a basic solution in water. The new product was insoluble in absolute alcohol and decomposed at 258–260°.

Anal. Calcd. for $(C_7H_{16}NBr)_x$: Br, 41.24. Found: total Br, 41.17; ionic Br, 40.44; mol. wt. (calcd. from ratio of total to ionic bromine) 10,864.

The cyclic salt which had been purified did not show signs of changing to the polymeric form over a long period of time. Heating the cyclic salt to its melting point (175–178°) did not change it into the polymeric form.

Diisoamyltrimethyleneammonium Bromide.—This cyclic salt was prepared from bromopropyldiisoamylamine by the method previously described for similar salts.[1b] After standing for one week without solvent, 6 g. of amine gave 3.5 g. of cyclic salt; m. p. 71–73°.

Anal. Calcd. for $C_{13}H_{28}NBr$: Br, 28.78. Found: Br, 28.94.

Miscellaneous Amines.—A number of tertiary amines have been prepared by methods analogous to those described for related compounds.[1] Their properties are listed in Table I.

The phenoxyamines other than the diisoamyl derivative could not be satisfactorily cleaved by hydrogen bromide to give the corresponding bromoamines.

Summary

γ-Bromopropyldimethylamine in very dilute solution reacts intramolecularly to give the crystalline cyclic salt dimethyltrimethyleneammonium bromide. At room temperature this cyclic quaternary ammonium salt rearranges slowly to the linear polymer previously described. Heating accelerates this rearrangement.

Impure diethyltrimethyleneammonium bromide will also rearrange to a polymeric salt, but this rearrangement proceeds less readily. No similar rearrangement to give polymeric salts has been observed when propyl, *n*-butyl and isoamyl groups are attached to the nitrogen atom.

A number of phenoxyalkyldialkylamines have been characterized.

URBANA, ILLINOIS RECEIVED MAY 6, 1935

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

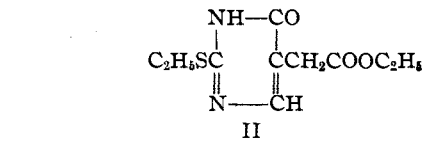
Researches on Pyrimidines. CXLVI. Synthesis of Uracil-5-methylamine

BY TREAT B. JOHNSON AND ANNE LITZINGER

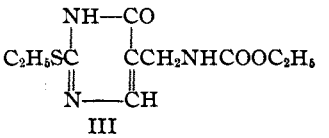
Of the different research programs now in progress in this Laboratory organized to develop the newer chemistry of purines and pyrimidines, our synthetic work dealing with the chemistry of thymine and its derivatives is of immediate interest on account of its bearing on the correct interpretation of the constitution of vitamin B_1. At the present time our knowledge of aliphatic chemistry as applied to the pyrimidine cycle is very limited. Side chain studies have thus far been restricted to very simple derivatives, and a research drive into this newer field promises to reveal information of immediate chemical and pharmacological interest.

We desire, therefore, to report in this preliminary paper, a successful application of a practical method for synthesizing the first aliphatic amine derivative of the uracil series to be described in the literature, namely, uracil-5-methylamine as represented by formula IV.[1] This is a true aliphatic amine, and bears a relationship to thymine corresponding to that existing between benzylamine and toluene. We believe that constructions of this type will prove to be of immediate interest in connection with the development of the newer chemistry of vitamin B_1. A pharmacological study of this new pyrimidine-amine and related compounds is now being carried on in the Department of Pharmacology of the Yale Medical School under the direction of Professor H. G. Barbour.[2]

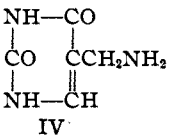
Our method of synthesizing this new amino derivative of thymine is based on the successful application of a Curtius reaction in the pyrimidine series. The starting point is the ethyl ester of 2-ethylmercapto-6-oxypyrimidine-5-acetic acid II,[3] which is easily converted into the corresponding urethan derivative represented by formula III.



II



III



IV

(1) A study of the chemistry of this interesting amine and its derivatives will be carried on in this Laboratory this coming year by Miss Anne Litzinger.

(2) This work will be partially supported by a special grant from the Research Committee of The American Medical Association.

(3) Johnson and Speh, *Am. Chem. J.*, **38**, 602 (1908).

This compound is then subjected to hydrolysis by the action of either sulfuric or hydrochloric acid when the corresponding salts of uracil-5 methylamine IV are obtained in excellent yields.

A complete discussion of the experimental technique of this interesting synthesis will be presented in a future publication from this Laboratory.

