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Abstract

Full Text

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ON THE STRUCTURE OF THALMINE AND THALMIDINE

The alkaloids thalmine and thalmidine, isolated from the aerial part of *Thalictrum minus* Z, belong to ether-like bimolecular bases ([1]).

Thalmine is insoluble both in alkalis and in Claisen reagent, and is not methylated by diazomethane. However, in the IR spectrum of thalmine absorption is observed in the region of 3400 cm^{-1}, characteristic of a hydroxyl group. In the IR spectrum of acetylthalmine there are bands at 1770 and 1195 cm^{-1}, characteristic of a phenol ester. Thalmine is methylated with methyl iodide in the presence of sodium methylate on prolonged heating, giving diiodomethylate-O-methylthalmine; with ethyl iodide the corresponding diiodomethylate-O-ethylthalmine was obtained.

On cleavage of thalmine with sodium in ammonia, phenolic and nonphenolic reactions were obtained. From the nonphenolic portion a crystalline base was isolated, m.p. 64-65°, $(\alpha)_D^{20} + 54.4$ (chloroform), +94.38° (alcohol). Hofmann degradation of this substance gave a des-base with m.p. 63°, $(\alpha)_D^{20} \pm 0°$ (methanol), a picrate of the des-base with m.p. 174-175°, and a nitrogen-free substance with m.p. 69-70°. All these constants coincide with the data for 1-(4′-methoxybenzyl)-2-methyl-6-methoxy-tetrahydroisoquinoline ([2]). As was to be expected, oxidation of this substance yielded anisic and phthalic acids.

Thus, the nonphenolic product of the cleavage of thalmine is 1-(4′-methoxybenzyl)-2-methyl-6-methoxy-tetrahydroisoquinoline. The phenolic portion could not be crystallized. No crystalline derivatives were obtained from it.

Cleavage of O-ethylthalmine with sodium in liquid ammonia gives phenolic and weakly phenolic fractions. From the first, an oxalate was obtained with m.p. 210-211°, $(\alpha)_D^{20}$ +80.4 (methanol). The phenol isolated from the oxalate has m.p. 140-141°, $(\alpha)_D^{20}$ + 81.2 (chloroform). The phenol readily gives an iodomethylate, which on heating with ethyl iodide in an alkaline medium gives an O-ethyl derivative with m.p. 156-157°. All these data indicate that the isolated phenol is 1-(4′-oxybenzyl)-6-ethoxy-7-methoxy-N-methyl-tetrahydroisoquinoline ([3]).

To confirm this, the phenol was oxidized in acetone solution with a calculated amount of potassium permanganate. A weakly basic substance with m.p. 96-

structural formula

Figure 1: structural formula

Structural formula of thalmin

Figure 2: Structural formula of thalmin

97° was obtained, which corresponds to the data for 1-keto-6-ethoxy-7-methoxy-N-methyl-tetrahydroisoquinoline ([4]). Thus, ethoxyl-

group in O-ethylthalmin, and, consequently, the hydroxyl group in thalmin is located in the tetrahydroisoquinoline part of the molecule at position 6.

The weakly phenolic fraction is an oil which, with methyl iodide in alkaline medium, gives a crystalline iodomethylate with m.p. 134–136°, identical with the iodomethylate of O-methylarmepavine (5). Consequently, the substituent groups in this substance must be at positions 4′, 6, and 7. Since the substance does not possess weakly phenolic properties, the hydroxyl group cannot occupy position 4′. To choose between positions 6 and 7, the substance was ethylated and oxidized in acetone solution with a calculated amount of potassium permanganate. This gave a weakly basic substance with m.p. 115–118°, which corresponds to 1-keto-6-methoxy-7-ethoxy-N-methyltetrahydroisoquinoline (4). Consequently, the weakly phenolic product of the cleavage of O-ethylthalmin by sodium in liquid ammonia is 1-(4′-methoxybenzyl)-6-methoxy-7-hydroxy-N-methyltetrahydroisoquinoline.

The hydroxyl group in it could have formed only through rupture of the ether bridge in the isoquinoline part of the thalmin molecule.

Proceeding from the fact that oxidation of thalmin gave 1,1′-diphenyl oxide-2-methoxy-4,5′-dicarboxylic acid, and that cleavage of O-ethylthalmin by sodium in ammonia yielded 1-(4′-methoxybenzyl)-6-methoxy-7-hydroxy-N-methyltetrahydroisoquinoline and 1-(4′-hydroxybenzyl)-6-ethoxy-7-methoxy-N-methyltetrahydroisoquinoline, we propose the following structure for thalmin:

Proceeding from the formula proposed above for thalmin, it is evident that 1-(4′-methoxybenzyl)-6-methoxy-N-methyltetrahydroisoquinoline is an anomalous cleavage product.

Upon cleavage of thalmidine by sodium in liquid ammonia, O-methylarmepavine and isococlaurine were obtained. Taking into account the closeness of the physicochemical properties of thalmidine and O-methyltalikberine, and also the fact that cleavage of O-methyltalikberine by sodium in liquid ammonia gives analogous products (6), we consider these two bases to be identical.

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CITED LITERATURE

1. S. Yu. Yunusov, M. V. Telezhenetskaya, Dokl. AN UzSSR, **5**, 22 (1963).

2. U. Inubushi, K. Nomura, *Tetrahedron Letters*, **24**, 1133 (1962); V. Sasaki, H. Ohnishi, N. Satoh. *Chem. Abstr.*, **8695** (1956).

3. E. Fujita, T. Tomimatsu, V. Kano, *J. Pharmac. Soc. Japan*, **82**, No. 3 (1962).

4. N. F. Proskurina, A. P. Orekhov, *ZhOKh*, **10**, 707 (1940).

5. S. Yu. Yunusov, R. A. Konovalova, A. P. Orekhov, *ZhOKh*, **10**, 641 (1940).

6. E. Fujita, T. Tomimatsu, *J. Pharmac. Soc. Japan*, **79**, No. 10 (1959); T. Tomimatsu, *J. Pharmac. Soc. Japan*, **79**, No. 11 (1959).

Note: Figure translations are in progress. See original paper for figures.