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 deacetylmethaplexigenin 12-nicotinate.

We have previously reported1 the presence of two alkaloids, rostratine and dihydorostratine, 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.

Rostratamine (1) has the molecular formula $C_{27}H_{35}NO_3$, 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 deacetylmethaplexigenin. Its n.m.r. spectrum2-4 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 ω-proton on a hydroxylated C3, while the one-proton quartet at δ 4·90 (J 5·0 and 11·0 Hz) represents the ω-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.

α-proton signal appears between δ 3.9 and 4.0.) The mass spectrum\(^5\) 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 C17 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 C12. That the nicotinoyl group is located on the C12 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,\(^5\) 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 n 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\(_3\)OD 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\(_2\)O (Found: C, 67.0; H, 7.4; N, 2.7. C\(_{27}\)H\(_{35}\)N\(_7\)O\(_7\) requires C, 66.8; H, 7.3; N, 2.9 %). [α]\(_D\)\(^{22}\) = 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\(_2\)O; 459 (0.3), M\(^+\)-2×H\(_2\)O; 442 (1.7), M\(^+\)-acetyl; 424 (0.6), M\(^+\)-H\(_2\)O-43; 406 (0.4), M\(^+\)-2×H\(_2\)O-43; 362 (0.6), M\(^+\)-nicotin acid; 344 (0.8), M\(^+\)-H\(_2\)O-123; 326 (0.7), M\(^+\)-2×H\(_2\)O-123; 319 (1.5), M\(^+\)-H\(_2\)O-123-43; 283 (8.0), M\(^+\)-3×H\(_2\)O-123-43; 265 (8.0), M\(^+\)-3×H\(_2\)O-123-43; 223 (8.0), C\(_{12}\)H\(_{15}\)O\(_2\); 193 (5.0), C\(_{12}\)H\(_{17}\)O\(_2\); 181 (9.0), C\(_{10}\)H\(_{13}\)O\(_3\); 175 (8.0), 193-H\(_2\)O; 169 (7.0), C\(_{9}\)H\(_{15}\)O\(_3\); 163 (21), 181-H\(_2\)O; 145 (36), 163-H\(_2\)O; 139 (19), C\(_{8}\)H\(_{15}\)O\(_2\); 138 (11.0), C\(_{9}\)H\(_{13}\)O; 124 (100), protonated nicotinic acid; 123 (60), nicotinic acid; 121 (51), 139-H\(_2\)O; 120 (39), 138-H\(_2\)O; 113 (49), C\(_{6}\)H\(_{15}\)O\(_2\); 106 (100), nicotinoyl; 95 (41), 113-H\(_2\)O; 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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