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ANTHOCEPHALUS ALKALOIDS: 3β-DIHYDROCADAMBINE AND 3β-ISODIHYDROCADAMBINE

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In a recent communication[1] we described the structures (1) of two indole alkaloids from Anthocephalus cadamba leaves and speculated that they might be formed from unknown 3β analogues of the glycoalkaloid isodihydrocadambine (2a), previously found in the heartwood.[2] We now report the isolation as their acetate derivatives of two new 3β glycoalkaloids - one corresponding to a presumed precursor - 3β-isodihydrocadambine (2b), and the other to 3β-dihydrocadambine (3b).

Ion exchange and silica chromatography of a methanolic extract of A. cadamba leaves gave a concentrate of glycosidic bases which were acetylated and chromatographed again on silica. Final purification by TLC afforded the acetate derivatives of the known strictosidine, cadambine[3] (4), 3α-isodihydrocadambine and 3α-dihydrocadambine[3,4] (3a) in addition to two new isomeric alkaloids $C_{37}H_{44}O_{15}N_2$. One was amorphous $[\alpha]_D^{25}$ -69° ($CHCl_3$), the other recrystallised from methanol as needles, m.p. 170-1° $[\alpha]_D^{25}$ 0° ($CHCl_3$). From UV, IR, NMR and mass spectra both structures had common indole and methyl β-alkoxyacrylate chromophores and a hexoside tetra-acetate moiety, but they differed particularly in their mass spectral fragmentation patterns.

The mass spectrum of the first base was very similar to that of 3α-dihydrocadambine penta-acetate. Since the CD spectrum exhibited a negative Cotton effect in the 290 nm region, the new compound differed from the latter in having 3β stereochemistry and it was possible that this was the only difference. Reduction of cadambine with $NaBH_4$ in acetic acid provided 3β-dihydrocadambine (3b) and direct comparison of its penta-acetate established identity with the acetylated natural product.

Distinguishing features of the mass spectrum of the second base were intense ions at m/e 683 and 335, the former attributable to loss of CH_2OAc from a carbon α to N(b), and overall it was virtually identical to that of 3α-isodihydrocadambine penta-acetate. Again the CD spectrum showed that H-3 was β, in accord with the lack of the trans quinolizidine IR bands observed with the latter, and hence one

possible structure was the C-3 epimer. Oxidation with $Pb(OAc)_4$ afforded a dihydro-β-carboline (λ_{max} ~355 nm) which on reduction with $NaBH_4$ in methanol gave a compound with 3α configuration, as shown by a positive Cotton effect in the CD spectrum. This inverted product was identical in all respects with authentic 3α-isodihydrocadambine penta-acetate confirming that the new alkaloid is the 3β epimer (2b) with the same (unknown) stereochemistry at C-19.

A. cadamba has thus provided cyclised derivatives of both vincoside and strictosidine with the novel N-4 ⟶ C-18 and C-19 bonds. Interestingly, no trace of vincoside or its more stable lactam could be found even though strictosidine is present.

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References

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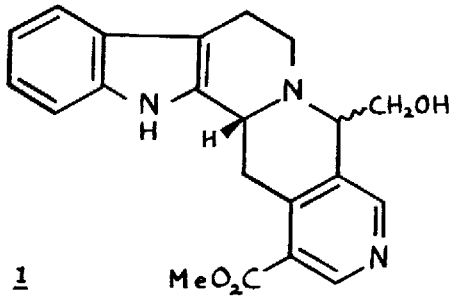

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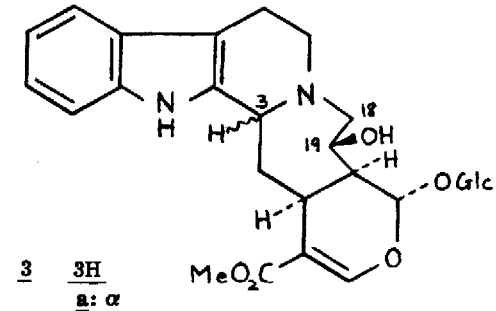

3 3H
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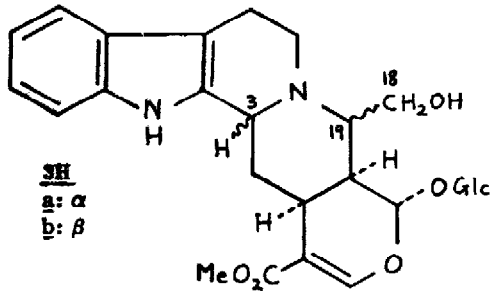
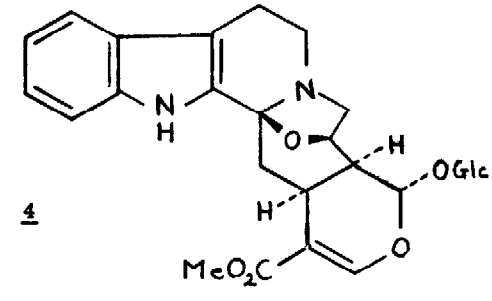
b: β



2 3H
a: α
b: β



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