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ANTHOCEPHALUS ALKALOIDS: CADAMINE AND ISOCADAMINE

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In previous communications we described the isolation and structure elucidation of three novel glycosidic indole alkaloids - cadambine, 3α-dihydrocadambine and isodihydrocadambine - from A.cadamba heartwood.[1,2] We now report the isolation of two related non-glycosidic alkaloids from A. cadamba leaves. The bases obtained from ion exchange chromatography of a methanolic extract were chromatographed on silica, the less polar fractions combined, acetylated and chromatographed again. Final purification by TLC [SiO_2,$CHCl_3$/MeOH 9:1] afforded small amounts of two isomeric alkaloids (0.006% original extract) R_f 0.54 (major, 2 mg) and 0.51 (minor, 0.5 mg).

The major alkaloid, cadamine, was characterised as its O-acetate, $C_{23}H_{23}N_3O_4$, $[\alpha]_D^{25}$ -65° ($CHCl_3$). Its UV spectrum corresponded to the sum of indole and nicotinic ester chromophores, and two carbonyl bands in the IR at 1740 and 1720 cm^{-1} were compatible with this together with the presence of an acetate. Typical ions at m/e 170 and 169 in the mass spectrum extended the indole to a tetrahydro-β-carboline part structure. The base peak at m/e 332 was due to a facile loss of CH_2OAc suggesting a bond α to nitrogen but which could not be in ring C due to the absence of an m/e 168 ion (cf.[2]). On the basis of these data and biosynthetic considerations structure **2** was suggested for the m/e 322 ion. The corresponding gross structure **1b** proposed for cadamine acetate was eventually confirmed by analysis of the 300 MHz NMR spectrum. Thus the methyl and acetate esters appeared as spikes at τ 6.07 and 7.94, and broad one-proton singlets at τ 1.86, 1.28 and 0.94 were due to the indolic NH and pyridine α- protons H-21 and H-17 respectively. The aromatic protons at C-9 and 12 were a pair of broadened doublets τ 2.43 and 2.30 and the other two formed a multiplet at τ 2.6. The C-5 and 6 methylene groups were evident as multiplets at τ 6.71 and 7.13, and the C-18 protons at τ5.46 formed an ABX system with H-19 at τ 5.66. A remaining ABX set at τ 5.68, 6.26 and 6.81 was attributed to H-3 and the two H-14 protons.

The postulated structure **1** has two chiral centres at C-3 and C-19. From the negative Cotton effect in the CD spectrum between 300 and 260 nm H-3 can be assigned a β (R) configuration, but H-19 remains undetermined. The minor alkaloid - isocadamine - acetate had virtually identical UV, NMR, CD and mass spectra and hence must differ only in the stereochemistry of H-19.

Both alkaloids - presumably occurring as the alcohols **1a** - have the unusual N-4—C-19 bond and are thus structurally analogous to isodihydrocadambine (**3**) since there are several precedents for the formation of pyridine from glycosidic dihydropyran rings. The striking difference is in the stereochemistry of C-3 which shows that they are derived from a 3β precursor rather than 3α and hence constitute the first vincoside derivatives to be found in the plant.

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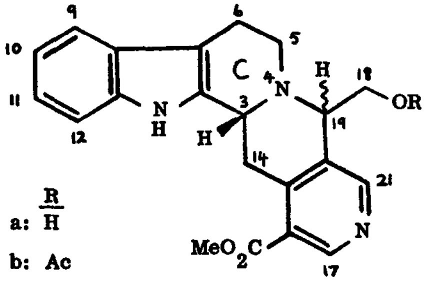
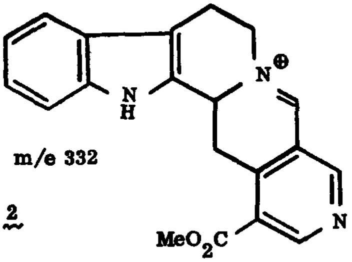
References

1. R. T. Brown and S. B. Fraser, Tet. Letters, 1957 (1974).
2. R. T. Brown, S. B. Fraser and J. Banerji, ibid., 3335 (1974).



	R
1 a:	H
b:	Ac



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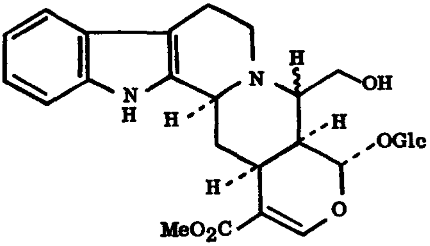

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