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NEW APORPHINE ALKALOIDS FROM CROTON WILSONII GRISEB.

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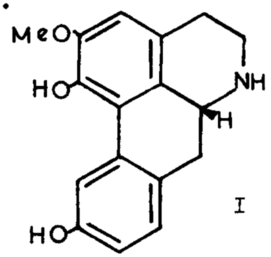
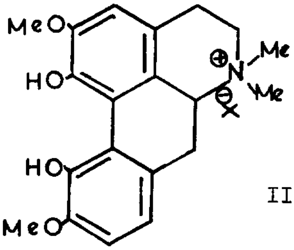
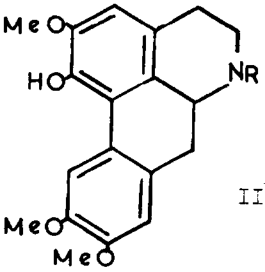
Two aporphine alkaloids, namely sparsiflorine (I) from *Croton sparsiflorus* Morung (1) and magnoflorine (II) from *C. cumingii* Muell et Arg.(2) have been reported from the *Croton* species. We now report the isolation and characterisation of five phenolic aporphines from *C. wilsonii* Griseb. These are wilsonirine (III; R = H) and the four derivatives of structure IV listed below.



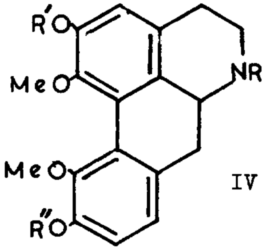
I



II



III



IV

(i) Hernovine (IV; R=R'=R"=H)

(ii) N-Methylhernovine (IV;R=Me,R'=R"=H)

(iii) 10-O-Methylhernovine (IV;R=R'=H,R"=Me)

(iv) N-Methyl-10-O-methylhernovine (IV;R=R"=Me, R'=H).

All these aporphines, with the exception of hernovine are new natural products, and were separated with the aid of countercurrent distribution techniques.

Hernovine, $C_{18}H_{19}NO_4$, m.p. 235-237°(dec.), $[\alpha]_D^{18}$+ 142° (c = 0.52 in pyridine), recently isolated from Hernandia ovigera L. (3) was identified by direct comparison (UV, IR, NMR,* TLC, mixed m.p., optical rotation) with an authentic sample.

The second alkaloid was characterised as the hydrochloride, $C_{19}H_{21}NO_4\cdot HCl$**, m.p. 244-245° (dec.), $[\alpha]_D^{23}+209°$ (c = 0.55 in MeOH), and had a UV, λ_{max}^{EtOH} 218 mμ (log ε 4.41), 273 (4.02), 305 (3.63), characteristic of 1,2,10,11-tetrasubstituted aporphines (4). N-Methylation (5) of hernovine gave an amorphous product which could be converted to the crystalline hydrochloride (3) and which was identical (IR, mixed m.p., TLC) to the hydrochloride of this base. This establishes the structure of this aporphine as N-methylhernovine (IV; R=Me, R'=R"=H). This assigned structure was fully supported by the NMR of the free base [2 OMe, δ 3.53, 3.56; C_8-H and C_9-H, 6.82; C_3-H 6.62 and N-Me, 2.43] (6).

Another new alkaloid was the $C_{19}H_{21}NO_4$ compound, m.p. 157-158° (dec.), $[\alpha]_D^{17}+188°$ (c = 1.0 in EtOH), λ_{max}^{EtOH} 220 mμ (log ε 4.56), 273 (4.11) and 305 (3.70). The NMR showed three methoxyls (δ 3.50, 3.60, 3.82), C_8-H and C_9-H at δ 6.91 and C_3-H at δ 6.63. The 1,2,10,11-tetrasubstitution pattern was confirmed by O-methylation (CH_2N_2) to give catalpifoline (IV; R = H, R' = R" = Me), identified by direct comparison with an authentic sample (7). The location of the phenolic group at C_2 was based on a comparison of the NMR spectrum of the new base with that of the NO-diacetyl derivative. The C_3-H experienced a marked shift (δ 6.63 → 7.01) on going from the base to the diacetate, while

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* All NMR spectra reported were determined at 60 Mc/sec. in CD_3SOCD_3 with TMS as the internal standard.

