limonene nitrosochloride has been investigated and the following equations are offered to explain the formation of the principal reaction products identified:

I. $C_{10}H_{16}\begin{cases}NO\\Cl\end{cases} + CH_2NH_2COOH \rightarrow$

Limonene nitrosochloride — Aminoacetic acid

$C_{10}H_{14}NOH + CH_2(NH_2.HCl)COOH$

Carvoxime — Aminoacetic acid hydrochloride

II. $C_{10}H_{14}NOH + H_2O \rightarrow$

$C_{10}H_{14}O + NH_2OH$

Carvone — Hydroxylamine

III. $C_{10}H_{16}\begin{cases}NO\\Cl\end{cases} + CH_2NH_2COOH \rightarrow$

$C_{10}H_{15}\begin{cases}NOH\\(NH.HCl)CH_2COOH\end{cases}$

Glycine, *N*-(2-oxo-1-$\Delta^{8(9)}$-*p*-menthenyl)-, oxime hydrochloride

The major portion of the limonene nitrosochloride is used to bring about the first two steps, only a small amount undergoing condensation with aminoacetic acid. No regenerated limonene could be found although considerable tarry residue was obtained during steam distillation of the reaction products.

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The Qualitative Detection of Methanol*

By Walter C. Gakenheimer† and Walter H. Hartung‡

An attempt was made to adapt, as a general laboratory exercise, the qualitative U. S. P. test for methanol in whisky (1) as a general method for detecting methyl alcohol in the presence of ethyl alcohol. In the class assignment, every student reported a positive reaction when no methanol was present. This is not surprising when it is realized that fuchsin-sulfurous acid T.S. is a general reagent for identifying aldehydes as a class (2). Under the U. S. P. conditions of the test, it is obvious that ethanol must be oxidized, at least in part, to acetaldehyde.

Eegriwe has reported (3) that chromotropic acid (1,8-dihydroxynaphthalene-3,6-disulfonic acid) is a sensitive, specific and characteristic reagent for formaldehyde. His procedure has been adopted by Feigl (4) to apply to methyl alcohol. In Feigl's discussion, he says that "with chromotropic acid in a concentrated sulfuric acid solution, a violet-red color appears" and "the following give no reaction: acetaldehyde, propionic aldehyde, butyric aldehyde, isobutyric aldehyde, isovaleric aldehyde, oenanthol, crotonaldehyde, chloral hydrate, glyoxal and aromatic aldehydes. Glyceryl aldehyde, furfural, arabinose, fructose and sucrose give yellow colors. Other sugars, acetone and carboxylic acids do not react. High concentrations of furfural give a red color."

Accordingly, several series of experiments were designed to show:

(*a*) the sensitivity of fuchsin-sulfurous acid T.S. to acetaldehyde;

(*b*) the sensitivity of fuchsin-sulfurous acid T.S. to ethanol (after oxidation according to the U. S. P. procedure);

(*c*) the sensitivity of chromotropic acid to methanol in ethanol;

(*d*) the sensitivity of chromotropic acid to methanol in whisky.

EXPERIMENTAL

Fuchsin-Sulfurous Acid T.S. and Acetaldehyde.—Five cc. of fuchsin-sulfurous acid T.S. was added to 10 cc. quantities of aqueous acetaldehyde solutions of the following concentrations: 1%, 0.1%, 0.01% and 0.001%. A positive reaction was obtained with concentrations of 0.01% or higher, and negative results with the 0.001% solution, showing a sensitivity of at least 1:10,000.

Fuchsin-Sulfurous Acid T.S. and Ethanol.—The U. S. P. procedure for detecting methanol was applied to aqueous solutions of ethanol varying in concentration from 50% to 0.01% and in every case a positive reaction was obtained. By using a blank, it was determined that the oxalic acid-sulfuric acid solution of the Pharmacopœia was sufficient in itself to restore the color to the fuchsin-sulfurous acid T.S.

Chromotropic Acid and Methanol in Ethanol.—The above facts indicate the necessity for an improved test for the presence of methyl alcohol in ethyl alcohol. Consequently, the procedure of Eegriwe, as outlined by Feigl, was applied to a series of solutions of methanol in 50% (by volume) ethanol. The concentrations of methanol used were: 1%, 0.75%, 0.50%, 0.25%, 0.10%, 0.075%, 0.050%, 0.025% and 0.01%. All concentrations as low as 0.1% gave a positive reaction to the naked eye. Those of 0.075% and less gave a negative reaction. It is noteworthy that this test is carried out with 0.02 cc. of the sample and is sensitive to 16γ (0.016 milligram) of methanol.

The procedure consists in mixing drop quantities of 5% phosphoric acid, 5% potassium permanganate solution and the sample. The mixture is allowed to stand a minute and is then decolorized with a little solid sodium bisulfite, after which 4 cc. of 72% sulfuric acid and a little finely powdered chromotropic acid are added. The mixture is well shaken and heated to 60° for 10 minutes. A violet

* From the Department of Chemistry, School of Pharmacy, University of Maryland.
† Alumni Fellow, 1939–1940.
‡ Professor of Pharmaceutical Chemistry.