LEUCOXYLONINE AND OCOXYLONINE - HEXAOXYGENATED APORPHINES FROM *OCOTEA LEUCOXYLON*

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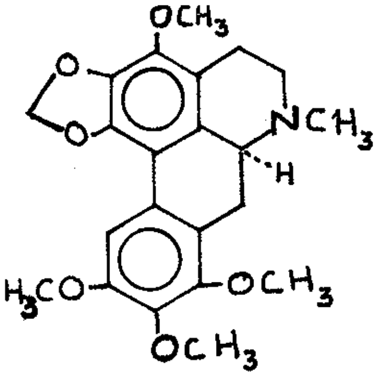
Leucoxylonine and ocoxylonine, two aporphine alkaloids isolated from *Ocotea leucoxylon* (Lauraceae) have been assigned structures **1** and **2**, respectively. They are the first examples of aporphine bases in which all but one of the aromatic positions are oxygenated.

In 1960, a preliminary phytochemical investigation of the leaf and stem alkaloids of *Ocotea leucoxylon* resulted in the isolation of the known dicentrine (**5**), and the two new alkaloids leucoxine and leucoxylonine.[1)] Subsequently, the structure and absolute configuration of leucoxine were established as shown in **4** by X-ray crystallography;[2)] this result has escaped general recognition in the chemical literature.[3)] We have now reinvestigated the leaf alkaloids of *O. leucoxylon*, resulting in the isolation of the known ocoteine (**6**), and the new aporphine ocoxylonine as well as the three above-mentioned alkaloids. Structures **1** and **2** are proposed for leucoxylonine and ocoxylonine, respectively, making these the first examples of hexaoxygenated aporphines.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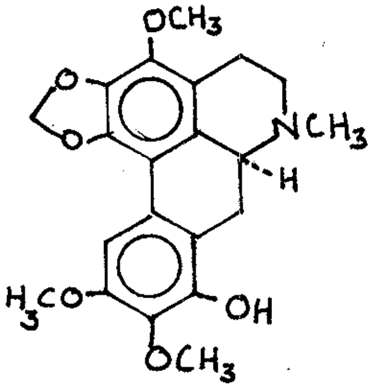
H
H3CO
OCH3
OCH3

1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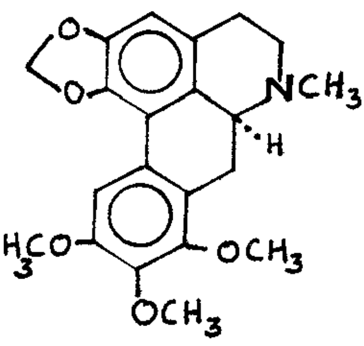
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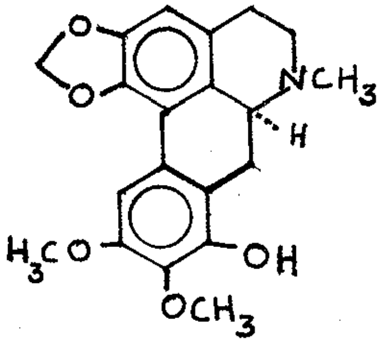
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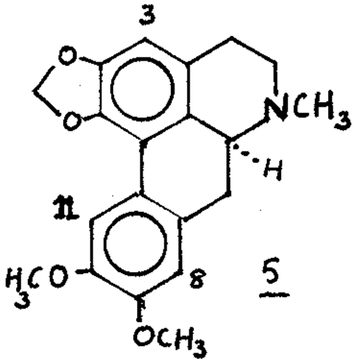
4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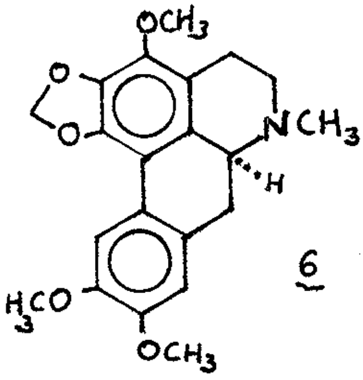
5


