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THALICTRUM ALKALOIDS I. THALIFENDLERINE AND THALIFENDINE[1]

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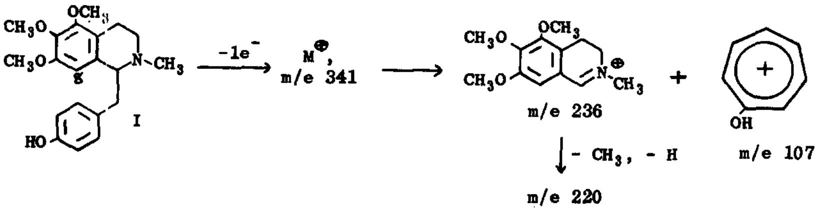
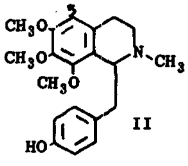
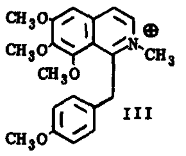
In some recent communications, the isolation and characterization of aporphine and liriodenine type alkaloids substituted at the unusual C-3 position have been described.[2,3] We now wish to report that we have found a new benzyltetrahydroisoquinoline alkaloid, thalifendlerine (I), in *Thalictrum fendleri*, which is also substituted at that position, corresponding to C-5 in a benzylisoquinoline system.

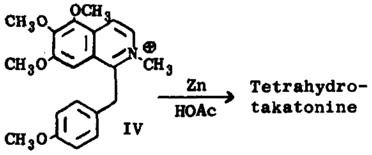
Thalifendlerine (I), $C_{20}H_{25}O_4N$, was obtained as colorless crystals, m.p. 177-178°, $[\alpha]_D^{25}$ -108° (MeOH), λ_{max}^{EtOH} 282 mμ (log e 3.49), positive $FeCl_3$ test. The nmr spectrum in deuteriochloroform solution exhibited one N-methyl peak at 2.49 p.p.m., and two O-methyl peaks at 3.51 (3 protons) and at 3.85 p.p.m. (6 protons). One aromatic hydrogen showed up relatively upfield at 5.83 p.p.m., and four others appeared as the four peaks of an A_2B_2 system centered at 6.6 and 6.85 p.p.m. (apparent J = 8.4 c.p.s.). The mass spectrum showed a molecular ion peak at m/e 341, a base peak at m/e 236, and other intense peaks at 220 and 107, all of which could be explained on the basis of the following cleavages:



That the phenolic function present in the benzyl moiety is in the para position was shown by a negative Gibbs test, and by the above mentioned A_2B_2 system in the nmr spectrum.


II

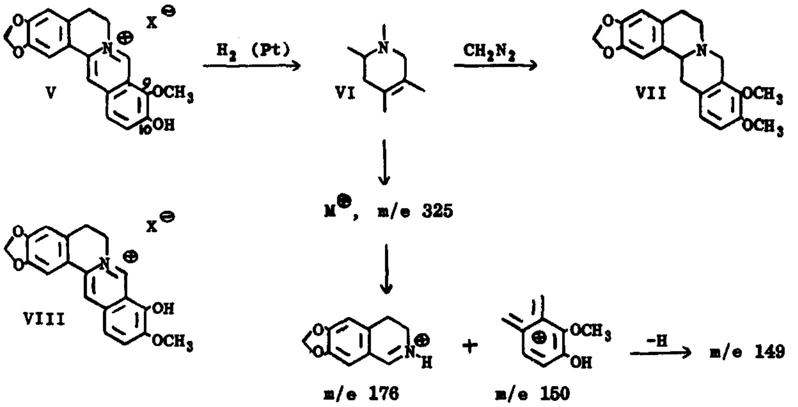

III


IV

To establish that the alkaloid was 5,6,7 and not 6,7,8 substituted, the isomeric (±)-base II was synthesized by the classical Bischler Napieralski route. Compound II melted 122° and was different from thalifendlerine (I) in its infrared spectrum and its TLC R_f values. Additionally, treatment of thalifendlerine with diazomethane gave an O-methyl derivative, m.p. 195-197°. This O-methyl derivative was compared with a sample of tetrahydrotakatonine obtained from Professor Fujita, and the two compounds were found to be identical in terms of nmr spectra and TLC R_f values. Before sending us a sample of tetrahydrotakatonine, Professor Fujita was kind enough to inform us that the old structure III for takatonine[4] had just been revised to IV, and that the structural studies were to be described in a forthcoming publication.[5] Thalifendlerine (I) and takatonine (IV) are, therefore, the first benzylisoquinoline alkaloids found to be substituted at C-5.

From the quaternary, water soluble, alkaloidal fraction, we have isolated, in addition to the known berberine, jatrorrhizine, and magnoflorine, a new optically inactive yellow crystalline alkaloid analyzing for $C_{19}H_{16}O_4N^{\oplus} X^{\ominus}$ which we have named thalifendine (V), chloride sintering >230°.

Thalifendine chloride exhibited λ_{max}^{EtOH} 348, 269, and 231 mμ (log e 4.10, 4.15, and 4.17), and the alkaloid turned orange upon the addition of even such a weak base as aq. $NaHCO_3$. The nmr spectrum in trifluoroacetic acid solution with TMS as an internal standard showed one methoxy group at 4.28 p.p.m., and a methylenedioxy function at 6.15 p.p.m. Six aromatic protons showed up at 6.95, 7.52, 7.95 (2 protons), 8.52 and 9.55 p.p.m.



Reduction of thalifendine (V) with Adams catalyst gave colorless crystals of tetrahydrothalifendine (VI), m.p. 209-211°, whose main mass spectral peaks were at m/e 325, 176 (base), 150 and 149. O-Methylation of tetrahydrothalifendine (VI) with diazomethane gave tetrahydroberberine (VII), identical with an authentic sample (mixture m.p. and TLC R_f comparisons). The phenolic function in thalifendine must be at C-10, since the alkaloid chloride was clearly different from an authentic sample of berberrubine chloride (VIII) prepared by heating berberine chloride in an inert atmosphere.[6]

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References

1. Melting points are uncorrected, and satisfactory analyses were obtained for all compounds in question.
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