New Histamine Alkaloids from a *Glochidion* Species

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THREE new inter-related histamine alkaloids, together with the previously known alkaloid, N^{α}-cinnamoylhistamine,[1] have been isolated from the leaves of a New Guinea *Glochidion* species, probably *G. philippicum* (Cav.) C. B. Rob. (Euphorbiaceae). Glochidine, $C_{15}H_{22}N_3O$, m.p. 65—67°, $[\alpha]$ $(CHCl_3)$ $\pm$ 0°, an alkaloid of a new type, has been shown to be (I). Hydrolysis of (I) with concentrated hydrochloric acid at 100° affords histamine hydrochloride and 4-oxodecanoic acid. The infrared spectrum shows a band at ν_{max} $(CHCl_3)$ 1690 cm.$^{-1}$ (five-membered-ring lactam) and the absence of NH absorption. Two singlet signals in the n.m.r. spectrum* at δ 7·42 and δ 6·72 are ascribed to the C-3 and C-1 imidazole ring protons respectively.

A second isomeric alkaloid, glochidicine, $C_{15}H_{23}N_3O$, hemihydrate m.p. 103—105°, $[\alpha]_D$ $(CHCl_3)$ $\pm$ 0°, is stable to refluxing concentrated hydrochloric acid and has been shown to be (II). The infrared spectrum shows bands at ν_{max} $(CHCl_3)$ 3500 (imidazole NH) and at ν_{max} $(CHCl_3)$ 1670 cm.$^{-1}$ (lactam carbonyl). A signal in the n.m.r. spectrum at δ 9·33, due to a proton exchangeable with deuterium oxide, can be ascribed to the imidazole NH, while the C-2 proton resonates as a singlet at δ 7·38.

The n.m.r. spectra of both (I) and (II) have broad eight-proton signals at δ 1·25 (four methylene groups) and a broadened three-proton triplet at δ 0·85 (terminal methyl group). The mass spectra of both alkaloids have a molecular ion at *m/e* 261 with a major peak at *m/e* 176 (M — 85), ascribed to loss of the n-hexyl chain at C-4.

The third new alkaloid is N^{α}-(4-oxodecanoyl)-histamine (III), $C_{15}H_{25}N_3O_2$, m.p. 117—118°, which on hydrolysis with concentrated hydrochloric acid gives histamine hydrochloride and 4-oxodecanoic

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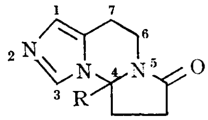
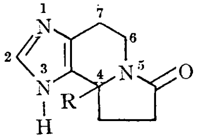
* Spectra were measured on a Varian A60 spectrometer in $CDCl_3$ solution with tetramethylsilane as internal standard (δ 0·00).

acid. The infrared spectrum of (III) shows the presence of both the amide carbonyl [$\nu_{\max}$ ($CHCl_3$) 1665 cm.$^{-1}$] and ketonic carbonyl groups [$\nu_{\max}$ ($CHCl_3$) 1710 cm.$^{-1}$). When base (I) is heated in 10% aqueous acetic acid, a mixture of (I), (II), and (III) is obtained, and prolonged boiling in acetic acid affords essentially pure base (II). Histamine and 4-oxodecanoyl chloride react in pyridine to give a mixture of the three bases. Bases (I) and (II) are alternative cyclisation products of base (III) resulting from ring closure to imidazole NH or CH respectively.

Because alkaloids (I) and (III) are readily converted into mixtures of (I), (II), and (III) by acid, the ratio of the three alkaloids present is uncertain, but we have consistently obtained alkaloid (I) as the major leaf alkaloid. *Glochidion* bark contains base (II) and N^{α}-cinnamoylhistamine, but not bases (I) or (III).

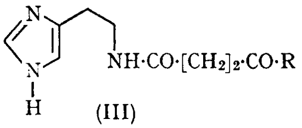


(I)



(II)

[R = n-hexyl]



(III)

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[1] J. S. Fitzgerald, *Austral. J. Chem.*, 1964, **17**, 375.