OCH3
NCH3
H
H3CO
OCH3

6

Leucoxylonine (1) was obtained as an amorphous solid $[\alpha]_D = +54^\circ$ (MeOH). The mass spectrum of 1 indicated the composition $C_{22}H_{25}NO_6$, and showed a strong molecular ion at m/e 399 (65%), and significant fragment ions at m/e 398 (90), 386 (30), 385 (50), 384 (90), 383 (100), 382 (20) and 356 (21). The nmr spectrum of 1 ($CDCl_3$) showed one N-methyl at δ 2.56 (3 H), four methoxyls at 3.86, 3.90, 3.91 and 4.01 (3 H each), and a diasteriotopic methylenedioxy group as a pair of doublets centered at 5.98 and 5.96 (J = 10 cps). In addition, only one aromatic proton was observed at 7.48 as a singlet. The uv absorption spectrum of 1 (EtOH) showed a maximum at 283 nm (ϵ = 20,860). Leucoxylonine formed a crystalline methiodide, mp 228-230° (decomp.), $[\alpha]_D = +32^\circ$ (MeOH). This sample was identical (ir, mixture mp) with a sample of the original preparation[1)] of leucoxylonine methiodide.

Ocoxylonine (2) crystallized from methanol as colorless needles, mp 161-162°, $[\alpha]_D = +45^\circ$ ($CHCl_3$). The mass spectrum of 2 indicated the composition $C_{21}H_{23}NO_6$, and showed a molecular ion at m/e 385 (78%) and significant fragment ions at 384 (100), 370 (15), 354 (20), 342 (34), 327 (9) and 311 (10). The nmr spectrum of 2 ($CDCl_3$) shows one N-methyl at δ 2.36 (3 H), three methoxyls at 3.90, 3.93 and 4.01 (3 H each) and a methylenedioxy group as a pair of doublets centered at 5.98 and 5.96 (J = 10 cps). In addition a single aromatic proton was observed at 7.30 as a singlet. The uv absorption spectrum of 2 (EtOH) showed maxima (ϵ) at 224 (35,280), 284 (23,760), and 305 sh (12,000); an alkaline bathochromic shift of the maxima to 294 nm indicated the presence of a phenolic function. O-Methylation of 2 with diazomethane afforded leucoxylonine (1), indicating the latter to be a monomethyl ether of ocoxylonine. Conversely, benzylselenolate demethylation[4] of leucoxylonine (1) occurred regiospecifically to give ocoxylonine (2) in 68% isolated yield.

The assignment of structures 1 and 2 to leucoxylonine and ocoxylonine rests upon a comparison of their spectral and chemical properties with those of the corresponding 3-desmethoxy aporphines ocopodine (3)[5] and leucoxine (4)[6]. The nmr spectrum of leucoxylonine (1) is virtually identical with that reported for ocopodine (3)[5] except that it shows an additional methoxyl at δ 4.01 in place of the C-3 proton at δ 6.48 in the ocopodine spectrum. Like leucoxine (4), ocoxylonine (2) gives a positive Gibbs test,[7] indicating that the sole aromatic proton of 2 must be para to the phenolic function. In ocoxylonine (2) this condition can only be met by a C-8 hydroxyl and an unsubstituted C-11 position; the only alternative structure containing a C-11 hydroxyl and C-8 proton is excluded, since its O-methylation product, leucoxylonine (1) does not show a characteristic high-field C-11 methoxyl[8] in its nmr spectrum. The selective benzylselenolate demethylation of leucoxylonine (1) to ocoxylonine (2) parallels the corresponding selective conversion[4] of ocopodine (3) to leucoxine (4).

All of the aporphines found so far in *O. leucoxylon* (1, 2, 4, 5 and 6) may be viewed as derivatives of dicentrine (5) in which further oxygenation has taken place at C-3 and or C-8.

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6 The following properties for leucoxine (**4**) have been recorded in our laboratory: mp 208-210°; $[\alpha]_D$ +84° (EtOH); mass spectrum: M^+, m/e 355; nmr spectrum: 2.46 (s, 3 H, N-methyl), 3.76, 3.83 (s, 3 H each, methoxyl) 6.07, 6.09 (d, 1 H each, J = 12 c/s), 6.65, 7.28 (s, 1 H each, Ar).

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