STEROIDAL ALKALOIDS OF *MARSDENIA ROSTRATA*

II.* THE ISOLATION AND STRUCTURE OF A NEW ALKALOID, ROSTRATAMINE

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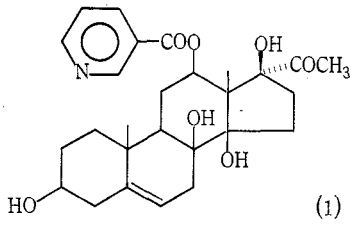
Abstract

A new alkaloid, rostratamine, was isolated from *Marsdenia rostrata* (Asclepiadaceae). Its structure was elucidated as deacetylmetaplexigenin 12-nicotinate.

We have previously reported[1] the presence of two alkaloids, rostratine and dihydrorostratine, in *Marsdenia rostrata* R.Br. of the Asclepiadaceae family. This paper describes the isolation and structure elucidation of a third new alkaloid from the Wollongong collection of the same plant material.



(1)

Rostratamine (1) has the molecular formula $C_{27}H_{35}NO_7$, and m.p. 277–279°. It was isolated from the alkaloid mixture by chromatography on silica gel impregnated with silver nitrate. Spectral evidence clearly indicated it to be a nicotinoyl ester of a polyhydroxypregnane which was shown, by hydrolysing rostratamine, to be deacetylmetaplexigenin. Its n.m.r. spectrum[2–4] shows a doublet at δ 9·05 (J 1·5 Hz), two quartets at 8·70 (J 4·5 and 1·5 Hz) and 7·43 (J 4·5 and 8·0 Hz), and a pair of triplets at δ 8·24 (J 8·0 Hz) characteristic of the C2′, C6′, C5′, and C4′ protons of a 3-substituted pyridine ring system. The three three-proton singlets at δ 2·09, 1·60, and 1·15 are assigned to the C21, C18, and C19 methyl protons of the pregnane ring system. The broad one-proton signal at δ 5·35 is assigned to the C6 vinylic proton at the 5,6 double bond. The single proton multiplet at δ 3·37 represents the α-proton on a hydroxylated C3, while the one-proton quartet at δ 4·90 (J 5·0 and 11·0 Hz) represents the α-proton on C12 when the hydroxyl group on C12 is esterified.[2] (If this hydroxyl group is not esterified the

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[1] Summons, R. E., Ellis, J., and Gellert, E., *Phytochemistry*, 1972, **11**, 3335.

[2] Schaub, F., Kaufmann, H., Stöcklin, W., and Reichstein, T., *Helv. chim. Acta*, 1968, **51**, 338.

[3] Shimizu, Y., Sato, Y., and Mitsuhasi, H., *Chem. Pharm. Bull., Tokyo*, 1969, **17**, 2394.

[4] Yamagishi, T., and Mitsuhasi, H., *Chem. Pharm. Bull., Tokyo*, 1972, **20**, 2070.

α-proton signal appears between δ 3·9 and 4·0.) The mass spectrum[5,6] shows ready losses of water and of an acetyl (*m/e* 43) fragment (but no acetic acid) which indicates the presence of an acetyl side chain on C 17 of polyhydroxy steroid molecules. The strong peaks at *m/e* 123 and 124 in conjunction with the loss of *m/e* 123 fragments in various combinations are indicative of an esterifying nicotinoyl group, probably on C 12. That the nicotinoyl group is located on the C 12 hydroxyl group and consequently rostratamine has structure (1) was shown, in addition to the n.m.r. data, also by the characteristic fragments observed in the mass spectrum,[5,6] e.g. *m/e* 138 and 139 together with their anhydro derivatives at *m/e* 120 and 121, and *m/e* 181 together with its anhydro derivatives at 163 and 145 when ring B is cleaved, or *m/e* 193 (with 175) and *m/e* 169 together with *m/e* 223 and 113 (with 95) when ring C is cleaved.

Experimental

Microanalyses were carried out by the Microanalytical Laboratory, Chemistry Department, Stanford University. The n.m.r. data were obtained on a Varian HA-100 instrument in $CDCl_3/CH_3OD$ solution using $SiMe_4$ as the internal reference. The mass spectrum was measured on a Varian Mat 711 instrument at 70 eV.

The alkaloid mixture from the Wollongong collection of *Marsdenia rostrata* was chromatographed on a preparative thin-layer plate prepared from silica gel GF 254 (Merck) impregnated with 25% $AgNO_3$ using $CHCl_3$: MeOH (9 : 1) as the developing solvent. Extraction of the appropriate zone (R_F 0·40) gave *rostratamine* in colourless needles from MeOH and Et_2O (Found: C, 67·0; H, 7·4; N, 2·7. $C_{27}H_{35}NO_7$ requires C, 66·8; H, 7·3; N, 2·9%). $[\alpha]_D^{22}$ −32±1° (*c*, 1·0 in MeOH). Mass spectrum: *m/e* 486 (0·2%), protonated parent ion; 485 (0·1), M^+; 467 (0·2), M^+-H_2O; 459 (0·3), $M^+-2\times H_2O$; 442 (1·7), M^+−acetyl; 424 (0·6), M^+-H_2O-43; 406 (0·4), $M^+-2\times H_2O-43$; 362 (0·6), M^+−nicotinic acid; 344 (0·8), M^+-H_2O-123; 326 (0·7), $M^+-2\times H_2O-123$; 319 (1·5), $M^+-123-43$; 301 (7·5), $M^+-H_2O-123-43$; 283 (15), $M^+-2\times H_2O-123-43$; 265 (8·0), $M^+-3\times H_2O-123-43$; 223 (8·0), $C_{13}H_{19}O_3$; 193 (5·0), $C_{12}H_{17}O_2$; 181 (9·0), $C_{10}H_{13}O_3$; 175 (8·0), 193−H_2O; 169 (7·0), $C_9H_{13}O_3$; 163 (21), 181−H_2O; 145 (36), 163−H_2O; 139 (19), $C_9H_{15}O$; 138 (11·0), $C_9H_{14}O$; 124 (100), protonated nicotinic acid; 123 (60), nicotinic acid; 121 (51), 139−H_2O; 120 (39), 138−H_2O; 113 (49), $C_6H_9O_2$; 106 (100), nicotinoyl; 95 (41), 113−H_2O; 78 (99), pyridyl; 43 (100), acetyl.

Rostratamine (5 mg) was refluxed in 5% methanolic KOH for 3 hr, cooled, diluted with water, and extracted with $CHCl_3$. Evaporation of the solvent gave deacetylmetaplexigenin, m.p. 218–222° (lit.[5] 218–223°), identical with a sample obtained from authentic metaplexigenin[1] (t.l.c., mixed m.p., mass spectrum).

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[6] Saner, A., Stöckel, K., and Reichstein, T., *Helv. chim. Acta*, 1972, **55**, 1221.