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ISOLATION OF (+)-MAACKIAMINE (NORAMMODENDRINE) FROM THE FLOWERS OF *MAACKIA AMURENSIS*

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Key Word Index—*Maackia amurensis*; Leguminosae; flowers; piperidine alkaloid; lupin alkaloid; maackiamine; ammodendrine.

Abstract—A new natural alkaloid, (+)-maackiamine, was isolated from the flowers of *Maackia amurensis* var. *buergeri* together with 10 known alkaloids. The structure of the new natural compound was determined as 1-acetyl-1,2,3,4-tetrahydro-5-(2′-pyrrolidinyl)pyridine by spectroscopic methods.

INTRODUCTION

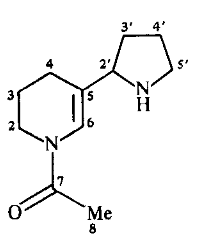
In the course of our recent phytochemical study on leguminous plants, we have already isolated two new lupin alkaloids from the stems of *Maackia amurensis* var. *buergeri* Rupr. et Maxim. [1, 2]. This plant is a deciduous tree widely grown in Eastern Asia and sometimes used as the source of folk medicine. In the present communication, we report the isolation and structure determination of (+)-maackiamine (**1**), a new natural pyrrolidinyl piperidine alkaloid, from the flowers of *M. amurensis* var. *buergeri*, together with the 10 known alkaloids.

RESULTS AND DISCUSSION

From the freshly harvested flowers of *M. amurensis*, the new alkaloid (**1**) was isolated as a colourless oil in a yield of 0.0014% of the fresh weight by repeated chromatography. We also isolated the 10 known alkaloids, (−)-*N*-methylcytisine (main base), (−)-camoensidine, (+)-sparteine, (−)-anagyrine, (−)-cytisine, (−)-lupanine, (−)-rhombifoline, (−)-lusitanine, 5,6-dehydrolupanine and ammodendrine.

The chromatographic behavior of **1** on a silica gel column was very similar to that of ammodendrine (**2**). The IR spectrum of **1** also showed a similar pattern to that of **2**, having an amide carbonyl band at 1640 cm^{-1} and a C–N stretching band at 1410 cm^{-1}. In the EIMS spectrum of **1**, $[M]^+$ at *m/z* 194.1420 ($C_{12}H_{18}N_2O$, calc. 194.1419) and other peaks suggested that **1** is one of the nor derivatives of **2**. The fragment peaks of *m/z* 151 $[M-MeCO]^+$ and *m/z* 177 $[M-OH]^+$ indicated the presence of an *N*-acetyl group of a pyrrolydinyltetrahydropyridine moiety. The peak at *m/z* 166 $[M-CH_2CH_2]$ also suggested the presence of *N*-acetyltetrahydropyridine [3]. In the ^{13}C NMR spectrum of **1** (Table 1), the signals corresponding to C-2 to C-8 coincided with those of **2**, suggesting the presence of an *N*-acetyltetrahydropyridine ring in **1** as well as in **2**. The signals of C-2′, C-3′, C-4′, and C-5′ corresponded to C-2′, C-3′, C-4′ or C-5′, and C-6′ of **2**, respectively. The differences in the chemical shifts of these carbons between **1** and **2** showed good coincidence with those of nornicotine and anabasine, which also have pyrrolidine and piperidine rings, respectively [4]. The ^{1}H NMR spectrum of **1** was similar to that of **2**, except for the signals of H-2′ and H-5′ which were shifted downfield by 0.01 to 0.45 ppm because of the presence of the five-membered ring [5]. Thus, the structure of **1** was proved as 1-acetyl-1,2,3,4-tetrahydro-5-(2′-pyrrolidinyl)pyridine.

Compound **1** had been already prepared and recorded as norammodendrine by Fitch and Djerassi [3] by mass spectrometry. However, as far as we know, this is the first isolation of **1** from natural sources. Thus, we propose to rename **1** as maackiamine.



