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ADINA ALKALOIDS: DESOXYCORDIFOLINE LACTAM

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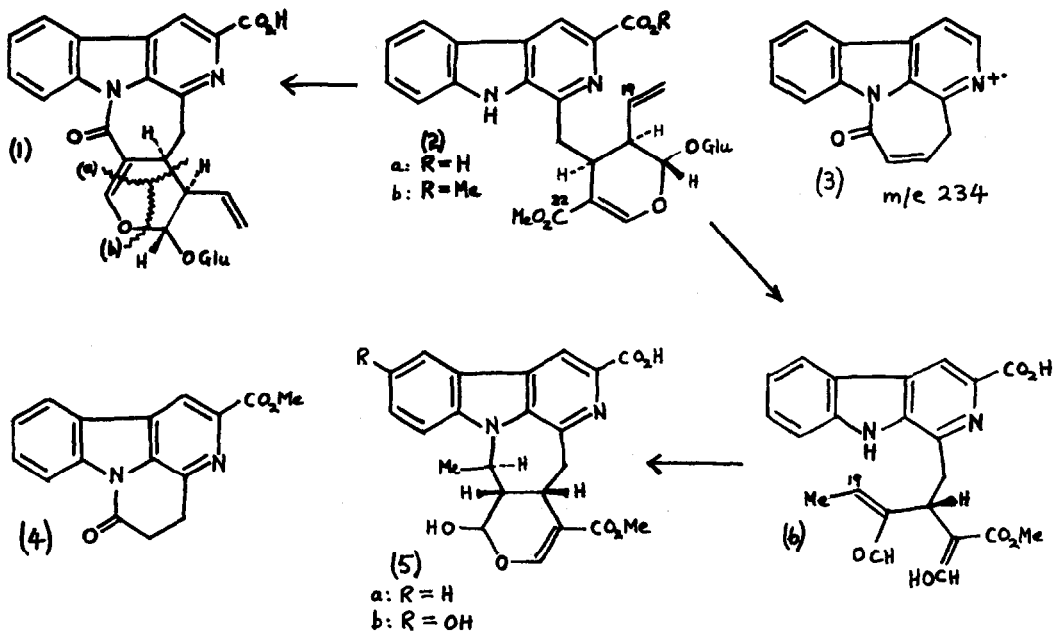
We have isolated from A. rubescens heartwood a new glycosidic alkaloid, characterised as the crystalline tetraacetate, $C_{37}H_{43}N_2O_{15}$, m.p. 165-8° $[\alpha]_D$ - 135° (MeOH) and the corresponding methyl ester, $C_{38}H_{45}N_2O_{15}$ $[\alpha]_D$ - 103° (MeOH). The UV spectrum [λ_{max} (log ϵ): 245 (4.51), 287 (4.13), 306 (3.73), 326 (4.02), 337 (4.07) nm] was not immediately informative, but on addition of alkali a rapid, irreversible change occurred to a 3-carboxy-β-carboline chromophore [$\lambda^{H^+}_{max}$ (log ϵ): 239 (4.40), 283 (4.60), 370 (3.70) nm]. Subsequently, treatment of the methyl ester with sodium methoxide in methanol followed by re-acetylation afforded the known[1,2] methyl desoxycordifoline tetraacetate (2), corresponding to the addition of a molecule of methanol to the original material.

This reaction with alkali was reminiscent of the facile cleavage of N-acyl indoles under similar conditions[3]. Furthermore, it was significant that no signals attributable to an indolic NH could be found in the NMR and IR spectra of either the acid or the ester. The only structure compatible with both observations is that of a N_a-lactam (1). This was supported by the mass spectra where series of ions corresponding to cleavages (a) and (b) could be detected in addition to the usual glycosidic and β-carboline fragmentations[4]; in particular, a strong peak ($C_{15}H_{10}N_2O$) at m/e 234 was attributable to ion (3).

Confirmation of this structure would be afforded by a UV spectral comparison with a N_a-acylated 3-carbomethoxy-β-carboline, but such a system was unknown. Hence 2-carbomethoxy-4,5-dihydrocanthin-6-one (4) was synthesised as a model by a route analogous to that used for canthin-6-one[5]. Heating the N_b-succinamide of methyl tryptophanate with $POCl_3$ and V_2O_5 in polyphosphoric acid gave a mixture of (4) and the corresponding carbomethoxycanthinone which were separated by preparative TLC. The anticipated structure for the former was substantiated by reduction of the lactam to produce a readily identified 3-carbomethoxy-β-carboline chromophore. After allowing for the absence of a β-alkoxyacrylamide chromophore

the UV spectrum of the dihydrocanthinone [λ_{max} (log ϵ):240 (4,69), 266 (4.51), 282 (4.32), 305 inf. (3.83), 316 (3.96), 329 (4.00) nm] was a fair match for that of the natural product and permitted assignment of structure (1) to desoxycordifoline lactam.

It is interesting to compare this compound and its unusual lactam ring with adifoline (5b) and desoxyadifoline (5a) where again N_a has formed a seven-membered ring.[2,6] The lactam is presumably produced in vivo by nucleophilic attack at the C-22 ester function in the glycosidic precursor (2a) - a reaction which as yet has not been possible to reproduce in vitro. When the sugar is removed, however, the aglucone is in equilibrium with the ring-opened form where a prototropic shift can occur to give an $\alpha\beta$-unsaturated aldehyde (6). An alternative nucleophilic attack by N_a on C-19 and re-closure of the heterocyclic ring then generates desoxyadifoline (5a).



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