Communications to the Editor

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(+)-13β-HYDROXYMAMANINE, A NEW LUPIN ALKALOID FROM MAACKIA AMURENSIS VAR. BUERGERI[1)]

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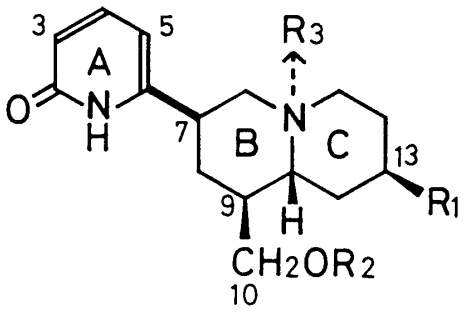
A new lupin alkaloid, (+)-13β-hydroxymamanine, was isolated from the stems of Maackia amurensis var. buergeri (Leguminosae). Its structure was determined by spectroscopic analysis and by chemical transformation to its acetate and N-oxide.

KEYWORDS ——— lupin alkaloid; quinolizidine alkaloid; (+)-13β-hydroxymamanine; 10,13-diacetyl-13β-hydroxymamanine; 13β-hydroxymamanine N-oxide; (-)-baptifoline; (+)-mamanine; biogenesis; Maackia amurensis; Leguminosae

As a result of screening plants belonging to the Leguminosae for lupin alkaloids, a new alkaloid, (+)-13β-hydroxymamanine 1, was isolated from Maackia amurensis Rupr. et Maxim. var. buergeri C. K. Schn. (Leguminosae), which is a deciduous tree widely distributed in Eastern Asia. In the present communication, we report the structure elucidation of 1 by spectroscopic data of this compound, its acetate 2 and N-oxide 3.

The new alkaloid 1 was isolated from the fresh stems of M. amurensis by repeated silica gel chromatography in a yield of 0.007% of the fresh weight as a colorless amorphous solid, $[\alpha]_D^{17}$ +31.2° (c=0.107, CH_3OH).[2)] The molecular formula, $C_{15}H_{22}N_2O_3$ (M^+, m/z 278.1651, calc. 278.1629), was established by high resolution electron impact mass spectrometry (HREIMS). The IR spectrum of 1 showed the bands 3100-3500, 2800-3000, 1650, 1610 and 1550 cm^{-1} and the UV spectrum revealed absorption maxima at 304 (log ε=3.82) and 226 nm (log ε=3.83). Both of these indicate the presence of a 2-pyridone moiety in the molecule.[3,4)]

In the HREIMS, fragment peaks were observed at m/z 261 (7%), 260 (6), 247(9) and 229 (13). These peaks were assigned to M^+-OH, M^+-H_2O, M^+-CH_2OH and M^+-CH_2OH-H_2O, respectively, suggesting the presence of hydroxy and hydroxymethyl groups in the molecule. The predominant fragment peaks at m/z 121 (64%) and 100 (base peak) were assigned by HREIMS to 6 (C_7H_7NO) and 7 ($C_5H_{10}NO$). These data indicate that 1 has a 2-pyridone moiety and quinolizidine ring substituted with hydroxy and hydroxymethyl groups. Thus, compound 1 is assumed to be a hydroxy



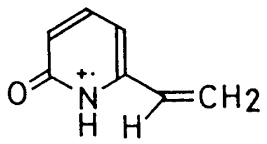
1: R_1=OH, R_2=H, R_3=lone pair

2: R_1=$OCOCH_3$, R_2=$COCH_3$, R_3=lone pair

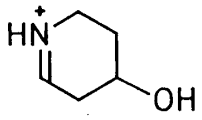
3: R_1=OH, R_2=H, R_3=O

4: R_1=H, R_2=H, R_3=lone pair

5: R_1=H, R_2=H, R_3=O



6: m/z 121 (C_7H_7NO)



7: m/z 100 ($C_5H_{10}NO$)

Table. ^{13}C-NMR Data of the Compounds 1 to 5 (67.8 MHz)

