A Biogenetically Patterned Conversion of Magnoflorine into Taspine

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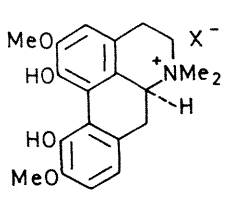
Summary Ozonization of diacetylmagnoflorine methine followed by oxidation and lactonization affords taspine.

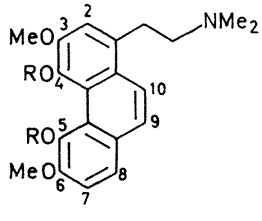
TASPINE (5) occupies a unique position in the realm of alkaloid chemistry. Found in *Leontice eversmanii* Bunge (*Berberidaceae*),[1] it is a high-melting dilactonic tertiary base with no close relative among other alkaloids. Its structure was derived through extensive degradative work,[1] and its synthesis has not previously been reported.

It appeared to us that the biogenesis of this interesting alkaloid probably proceeds through enzyme-catalysed Hofmann elimination of the widespread quaternary aporphine (+)-magnoflorine (1) to magnoflorine methine (2). Oxidation of the 9,10 double bond followed by lactonization can then afford taspine (5).[2]

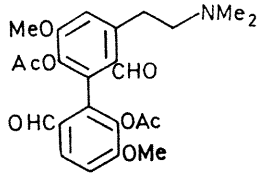
In an effort to emulate this sequence *in vitro*, naturally occurring (+)-magnoflorine chloride (1)[3] was heated under reflux with ethanolamine to provide the methine base (2)[4] which was acetylated with acetic anhydride in pyridine to afford diacetylmagnoflorine methine (3), $C_{24}H_{27}O_6N$, tan crystals m.p. 244—245°, *m/e* 425 (M^+), 59% from (1).



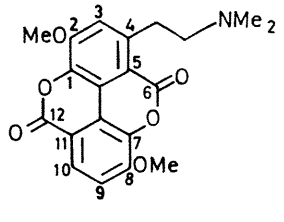
(1)



(2) R = H
(3) R = Ac



(4)



(5)

Ozonolysis of (3) in methanol for 15 min followed by treatment with sodium iodide gave the dialdehyde diacetate (4) (77%) as a yellow foam, *m/e* 457 (M^+) for $C_{24}H_{27}O_8N$, n m r ($CDCl_3$) δ 7 94 d (1H, *J* 9 Hz aromatic proton *ortho* to aldehyde function) An aqueous solution of (4) was oxidized with basic silver oxide, and the filtrate made strongly acidic with hydrochloric acid and heated under reflux for ½ h Basification with sodium hydrogen carbonate, chloroform extraction, and treatment with hydrogen chloride provided crystals of taspine (5) hydrochloride [14% from (4)] m p 252—253°, λ_{max} (EtOH) 246 285, 297sh, 330, and 346 nm (log ε 4 79, 3 94 3 88, 3 86, and 3 94) identical with the u v spectrum for a sample of authentic taspine hydrochloride [5]

Our synthetic taspine free-base also proved to be indistinguishable from the natural product in terms of t l c R_f values, u v i r , and mass spectra Additionally, no mixed m p depression was observed

Taspine free-base darkens upon standing, n m r ($CDCl_3$ δ 2 40 s [6H, $N(CH_3)_2$], 2 70 broad t (2H *J* 7 Hz, $ArCH_2$), 3 48 broad t [2H, *J* 7 Hz, $CH_2N(CH_3)_2$], 4 10 s (6H, OCH_3), 7 19 s (1H, 3-*H*), δ 7 27 d (1H *J* 9 Hz, 9-*H*), and 8 14 d (1H *J* 9 Hz, 10-*H*)

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[1] T F Platonova A D Kusovkov and Yu N Sheinker, *Zhur obshchei Khim* , 1965, **26**, 2651

[2] For a related biogenetic scheme which however, does not specifically postulate the intermediacy of an aporphine methine see H -G Boit, ' Ergebnisse der Alkaloid Chemie bis 1960, ' Akademie Verlag, Berlin, 1961, p 270

[3] Isolated by us from *Thalictrum polygamum* Muhl (*Ranunculaceae*)

[4] M Tomita and Y Takano *J Pharm Soc Japan*, 1960, **80**, 1645 [*Chem Abs* , 1961, **55**, 7452]

[5] J Holubek and O Štrouf "Spectral Data and Physical Constants of Alkaloids," Publishing House of the Czechoslovak Academy of Science Prague, 1966, Spectrum No 393