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STUDIES ON ALKALOIDS FROM *THALICTRUM* SPECIES. STRUCTURE OF THALMELATINE, A NEW EXAMPLE OF DIMERIC APORPHINE-BENZYLISOQUINOLINE ALKALOIDS

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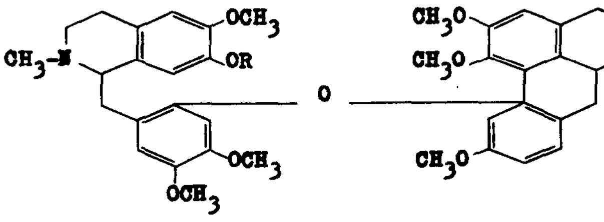
The isolation of three new alkaloids from the overground parts of *Thalictrum minus var.elatum Jacq.*, wide spread in Bulgaria, has recently been reported (1). The first alkaloid with the molecular formula $C_{41}H_{48}O_8N_2$ was found to be identical with thalicarpine (I), the first representative of the novel type of dimeric aporphine-benzylisoquinoline alkaloids, the structure of which has been established by S.M. Kupchan and coll.(2).



I, R = CH_3
II, R = H
V, R = C_2H_5

Because of the small quantity available the characterisation of the second alkaloid was not completed. The third alkaloid, given by us the name of thal-

melatine (II), represents a phenolic base, m.p.131-5° (EtOH) and 120-3° (abs.EtOH), $[\alpha]_D^{21}$ + 110° (c=1%, EtOH), and molecular weight ca 670. Its molecular formula is $C_{40}H_{46}O_8N_2$ and contains as substituents six methoxyl and one hydroxyl groups. Treatment of thalmelatine (II) with diazomethane converted it into I (by comparison of mixture melting point and infrared spectra). It represents therefore a second example of the novel type of dimeric aporphine-benzylisoquinoline alkaloids.

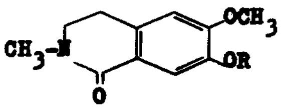
This paper summarizes the results of our research on the structure of thalmelatine (II).

The confirmation of the structure of I was proved by sodium in liquid ammonia reduction. This degradation resulted in (-)-6'-hydroxylaudanosine(III) and (+)-3,6-dimethoxyaporphine (IV) (2).

Treatment of II with diazoethane yielded O-ethylthalmelatine (V),m.p.133-5° (EtOH).(Analysis.Calcd. for $C_{42}H_{50}O_8N_2$: C, 70.96; H, 7.09; N, 3.94. Found: C, 70.57; H, 7.19; N, 3.84). The infrared spectrum of V showed no bands of hydroxyl groups. The spectrum is similar to that of I; an insignificant difference was observed only in the fingerprint region. When V was reduced with sodium in liquid ammonia (+)-3,6-dimethoxyaporphine (IV) was isolated from the reaction mixure (identity of infrared spectra). But the infrared spectrum of the 6'-hydroxylaudanosine, isolated by us, differed from that of III in the fingerprint region. The hydroxyl group of II was, therefore, to be found in its benzylisoquinoline part. In order to determine the exact position of the hydroxyl group, I as well as V were oxidized with potassium permanganate in acetone and the obtained products were compared.

By the oxidation of I a nitrogen containing compound (VI) m.p.124-6° was isolated from the reaction mixure.(Analysis.Calcd.for $C_{12}H_{15}O_3N$:C, 65.14; H, 6.83; N, 6.33. Found: C, 64.84; H, 6.93; N, 6.12). Infrared spectrum: 1645 cm^{-1} (δ -lactame). Melting point and analysis of VI corresponded with 1-oxo-6,7-dimethoxy-N-methyltetrahydroisoquinoline, synthesized from E. Späth and J.Pikl (3). The infrared spectrum came in favour of our conclusion about the structure of VI.

On oxidation of O-ethylthalmelatine (V) a nitrogen containing compound (VII), m.p.118-120°was isolated. (Analysis.Calcd.for $C_{13}H_{17}O_3N$: C, 66.36; H, 7.28; N, 5.95. Found: C, 65.95; H, 7.69; N, 5.54). Its infrared spectrum is similar to that of VI, differing only in the fingerprint region. VI and VII showed depression in their melting points on mixing. Melting point and analysis of VII corresponded to 1-oxo-6-methoxy-7-ethoxy-N-methyltetrahydroisoquinoline, synthesized by E.Späth and H.Epstein (4).



VI, R = CH_3
VII, R = C_2H_5

After oxidation of I and II with potassium permanganate in acetone, the same nitrogen containing compound was isolated from the reaktion mixure as a main product (about 50%) (compared melting points and identical infrared spectra). Yellow cristalline needles, m.p. 153-5°, optically inactive. (Analysis. Calcd. for $C_{29}H_{31}O_7N$: C, 68.91; H, 6.18; N, 2.77; Found: C, 68.92; H, 6.02; N, 2.78). The compound was weekly basic and dissolved in concentrated acids. By passing dry HCl through a benzen solution of VIII an unstable HCl-salt precipitated. Its structure will be further communicated.

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