Experimental Part

Uracil-5-methylamine Sulfate, $(C_5H_7O_2N_3)_2 \cdot H_2SO_4$.—This salt is very soluble in cold water and insoluble in alcohol. It separates from alcohol–water mixtures in the form of colorless, glistening plates, m. p. 245–246° with decomposition. Aqueous solutions of this salt are acid to litmus and are apparently very stable.

Anal. Calcd. for $(C_5H_7O_2N_3)_2 \cdot H_2SO_4 \cdot H_2O$: H_2O, 4.50; N, 21.11. Found: H_2O, 3.60; N, 21.18.

Uracil-5-methylamine Hydrochloride, $C_5H_7O_2N_3 \cdot HCl$.—This salt is more soluble in water than the sulfate. Alcohol–water solutions slowly deposit colorless elongated, glistening plates, m. p. 242–243° with decomposition.

Anal. Calcd. for $C_5H_7O_2N_3 \cdot HCl \cdot 0.5H_2O$: H_2O, 4.88; N, 23.66 (anhyd.). Found: H_2O, 4.82; N, 23.86 (anhyd.).

Both salts are decomposed by the action of alkali and the free amine separates from hot aqueous solutions as a fine amorphous powder melting at about 295–300° with decomposition. Aqueous solutions of the amine are strongly basic to litmus. The study of this interesting base is now in progress.

NEW HAVEN, CONN. RECEIVED MAY 17, 1935

[CONTRIBUTION FROM THE GEORGE HERBERT JONES CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO]

Ergotocin

BY M. S. KHARASCH AND R. R. LEGAULT

Empirical Formula.—In a recent note[1] we announced the isolation of ergotocin (the active component responsible for the oral effectiveness of some ergot extracts), and recorded some of its chemical and physical properties. It now appears desirable to present more detailed data on the chemistry of this substance.

The empirical formula which best accords with our analyses of the free base (ergotocin), the picrate, the oxalate and the maleate, is $C_{21}H_{27}N_3O_3$ (calculated for $C_{21}H_{27}N_3O_3$: C, 68.30; H, 7.32; N, 11.38. Found: C, 68.41; H, 7.35; N, 11.43. $C_{25}H_{31}N_3O_7$ (maleate salt): C, 61.86; H, 6.39; N, 8.66. Found: C, 61.84; H, 6.48; N, 8.73. $C_{23}H_{29}N_3O_7$ (oxalate salt): C, 60.13; H, 6.32; N, 9.15. Found: C, 60.41; H, 6.25; N, 9.19). Due caution, however, forbids summary dismissal from consideration of the alternative compositions, $C_{21}H_{25}N_3O_3$ and $C_{21}H_{29}N_3O_3$; a critical evaluation of the evidence will be undertaken in a future paper. In either case, it is obvious that the ergotocin molecule is much simpler than those of ergotamine, ergotoxine, sensibamine or ergoclavine.

Chemical Properties—Ergotocin gives the characteristic blue color with *p*-dimethylaminobenzaldehyde (Ehrlich's reagent). It differs from the other alkaloids, however, in that the blue color has a reddish tinge. On a weight basis ergotocin produces more color than pure commercial samples of either ergotamine or ergotoxine; on a mole basis, however, the color is somewhat weaker (10–20%). Ergotocin gives a blue color with the Folin–Denis phenol reagent.

The *p*H value of a 0.012 *M* solution of ergotocin in 50% alcohol is 7.5. The neutralization equivalent (in 30% alcohol) is 374, in excellent agreement with a calculated molecular weight of 369. Treatment of a solution of ergotocin in quinoline with a dibutyl ether solution of methylmagnesium bromide according to the Zerewitinoff method indicates the presence of three active hydrogens. (Calcd. change in volume for three active hydrogens, 1.18 cc.; found, 1.12 cc.) This fact may account for the observation that ergotocin apparently combines with alkali metal ions to form salts. We have also noticed that upon chloroform extraction of ergotocin from aqueous solution made alkaline with either sodium carbonate or bicarbonate and evaporation of the solvent, the product, even when crystallized twice from benzene or chloroform, still contained about one per cent. of ash upon ignition. In spite of this fact the substance begins to darken at 155° and melts with decomposition at 158–160°.[2] The ash is unquestionably sodium carbonate for it is alkaline to litmus and liberates carbon dioxide with acids.

(1) Kharasch and Legault, THIS JOURNAL, **57**, 956 (1935).

(2) The isolation of a substance from ergot melting at 152 or 155–158° with decomposition is not in itself a criterion that a new substance has been obtained, for a melting point of 162° has been recorded for ergotoxine (presumably impure). It is the chemical reactions, analyses and the effect on human mothers that differentiate ergotocin from ergotoxine, but not necessarily the melting point.