

Communications.

Structure of Tabernoxidine, a Novel Oxindole Alkaloid from *Tabernaemontana heyneana* Wall†

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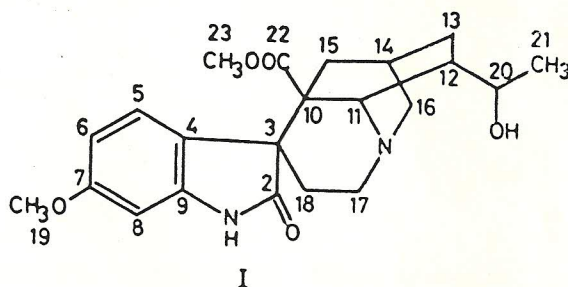
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Tabernoxidine, an oxindole alkaloid isolated from the leaves of
Tabernaemontana heyneana Wall. is shown to have the structure (I)
on the basis of spectral data and X-ray crystallography.

The occurrence of heyneanine¹, coronaridine^{2,3}, 3-oxocoronaridine³, isovoacristine⁴, ibogamine³, voacangine^{3,5}, and voacangine-pseudoindoxyl³ in *Tabernaemontana heyneana* Wall. (family Apocynaceae) has been reported earlier. From the leaves collected in Manipal, a minor alkaloid, m.p. 291-92°, designated as tabernoxidine was isolated by chromatography on silica gel. Structure elucidation of the minor alkaloid forms the subject of the present communication.

Tabernoxidine C₂₂H₂₈N₂O₃ (M⁺, m/z 400) exhibited in the UV spectrum in ethanol peaks at 220, 258, 286 and 293 nm (log ε, 4.55, 3.68, 3.48 and 3.37) indicating an oxindole chromophore⁶. Its IR spectrum in nujol displayed peaks at 3450, 2950 (NH, OH), 1720 (CO₂CH₃), 1700 (C=O), 1620, 1590 (aromatic) cm⁻¹. The ORD curve showed a negative Cotton effect: [φ]₃₇₀ -24°; [φ]₂₉₈ -15,280°; [φ]₂₅₂ +23,600°; [φ]₂₂₀ -34,400°; [φ]₂₁₀ -12,000°; CD: [θ]₃₂₅ -0; [θ]₂₈₆ -24,800; [θ]₂₃₇ +66,800; [θ]₂₀₉ -56,000. The PMR spectrum of tabernoxidine indicated a 1,2,4-substituted benzene ring: δ 7.28 (1H, d, J=7 Hz, H-5 or H-8). The indolic NH appeared at 7.48 (bs, disappears on addition of D₂O) and methoxyls at δ 3.78, 3.48 (each 3H, s, Ar-OCH₃ and COOCH₃). A doublet at 1.06 (3H, d, J=6.5 Hz) and a methine proton at 4.1 (1H, t, J=6.5 Hz) were assigned to an HO-C(H)-CH₃ group. The proton decoupled carbon-13 MNR spectrum of the alkaloid (DMSO-d₆) showed 21 lines and the SFORD spectrum led to the following



assignments for tabernoxidine (I); (ppm downfield from TMS): 180.2 (s, C-2), 174.0 (s, C-22), 159.4 (s, C-7), 142.9 (s, C-9), 124.9 (d, C-5), 123.4 (s, C-4), 105.6 (d, C-6), 95.7 (d, C-8), 70.1 (d, C-20), 55.0 (q, C-19), 52.5 (t, C-17), 51.5 (q, C-23), 50.3 (s, C-3), 50.3 (d, C-11), 49.9 (s, C-10), 47.0 (t, C-16), 40.3 (d, C-12), 29.9 (t, C-18), 25.8 (d, C-14), 25.3 (t, C-15), 25.1 (t, C-13) and 21.3 (q, C-21).

Mass spectral fragments were consistent with the formulation (I). Tabernoxidine is the third example of a naturally occurring oxindole alkaloid of the iboga class⁷, the other two being kisanine⁸ and crassinine⁹.

The structure and stereochemistry were established by a single crystal X-ray analysis. Crystals of the alkaloid are orthorhombic: *a* = 6.641 (1); *b* = 15.938 (2); and *c* = 18.759 (2). Å; *u* = 1986 Å³; space group *P* 2₁ 2₁ 2₁; *Z* = 4. Of the 1574 independent reflexions (θ ≤ 58°) measured on a diffractometer using Cu Kα radiation, 49 were classified as observed. The structure was solved by direct methods and refined anisotropically to give *R* = 0.049 (ref. 10). An indication of the absolute configuration was obtained by refinement of a variable, *η* which multiplies all *f* (ref. 11). This variable refined to a value of +1.2 (8) indicating with low confidence that the coordinate set represented the correct chirality as in fig. 1. There is an intramolecular hydrogen bond (2.71 Å) between the hydroxy oxygen and the bridgehead nitrogen N(2). There is also an intermolecular hydrogen bond (2.84 Å) between the indole nitrogen and the hydroxyl oxygen.

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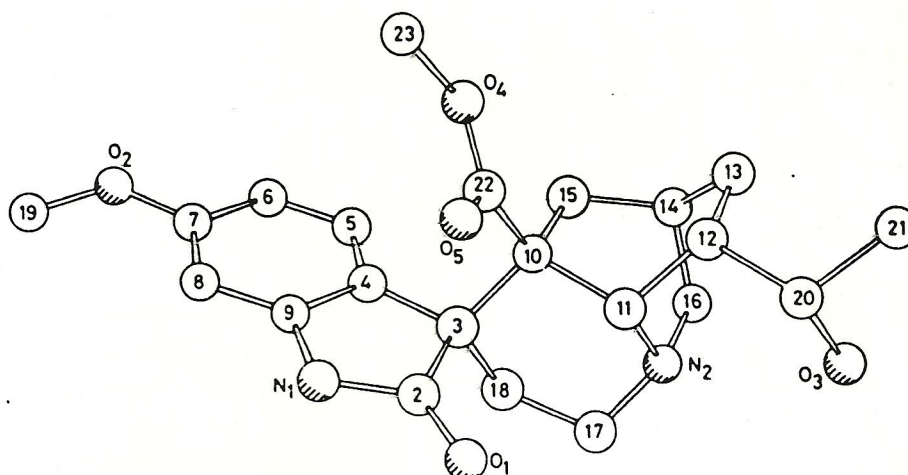


Fig. 1

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