The Alkaloids 8,14-Dihydrosalutaridine and 8,14-Dihydronorsalutaridine from *Croton linearis* Jacq.

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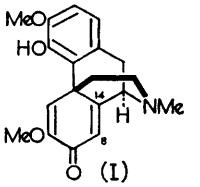
RECENTLY we reported the isolation of norsinoacutine and salutaridine (I) from *Croton balsamifera* Jacq.,[1] and now communicate the characterisation of two new related alkaloids from *C. linearis*. They are 8,14-dihydrosalutaridine,* $C_{19}H_{23}NO_4$ (II; R = Me, R′ = H) and 8,14-dihydronorsalutaridine, $C_{18}H_{21}NO_4$ (II; R = R′ = H).

8,14-Dihydrosalutaridine was first isolated as its *O*-acetyl derivative (designated base BIA), m.p. 210°, $[\alpha]_D^{15}$ −22·1° (MeOH) from *C. linearis*,[2] but the free base, m.p. 198—203°, $[\alpha]_D^{15}$ −76·1° (MeOH), λ_{max} 206 mμ (ε, 32,730), 238 mμ (ε, 6960), 265 mμ (ε 7550) has subsequently been isolated from *C. discolor* Willd.[3]

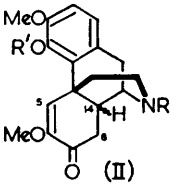
Hydrogenation of the dihydrosalutaridine compound (II; R = Me, R′ = H), ν_{max} 1681, 1613 (αβ-unsaturated CO), gave two products. One product, m.p. 214—217° (ethanol of crystallisation), $[\alpha]_D^{15}$ −20° (MeOH) was shown to be tetrahydrosalutaridinol (III). Mass-spectral data of the latter[4] showed the parent peak at *m/e* 333 [$\%\Sigma_{40}$ = 14·1], and the expected fragmentation[5] with the base peak (IV) at *m/e* 196 [$\%\Sigma_{40}$ = 14·8]. Along with the other fragments was a peak at *m/e* 59 [$\%\Sigma_{40}$ = 3·4]. This fragmentation pattern taken in conjunction with the relative abundance of these peaks strongly suggests *trans*-fused B : C rings.[5] As the stereochemistry of the C-14 centre is the same as that of the naturally occurring base, BIA, a study is being made of the complete stereochemistry of tetrahydrosalutaridinol (III). The other hydrogenation product, m.p. 218—220° was dihydrosalutaridinol, $C_{19}H_{25}NO_4$ (V).

The structure of the new base, 8,14-dihydrosalutaridine, (II; R = Me, R′ = H), molecular ion at *m/e* 329,[6] was fully supported by n.m.r. ($CDCl_3$) evidence. The aryl protons appeared at δ 6·68, the two methoxyl groups at δ 3·85 and 3·68, the *N*-methyl at δ 2·38 and the C-5 proton at δ 6·76. The spectrum of the *O*-acetyl derivative (II; R = Me, R′ = Ac) showed two aromatic protons (δ 6·96, 6·88; *J* = 9 c./sec.), two methoxyl groups (δ 3·70, 3·80), one *N*-methyl group (δ 2·32), a phenolic acetate (δ 2·45) and the C-5 proton shifted to δ 6·3.

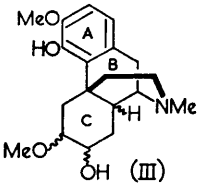
8,14-Dihydronorsalutaridine (II; R = R′ = H), molecular ion at *m/e* 315,[6] m.p. 208—212° (ethyl acetate of crystallisation), $[\alpha]_D^{15}$ −69·1° (MeOH), ν_{max} 3170 (NH), 1670 and 1600 (αβ-unsaturated CO) cm.$^{-1}$ (Nujol) was isolated by re-examination of residual material from fractions E and F of earlier countercurrent experiments.[2] The gross



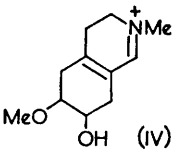
(I)



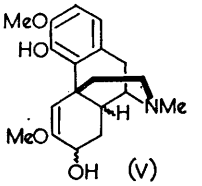
(II)



(III)



(IV)



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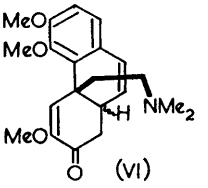

(VI)

structure was established by correlating the fully methylated quaternary compound, $[\alpha]_D^{15}$ −34° (MeOH) derived from this base with that from 8,14-dihydrosalutaridine. These compounds from both sources were identical and gave an identical Hofmann product (VI), m.p. 50—55°. The hydroxyl group in 8,14-dihydronorsalutaridine could be correctly located at C-4 by examination of the n.m.r. ($CDCl_3$) of the base and its neutral *NO*-diacetyl derivative, m.p. 252—255°, (II; R = R′ = Ac), 8,14-dihydronorsalutaridine showed two aryl protons (δ 6·7), two methoxyl groups (δ 3·67 and 3·85), one hydroxyl group (δ 3·56, exchangeable

* Professor D. H. R. Barton has suggested on the basis of his unpublished work that this alkaloid should be the enantiomer of isosinomenine; we have established that this is so by direct comparison of our material with a sample of isosinomenine which he kindly provided.

with D_2O) and one olefinic proton (C-5; δ 6·67). In the spectrum of the *NO*-diacetyl derivative (II; R = R′ = Ac) the aryl protons appeared at δ 6·93 and δ 6·97 (J = 9 c./sec.), the methoxyl groups at δ 3·67 and 3·80. Also present was one phenolic acetate (δ 2·35) one *N*-acetate (δ 2·12) and the C-5 olefinic proton was shifted to δ 6·26, again due to the influence of the *O*-acetyl group at C-4.

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[1] C. Chambers, L. J. Haynes, and K. L. Stuart, *Chem. Comm.*, 1966, 449.
[2] L. J. Haynes and K. L. Stuart, *J. Chem. Soc.*, 1963, 1784.
[3] Unpublished results, K. L. Stuart and C. Chambers.
[4] Spectrum kindly determined by Dr. H. W. Fehlhaber and Dr. D. R. Taylor.
[5] A. Mandelbaum and D. Ginsburg, *Tetrahedron Letters*, 1965, 2479.
[6] Mass-spectral data were obtained on the A.E.I. MS9 instrument through the courtesy of Professor Allan Maccoll and Dr. A. Loudon.