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SYNTHESIS OF ISOQUINOLINE ALKALOIDS - III[1]
PILOCEREINE AND "ISOPILOCEREINE"

J. M. Bobbitt, R. Ebermann[2] and Marcelle Schubert[3]
Department of Chemistry, University of Connecticut, Storrs, Conn.

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THE ALKALOIDS, pilocereine,[4,5] II, and piloceredine,[6] are postulated[6] to arise from the oxidative condensation of lophocerine, I.[6] We have previously synthesized I.[7] We now wish to report that I has been converted to a complex mixture containing "isopilocereine",[8] III, pilocereine, II, and probably piloceredine[9] by oxidation with potassium ferricyanide in an ammonium acetate buffer (pH 6.0). The reaction is based upon the elegant, but relatively

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1 J. M. Bobbitt and D. A. Scola, J. Org. Chem. 25, 560 (1960).

2 On leave from the Agricultural Institute, Vienna, Austria.

3 Deceased, July 1961.

4 C. Djerassi, S. K. Figdor, J. M. Bobbitt and F. X. Markley, J. Am. Chem. Soc. 79, 2203 (1957).

5 C. Djerassi, H. W. Brewer, C. Clarke and L. J. Durham, J. Am. Chem. Soc. 84, 3210 (1962).

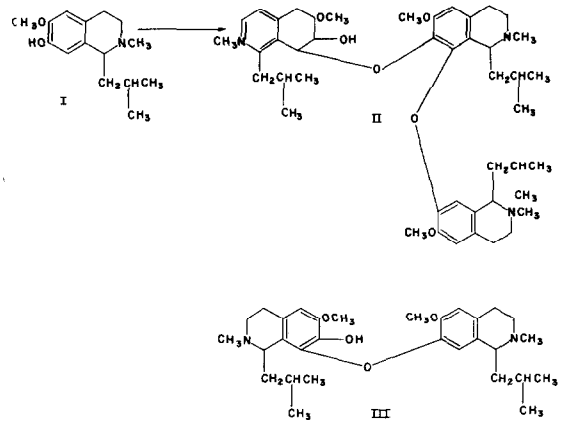
6 C. Djerassi, T. Nakano and J. M. Bobbitt, Tetrahedron 2, 58 (1958).

7 J. M. Bobbitt and T.-t. Chou, J. Org. Chem. 24, 1106 (1959).

8 This compound was erroneously thought[4] to be an isomer of pilocereine, but has now[5] been shown to possess the dimeric structure III.

9 A structure has been published[4] for this compound, but recent work[5] has shown that the substance is actually trimeric.

unappreciated, synthesis of libocedrol by Zavarin and Anderson[10] and is analogous to the present work of Franck.[11,12]



Lophocerine bisulfate (1.5 g., 4.3 m moles) and potassium ferricyanide (3 g., 9 m moles) were allowed to stand in 150 ml. of aqueous ammonium acetate (8%) for 24 hrs. at 4-5°. The mixture was made basic with ammonia and extracted with chloroform to yield a mixture of bases which showed three discrete spots on a thin-layer chromatogram (1% ammonium hydroxide in methanol as developer on Silica Gel G,[13] sprayed with Dragendorff's solution). Column chromatography over silica gel yielded 350 mg. of a substance corresponding to the fastest moving spot, 350 mg. of a mixture of all three components and 156 mg. of substance corresponding to the slowest moving spot. A gradient elution system of increasing amounts of methanol in benzene-ether (2:1) was

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10 E. Zavarin and A. B. Anderson, J. Org. Chem. 22, 1122 (1957).

11 B. Franck, G. Blaschke and G. Schlingloff, Tetrahedron Letters 439 (1962).

12 See preceding paper.

13 E. Merck, Darmstadt, Germany.

used. The fastest moving component gave a crystalline picrate, m.p. 234-236°, which had an identical infrared spectrum and X-ray powder pattern with the authentic picrate of "isopilocereine", lit. m.p. 235-237°.[4] The 350 mg. corresponded to a yield of 32%.

The slowest moving material had an Rf corresponding to authentic pilocereine and piloceredine on both Alumina G and Silica Gel G,[13] but could not be separated by thin-layer chromatography. However, the material and its amorphous oxalate did have infrared spectra identical with mixtures of the appropriate natural products. The mixture (100 mg.) was acetylated. The mixed acetates were resolvable by thin-layer chromatography (0.2% ammonia in methanol as developer on Silica Gel G) into two spots which corresponded to the acetates of authentic pilocereine and piloceredine, with pilocereine acetate having the higher Rf. Preparative thin-layer chromatography yielded, after crystallization and recrystallization from hexane, 3.5 mg. of pilocereine acetate m.p. 182.5-185.5, lit.[6] 185-186°. The mixture m.p. with authentic pilocereine acetate was not depressed and the infrared spectra and crystal forms were identical.

We have not yet been able to crystallize a derivative of piloceredine nor do we know the structure of the mixture component having the intermediate Rf. A detailed paper will be published when the reaction is more completely understood.

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