Flavinantine and Flavinine, Novel Morphinandienone Alkaloids from *Croton flavens* L.

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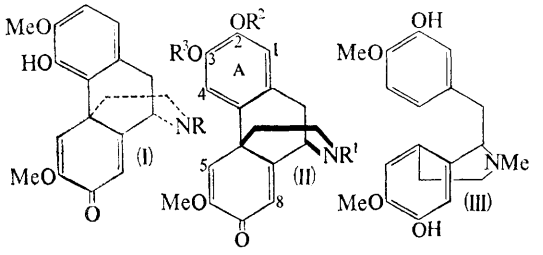
IN an attempt to obtain adequate supplies of the alkaloid flavinine[1] for complete structural characterisation, the plant *Croton flavens* was reaped from the same location as before. Counter-current separation again afforded norsinoacutine (I; R=H), but we were surprised not only by the absence of flavinine but also by the presence of sinoacutine (I; R=Me) and a new alkaloid flavinantine (II; $R^1=R^2=Me$, $R^3=H$), $C_{19}H_{21}NO_4$, m.p. 130—132°, $[\alpha]_D$ − 14·5° (EtOH). By using two-dimensional t.l.c. to examine the alkaloids of entire and serrate leaf specimens of *C. flavens*,[2] it is now evident that the species is not homogeneous. The serrate-leaf variety contains flavinine and norsinoacutine, while the entire-leaf type has the facility for performing *N*-methylations and contains flavinantine, sinoacutine, and norsinoacutine.

The u.v. (EtOH) of flavinantine, λ_{max} 239 mμ (ε 14,910), 286 (7078), i.r. ν_{max} ($CHCl_3$) 3448 (OH), 1667, 1639, 1626 (dienone), 1508 cm.$^{-1}$, and the n.m.r. [$(CD_3)_2SO$], [δ 2·32 (3H; NMe), 3·72, 3·79 (3H each; 2 OMe), 6·22, 6·72, 7·02 (2H, 1H, 1H respectively; H-1, H-4, H-5, and H-8)] are consistent with that of a morphaninandienone structure. The n.m.r. of the acetyl derivative, m.p. 196—197°, in $(CD_3)_2SO$, showed signals at δ 2·33, (3H; NMe), 2·25 (3H; ArOAc), 3·72, 3·80 (3H each; 2 OMe), 6·28 (1H; H-8), 6·80, 6·95, 7·40 (1H each; H-1, H-4, H-5). The lack of coupling of the clearly separated bands in the aromatic-olefinic region of the spectrum support a C-2,C-3 substitution pattern. The circular dichroism spectrum in dioxan was similar to that obtained for amurine[3] and flavinine.[1] The C-2,C-3 substitution pattern and the c.d.-determined stereochemistry was further supported by the fact that flavinantine could be converted into a compound which was identical to *NO*-dimethylflavinine methiodide in all respects.

A final decision as to the location of the hydroxy- and methoxy-groups on ring A was influenced by the timely synthesis of isosalutaridine (racemate of II; $R^1=R^3=Me$, $R^2=H$). Isosalutaridine was prepared by oxidising reticuline (III) with manganese dioxide in chloroform.[4] A comparison of flavinantine and isosalutaridine, kindly carried out by Professor Franck, showed that both compounds had similar mass spectra [*m/e* 327 (M^+), 312

(M — CH_3), 299 (M — CO), 284 (312 — CO)], but the t.l.c. behaviour and i.r. spectrum of flavinantine methiodide, m.p. 201—203°, and isosalutaridine methiodide were different. This comparison therefore establishes the structure of flavinantine as (II; R^1=R^2=Me, R^3=H). Flavinantine methiodide was shown to be identical to *N*-methylflavinine methiodide, and this therefore defines the structure of flavinine as (II; R^1=R^3=H; R^2=Me).



Deuterium exchange in dimethylformamide of the C-4 proton in flavinantine (n.m.r. control) was accompanied by a replacement of the i.r. band at 1508 cm.$^{-1}$ by one at 1488 cm.$^{-1}$ in the deuteriated compound. These i.r. changes can therefore no longer be ascribed solely to an introduction of a substituent at C-1 in the morphinandienone series.[6]

Flavinine and flavinantine are probably biosynthesised from reticuline-type precursors. *para–para*-Intramolecular oxidative coupling would then be followed by demethylation and re-methylation to give the observed ring A substitution, in an analogous manner to the formation of crotonosine from coclaurine.[7]

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