Cordifoline: a Novel Indole Alkaloid of Biogenetic Interest

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PREVIOUS investigations on the constituents of the Asiatic tree *Adina cordifolia* yielded the alkaloid adifoline, shown by King and his co-workers to be a β-carboline derivative.[1] We now report the isolation of a new alkaloid, cordifoline, which has been assigned the novel structure (Ia) on the basis of chemical and spectral evidence summarised below.

Cordifoline was obtained as the penta-acetate, m.p. 142—144°, which had the constitution $C_{38}H_{40}O_{17}N_2$.‡ It contained two active hydrogens, one of which was removed by methylation with diazomethane to give methylcordifoline penta-acetate, $C_{39}H_{42}O_{17}N_2$. This was hydrogenated to methyldihydrocordifoline penta-acetate, $C_{39}H_{44}O_{17}N_2$. Mild hydrolysis of cordifoline penta-acetate, followed by methylation and re-acetylation, afforded dimethylcordifoline tetra-acetate, $C_{38}H_{42}O_{16}N_2$. These reactions suggested that cordifoline contained phenolic, carboxyl, and olefinic groups—deductions which were amply supported by spectral data.

A common factor in the mass spectra of all the compounds was a strong peak at *m/e* 331 ($C_{14}H_{19}O_9$), attributed to the oxonium ion (II), which appropriate metastable peaks showed to be the parent of intense ions at *m/e* 169, 127, and 109 formed by loss of acetic acid and keten molecules. Complementary ions were found at $M-331$ ($C_{14}H_{19}O_9$) and $M-347$ ($C_{14}H_{19}O_{10}$) corresponding to cleavages (a) and (b). From double irradiation n.m.r. spectra it was evident that the sugar was an aldohexose with the 6′-methylene group at τ 4·80 coupled to the H-5′ at τ 6·30; the other four hydrogens appeared between τ 4·7 and 5·2. Moreover since the four acetyl signals were between τ 7·94 and 8·04, indicating equatorial acetoxy-groups,[2] the sugar was probably glucose.

The carboline partial structure was suggested by a major peak at *m/e* 284 ($C_{15}H_{14}O_4N_2$) in the mass spectrum of cordifoline penta-acetate which was assigned structure (IIIa), formed by the favourable cleavage (c) and hydrogen transfer; lesser fragments at *m/e* 240 and 198 were plausibly derived by loss of carbon dioxide and keten. Corresponding ions were given at *m/e* 298 (IVb) by methylcordifoline and methyldihydrocordifoline penta-acetates, and at *m/e* 270 (IVc) by dimethylcordifoline tetra-acetate. Further evidence in support of the β-carboline system was supplied by n.m.r. spectra which showed phenolic acetate and NH groups and four aromatic protons. One of the latter was a sharp singlet at τ 1·27 attributed to the ring C hydrogen since it coincided exactly with the corresponding hydrogen in 3-methoxycarbonylharman (IVb) and in 3-methoxycarbonyl-β-carboline (IVc); spin decoupling of the other

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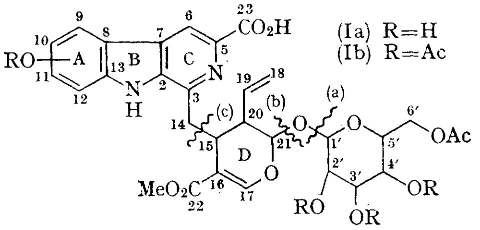
‡ Since only a small amount of alkaloid was available all formulae were determined by accurate mass measurement.

aromatic hydrogens established that the acetoxy-group must be at either C-10 or C-11. Finally, the u.v. spectrum of cordifoline penta-acetate [λ_{max}(log ϵ): 239 (4·66), 271 (4·60), 305 inf. (3·82), 338 (3·61), 350 (3·61) mμ] with a bathochromic shift in acid solution was very similar to that of (IVb) [λ_{max} (log ϵ): 235 (4·43), 271 (4·58), 305 (3·84), 330 (3·63), 345 (3·63) mμ]. Since an acetoxy-substituent has relatively little effect upon an aromatic chromophore,[3] a summation spectrum of harman-3-carboxylic acid (IVa) and loganin penta-acetate (V)§ should, and did, give a fair approximation to that of cordifoline penta-acetate.

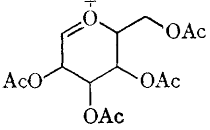
The remainder of the molecule was represented by a peak at *m/e* 165 ($C_9H_9O_3$), corresponding to the pyrylium ion (VI), in the mass spectra of cordifoline derivatives, which shifted to *m/e* 167 ($C_9H_{11}O_3$) after hydrogenation. A vinyl group was indicated by n.m.r. spectra and confirmed when Kuhn–Roth oxidation of methyldihydrocordifoline yielded propionic acid. The presence of the chromophore $MeO_2C–CH=CHO\cdot$ was shown by two strong i.r. bands at 1680 and 1635 cm.$^{-1}$, u.v. absorption in the 240 mμ region and n.m.r. signals at τ 2·51 (=CHO·) and τ 6·15 (CH_3O).

Most importantly, in the n.m.r. spectrum of cordifoline penta-acetate it was possible to locate the hydrogens around ring D and to confirm the assignments by spin-decoupling experiments. Briefly, it was established that the C-20 hydrogen (τ 7·42) was coupled to hydrogens at C-15 (τ 6·75), C-19 (τ 4·25), and C-21 (τ 4·61); the C-15 hydrogen was coupled to the C-14 methylene group (τ 6·25) and also showed a small allylic interaction with the C-17 hydrogen (τ 2·51).

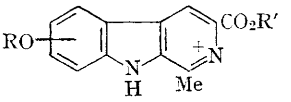
The above evidence leads to the structure (Ib) for cordifoline penta-acetate and hence cordifoline is presumed to have structure (Ia). This is of interest because of its close resemblance to a possible intermediate on the biogenetic pathway to monoterpenoid indole alkaloids from tryptophan[4] and loganin.[5,6] Ipecoside[6,7] may have a similar relationship to the *Ipecacuanha* alkaloids.



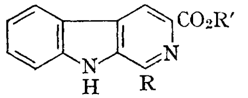
(Ia) R=H
(Ib) R=Ac



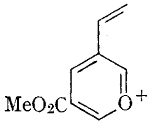
(II) *m/e* 331



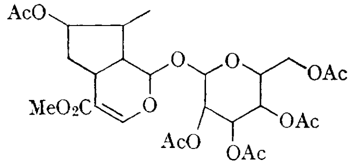
(IIIa) R=Ac, R'=H
(IIIb) R=Ac, R'=Me
(IIIc) R=R'=Me



(IVa) R=Me, R'=H
(IVb) R=R'=Me
(IVc) R=H, R'=Me



(VI) *m/e* 165



(V)

(*Received, March* 23*rd*, 1967; *Com.* 285.)

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§ We thank Professor A. R. Battersby for a generous gift of loganin penta-acetate.

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