THE STRUCTURE OF THALICMININE

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Four alkaloids have previously been isolated from the roots of Thalicrum minus L. (lesser meadowrue): glaucine, thalicmine, thalicmidine, and base 5 [1–3].

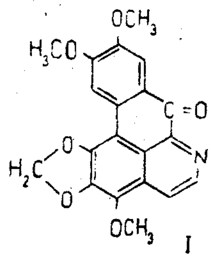
We have investigated the roots of this plant collected in the early vegetation period on 5 May 1963 in Lyash-Karaksa, Tashkent Oblast, and have isolated thalicmine, thalicmidine, and base 5. In this case, the yield of thalicmidine and base 5 was far greater than described in the literature.

Base 5, which we have called thalicminine (I) has properties differing from those of known alkaloids. Its IR spectrum has a band at 1650 cm^{-1} which is characteristic for a conjugated ketone group. The base contains three methoxy groups and one methylenedioxy group. The UV spectrum has the four maxima characteristic of alkaloids of the litiodenine type [4–6]. This enables us to assume that thalicminine is also a 10-oxoaporphine.

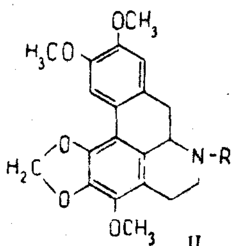
In the plant, thalicminine (I) is found together with the alkaloid thalicmine (IIb), which also contains three methoxy groups and one methylenedioxy group. We have assumed that thalicminine is formed in the plant organism from thalicmine by an oxidation process; its empirically calculated composition is $C_{20}H_{15}O_6N$ and its analytical formula is $C_{15}H_4(CO)\,(=N-)\,(OCH_3)_3(O_2CH_2)$. This was confirmed by the following investigation.

The oxidation of thalicmine with potassium permanganate in acetone solution and with chromic anhydride in pyridine does in fact give rise to thalicminine.

The passage from thalicminine (I) to dl-thalicmine (IIb) has been carried out. For this purpose, the base (I) was reduced with zinc in sulfuric acid to give the aporphine base (IIa) with a characteristic UV spectrum [7]. Its IR spectrum exhibited a band for a secondary amino group in the 3300 cm^{-1} region. The methylation of the base (IIa) led to the formation of the optically inactive N-methyl derivative (IIb). The UV and IR spectra of substance (IIb) were identical with those of thalicmine.



I



II

a) R = H

b) R = CH_3

The Hofman degradation of the methiodide of the N-methyl derivative (IIb) gave a des-base, a mixture of which with des-N-methylthalicmine [2] gave no depression of the melting point. The UV and IR spectra of the two des-bases were also identical.

Experimental

Isolation of the alkaloids. 28 kg of the roots was extracted with chloroform with subsequent extraction of the bases from an alkaline solution with ether (A) and then with chloroform (75.6 g) (B). The ethereal extract A was concentrated and washed with water and 5% caustic soda, and the ether was distilled off. The yield of crystalline thalicmine was 53.2 g.

The alkaloids were extracted from the aqueous solution with ether (4.8 g) and chloroform (5.2 g). 4.8 g of the total chloroform extract gave 3.5 g of thalicminine. The phenolic bases were extracted from the alkaline solution with ether (90.8 g) and chloroform (2.3 g). 90.8 g of the total ethereal extract yielded 85.5 g of thalicmidine via the tartrate.

Thalicminine (I). The chloroform fraction (B) was treated with methanol. This gave 72.8 g of golden orange crystals of thalicminine with mp 263°–265° C [chloroform (1:50)].

UV spectrum: λ_{max} 252, 282, 364, 456 mμ (log ε 4.29, 4.43, 3.91, 3.72) (chloroform—alcohol). IR spectrum: 2850, 1280, 1150 (OCH_3), 1650 (C = O) cm^{-1}.

Found, %: N 3.56; 3.52; OCH_3 24.6; 24.3. Calculated for $C_{20}H_{15}O_6N$, %: N 3.73; 3 OCH_3 24.8.

Thalicminine (I) from thalicmine (IIb). 1. With stirring, 0.57 g of potassium permanganate in 100 ml of acetone was added over 2.5 hr at 10°–15° C to 1.0 g of thalicmine (IIb) in 100 ml of acetone. After the acetone had been distilled off, the residue was treated with chloroform. This yielded 0.3 g of thalicminine.

2. A mixture of 0.5 g of thalicmine in 5 ml of pyridine and 75 g of anhydrous chromic anhydride in 30 ml of pyridine was left for 44 hr. Then 10 ml of alcohol was added, the mixture was stirred for 30 min, and the precipitate was filtered off and washed with chloroform. The latter was evaporated to dryness, the residue was dissolved in chloroform, and the reaction product was extracted with 5% hydrochloric acid. The acid solution was made alkaline with 25% ammonia. The base was extracted with chloroform. The residue after the elimination of the solvent was recrystallized from chloroform, mp 260°–262° C. Yield 0.15 g. The IR spectra of the oxidation products both in experiment 1 and in experiment 2 were identical with that of thalicminine (I).

Hexahydrothalicminine (IIa). A mixture of 0.5 g of thalicminine (I), dissolved in 50% of acetic acid, 10 g of zinc dust, and 50 ml of 20% sulfuric acid was heated in a boiling water bath for 60 hr. After every 10 hr, 50 ml of 20% sulfuric acid and 2 g of zinc dust were added. The solution was filtered, the residue was washed with hot water, the filtrate and washings were made alkaline with 25% ammonia, and the base was extracted with ether. Yield 0.2 g, mp 180°–182°C. UV spectrum (in alcohol): λ_{max} 218, 280, 302 mμ (log ε 4.30; 4.12; 4.06).

Thalicmine (IIb). A mixture of 0.2 g of hexahydrothalicmine (IIa), 12 ml of formic acid, and 12 ml of formaldehyde was heated in the water bath for 7 hr. The solution was made alkaline with 25% ammonia, and the reaction product was extracted with ether. The ether was distilled off and the residue was treated with alcoholic hydrochloric acid. Crystals of a hydrochloride with mp 258°–260° C (from methanol) deposited. The base obtained from the hydrochloride had mp 140°–142° C. Yield 0.2 g. UV spectrum: λ_{max} 220, 282, 304 mμ (log ε 4.46; 4.22; 4.22) in alcohol.

The des-base. 1 ml of methyl iodide was added to 0.4 g of N-methylhexahydrothalicminine (IIb) in 10 ml of methanol. Needles of the methiodide with mp 233°–234° C deposited. Yield 0.45 g.

A mixture of 0.45 g of the methiodide of (IIb), 5 ml of methanol, and 1.5 g of caustic potash was heated for 2 hr. The solvent was evaporated off, 30 ml of water was added and the precipitate was separated off (0.2 g) and crystallized from ethanol. This gave needles with mp 149.5°–150°C, a mixture of which with des-N-methylthalicmine melted at 149.5° C.

UV spectrum: λ_{max} 218, 266, 316, 326, 345, 370 mμ (log ε 4.22; 4.91; 4.08; 4.09; 3.50; 3.60 respectively).

Summary

The structure of thalicminine (I) has been established; it is 2, 3, 7-trimethoxy-5, 6-methylenedioxy-10-oxotetradehydronoraporphine. The conversions of thalicmine (IIb) into thalicminine (I) and of thalicminine (I) into dl-thalicmine (IIb) have been effected.

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