Carbon number	Chemical shift (ppm)		Difference of chemical shift	Chemical shift (ppm)		
	1[a]	4[b]	Δ(1-4)	2[b]	3[a]	5[c]
2	166.5 (s)	165.3 (s)	+1.2	165.6 (s)	166.4 (s)	164.8 (s)
3	118.2 (d)	117.5 (d)	+0.7	117.8 (d)	118.9 (d)	118.9 (d)
4	143.7 (d)	141.8 (d)	+1.9	141.7 (d)	143.7 (d)	141.8 (d)
5	105.2 (d)	104.2 (d)	+1.0	103.6 (d)	105.8 (d)	104.3 (d)
6	152.7 (s)	151.1 (s)	+1.6	150.9 (s)	150.6 (s)	148.2 (s)
7	40.5 (d)	39.9 (d)	+0.6	39.5 (d)	36.0 (d)	34.6 (d)
8	32.8 (t)	32.4 (t)	+0.4	29.4 (t)	31.6 (t)	31.5 (t)
9	44.6 (d)	43.4 (d)	+1.2	40.7 (d)	39.2 (d)	37.9 (d)
10	63.9 (t)	63.8 (t)	+0.1	65.4 (t)	63.1 (t)	62.5 (t)
11	58.6 (d)	63.0 (d)	-4.4	57.9 (d)	68.1 (d)	73.0 (d)
12	37.0 (t)	29.5 (t)	+7.5	33.8 (t)	33.9 (t)	22.9 (t)
13	64.7 (d)	24.4 (t)	+40.3	67.6 (d)	63.0 (d)	23.2 (t)
14	34.8 (t)	25.7 (t)	+9.1	33.1 (t)	28.2 (t)	20.1 (t)
15	51.0 (t)	56.6 (t)	-5.6	50.4 (t)	64.4 (t)	69.2 (t)
17	60.9 (t)	60.6 (t)	+0.3	60.2 (t)	71.0 (t)	70.9 (t)
-O-CO-	-	-	-	170.2 (s)	-	-
	-	-	-	170.9 (s)	-	-
$-CH_3$	-	-	-	20.9 (q)	-	-
	-	-	-	21.3 (q)	-	-

a) In CD_3OD.

b) In $CDCl_3$.

c) In 5% CD_3OD - 95% $CDCl_3$, data from ref. 6.

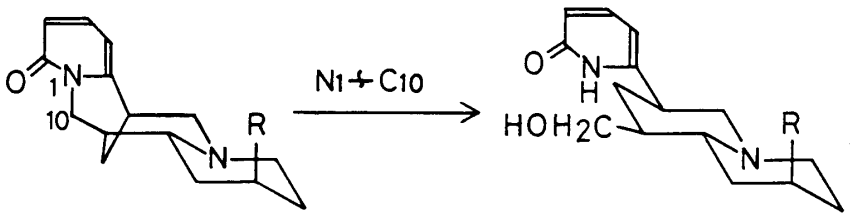
derivative of (+)-mamanine 4, which had been isolated from Sophora chrysophylla[5,6] and S. flavescens.[7]

Signals appearing in ^{13}C- and ^{1}H-NMR spectra were assigned by selective proton decoupling and homonuclear decoupling experiments. In the ^{13}C-NMR spectrum of 1, the signals corresponding to the carbons of ring A and B coincided with those of 4 (Table). This indicates that the relative stereochemistry of the substituents on ring B in 1 is the same as in 4. The remaining five signals were assigned to C-11 to C-15 by considering the substitution effects of a hydroxy group. The position and configuration of the hydroxy group was determined to be 13β (axial) on the basis of the shift effect of a hydroxy residue on decaline[8] and 13-hydroxylupanine.[9] The alpha effects of an axial and an equatorial hydroxy group are reported to be low-field shifts of ca. 40 ppm and ca. 44 ppm, respectively.[8,9] The low-field shift of 40.3 ppm of C-13 supported the existence of an axial hydroxy group. The beta and gamma effects also showed good agreement with those reported for an axial configuration. Therefore, the hydroxy group of 1 was determined to be in the 13β (axial) position.

The structure of 1 was confirmed by the ^{1}H-NMR spectrum (270 MHz, CD_3OD). The olefinic protons of C-3, C-4 and C-5 resonated at δ 6.38 ppm (1H, d, J=9.5), 7.52 (1H, dd, J=9.5 and 7) and 6.25 (1H, d, J=7), respectively. The signal at δ 4.09 (1H, quintet, J=3) was assigned to an equatorial proton on C-13. The two protons on C-10 exhibited the AB parts of the ABX pattern ($J_{A,B}$=11, $J_{A,X}$=2.5 and $J_{B,X}$=5) centered at δ 3.52 and 3.62. The signal at δ 2.84 (1H, tt, J=11 and 4) was assigned to an axial proton at C-7.