**Satisfactory elemental analyses were obtained for all new compounds reported.

the C_8-H and C_9-H were little affected (δ 6.91 → 7.01). This is in good agreement with the spectra of similarly substituted tetrahydroisoquinolines. For example crotonosine (8) and its NO-diacetyl derivative showed a similar shift (δ 6.57 → 7.02). These results establish this $C_{19}H_{21}NO_4$ alkaloid as 10-O-methylhernovine (IV; R=R'=H, R"=Me).

The fourth alkaloid, although homogeneous on TLC was amorphous and was characterised as the hydrochloride, $C_{20}H_{23}NO_4$.HCl, m.p. 218-219° (dec.), $[\alpha]_D^{23}$ + 139° (c=0.51 in MeOH). The UV, λ_{max}^{EtOH} 220 mμ (log ε 4.55), 273 (4.11), 304 (3.69) suggested a 1,2,10,11-tetrasubstituted aporphine (4). O-Methylation (CH_2N_2) followed by treatment with methyl iodide gave a product, m.p. 242 - 244° (dec.) which was identical to O-O-dimethylmagnoflorine iodide. This fourth alkaloid could also be obtained by N-methylating 10-O-methylhernovine, and a NMR comparison of the base and its O-acetyl derivative fully supported the location of the phenolic group at C_2. The preceding evidence clearly establishes this alkaloid as N-methyl-10-O-methylhernovine (IV; R=R"=Me,R'=H).

The fifth base, named wilsonirine, $C_{19}H_{21}NO_4$, m.p. 211-213° (dec.) gave a neutral diacetate, m.p. 229-231°, $[\alpha]_D^{23}$ + 56° (c=0.59 in MeOH). The UV of wilsonirine was characteristic of a 1,2,9,10-tetrasubstituted aporphine, λ_{max}^{EtOH} 221 mμ (log ε 4.45), sh.271 (3.92), 281 (4.02), 306 (4.02) and the NMR supported this substitution pattern (6) [3 OMe, δ 3.73, 3.80, 3.80; C_{11}-H, 8.05; C_8-H, 6.83; C_3-H, 6.60]. This alkaloid could be converted by N-methylation to a crystalline product, m.p. 188-189°. This was shown to be O-methylisoboldine (III; R=Me) by direct comparison with an authentic sample (9) and so establishes the structure of wilsonirine as (III; R=H). Compound (III; R=Me, has recently been isolated and synthesised (10).

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REFERENCES

1. A. Chatterjee, P.L. Majumder, R. Mukherjee, S.K. Saha and S.K. Talapatra, Tetrahedron Letters, 1539 (1965).
2. M. Tomita, K-H. Lee and T. Nakano, J.Pharm.Soc.Japan, 85, 276 (1965).
3. M.P. Cava, K. Bessho, B. Douglas, S. Markey, R.F. Raffauf and J.A. Weisbach, Tetrahedron Letters, 1577 (1966).
4. A.W. Sangster and K.L. Stuart, Chem.Rev., 65, 69 (1965).
5. A.O. Hawtrey, S.I. Biedron and S.H. Eggers, Tetrahedron Letters, 1693 (1967)
6. W.H. Baarschers, R.R. Arndt, K. Pachler, J.A. Weisbach and B. Douglas, J.Chem.Soc., 4778 (1964).
7. M.P. Cava, K. Bessho, B. Douglas, S. Markey and J.A. Weisbach, Tetrahedron Letters, 4279 (1966).
8. L.J. Haynes, K.L. Stuart, D.H.R. Barton and G.W. Kirby, J.Chem.Soc.(C), 1676 (1966).
9. P.S. Clezy, E. Gellert, D.Y.K. Lau and A.W. Nichol, Aust.J.Chem., 19, 135 (1966).
10. M. Shamma and W.A. Slusarchyk, Tetrahedron, 23, 2563 (1967).