For further confirmation of the structure of 1, the 10,13-diacetate 2[10] and the N-oxide 3[11] were synthesized from 1. The substituent effects on the ^{13}C-chemical shifts of 2 induced by 13β-acetoxy group showed good agreement with those reported in 13(axial)-acetoxysparteine.[9] In the ^{13}C-NMR spectrum of 3, the low-field shifts of C-11, C-15, C-17 in the range of 9 to 14 ppm and the up-field shifts of C-7, C-9, C-12, C-14 in the range of 3 to 7 ppm were induced by N-oxidation. These substituent effects of N-oxide were also observed in the spectrum of mamanine N-oxide 5.[6] From these several lines of evidence, the structure of the new base was determined to be (+)-13β-hydroxymamanine 1 or its enantiomer.

The structure of 1 corresponds to an oxidative product derived from the N_1-C_{10} cleavage of (-)-baptifoline 8 coexisting in M. amurensis. Similar relationships in the structures involving oxidative bond cleavage have been found between (+)-mamanine 4 and (-)-anagyrine 9, (+)-kuraramine and (-)-N-methylcytisine, and (-)-pohakuline and (-)-lupanine.[6,7] Biosynthetic relations are suggested between these bridged quinolizidine alkaloids and the unbridged bases.



8: R=OH; (-)-baptifoline
9: R=H; (-)-anagyrine

1: R=OH
4: R=H

Further studies of the absolute configuration and the biosynthetic relations of these alkaloids are being undertaken in our laboratories.

REFERENCES AND NOTES

1) Studies on Plant Constituents of Genus Maackia. Part I.

2) 1 was isolated from 75% EtOH extracts of the fresh stems of M. amurensis harvested in September 1984 at Medicinal Plant Gardens, Chiba University, together with eight known alkaloids, (-)-cytisine (main base), (-)-anagyrine, (-)-N-methylcytisine, (-)-lupanine, (-)-baptifoline, N-formylcytisine, ammodendrine, and camoensidine.

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10) 2 was obtained by acetylation of 1 with Ac_2O/pyridine. Colorless amorphous solid, MS (70 eV): m/z (rel.%) 362 (5, M^+), 302 (24, M^+-CH_3COOH), 243 (100), 229 (7), 202 (44), 121 (39), 96 (34), 82 (45), 43 (34). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2750-2850 (trans-quinolizidine), 1730, 1650, 1620, 1250. ^{13}C-NMR in Table. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 1.48 (2H, m), 1.70-2.00 (4H, m), 2.05 (3H, s, $-COCH_3$), 2.08 (3H, s, $-COCH_3$), 2.09-2.50 (4H, m), 2.69 (1H, dt, J=12 and 5), 2.88-3.07 (2H, m), 4.01 (1H, dd, J=11 and 6.5, H-10), 4.09 (1H, dd, J=11 and 4, H-10), 5.11 (1H, m, $W_{1/2}$=7.5, H-13), 6.07 (1H, d, J=6.5, H-5), 6.43 (1H, d, J=9, H-3), 7.39 (1H, dd, J=9 and 6.5, H-4), 12.3 (1H, br, H-1).

11) The oxidation of 1 with m-chloroperbenzoic acid in CH_2Cl_2-MeOH gave 3. Colorless needle, mp 207-210° (benzene-EtOH). MS (20 eV): m/z (rel.%) 294 (3, M^+), 278 (62, M^+-O), 277 (23, M^+-OH), 276 (77, M^+-H_2O), 220 (43), 121 (64), 100 (100). IR ν_{max}^{KBr} cm^{-1}: 1650, 1610, 1000. ^{13}C-NMR in Table. ^{1}H-NMR (270 MHz, CD_3OD) δ: 1.61-2.20 (4H, m), 2.52 (1H, br t, J=13.5), 3.09 (1H, br d, J=11), 3.25 (1H, br d, J=13.5), 3.38-3.80 (5H, m), 4.10 (1H, m, $W_{1/2}$=7.5, H-13), 6.29 (1H, d, J=7, H-5), 6.42 (1H, d, J=9.5, H-3), 7.53 (1H, dd, J=9.5 and 7, H-4).

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