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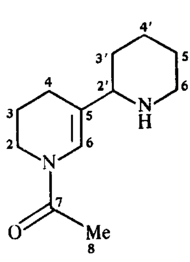

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*Part 3 in the series 'Studies on Plant Constituents of Genus *Maackia*'. For Part 2 see ref. [2].

Table 1. ^{13}C NMR spectral data of compounds **1** and **2** ($CDCl_3$, TMS as int. stand.)

C	**1**	C	**2**	Δ(**1**–**2**)
2	40.4 (*t*)	2	40.4 (*t*)	0
	(44.5)*		(44.5)	0
3	21.5 (*t*)	3	21.5 (*t*)	0
4	25.4 (*t*)	4	25.9 (*t*)	−0.5
5	122.1 (*s*)	5	123.7 (*s*)	−1.6
	(122.8)		(124.0)	−1.2
6	121.1 (*d*)	6	121.4 (*d*)	−0.3
	(119.4)		(120.4)	−1.0
7	168.0 (*s*)	7	168.1 (*s*)	−0.1
	—†		(167.7)	
8	21.5 (*q*)	8	21.5 (*q*)	0
	(21.9)		(22.0)	−0.1
2′	62.3 (*d*)	2′	61.7 (*d*)	+0.6
	(62.5)		(61.8)	+0.7
3′	30.4 (*t*)	3′	31.8 (*t*)	−1.4
		4′	22.8 (*t*)	
4′	22.6 (*t*)	5′	25.1 (*t*)	
5′	46.7 (*t*)	6′	47.5 (*t*)	−0.8

*Two peaks were observed because of the configuration of the *N*-acetyl group. Data in parentheses are the smaller peaks.

†The peak was in the noise range.

It is interesting that *M. amurensis* accumulates two alkaloids containing a pyrrolidine ring. These compounds, maackiamine (**1**) and cammoensidine, which was also isolated by Kinghorn *et al.* from *M. amurensis* [6], were found together with the corresponding piperidine alkaloids, ammodendrine (**2**) and lupanine. It can be speculated that *M. amurensis* has the biosynthetic ability to utilize ornithine instead of lysine as the precursor amino acid for the alkaloids or has the enzymatic activity to transform the piperidine moiety to the corresponding pyrrolidine group.

EXPERIMENTAL

Isolation of **1**. The basic fraction (4g) was prepared from the fresh flowers (0.9 kg) of *M. amurensis* var. *buergeri* harvested in August in Chiba by the methods of ref. [1]. This fraction was subjected to silica gel chromatography (Merck, type 60, 70–230 mesh, 250 g, 3.8 × 44 cm) using gradient elution with 1% MeOH in CH_2Cl_2–28% NH_4OH (500:1) to 10% MeOH in CH_2Cl_2–28% NH_4OH (500:1). The fraction containing **1** and **2** eluted with 5% MeOH in CH_2Cl_2–28% NH_4OH (500:1) was further separated on a silica gel column (Merck, type 60, 230–400 mesh, 12 g, 1.5 × 12 cm) with Et_2O–MeOH–28% NH_4OH (36:3:1). The **1**-rich fractions were purified by prep. TLC (Whatman, PKSF silica gel, 1 mm) using the solvent system cyclohexane–Et_2NH (7:3) to give 13 mg of **1**. The other ten compounds were also isolated by repeated silica gel chromatography using three solvent systems: 1–10% MeOH in CH_2Cl_2–28% NH_4OH (500:1), Et_2O–MeOH–28% NH_4OH (16:3:1), cyclohexane–Et_2NH (9:1).

Maackiamine (**1**). Colourless oil, **1**$[\alpha]_D^{22}$ + 110° (EtOH; *c* 0.01); UV λ_{max}^{MeOH} nm (log ε): 244 (4.22); EIMS (probe, 70 eV) *m/z* (rel. int.): 194.1240 $[M]^+$ (82) ($C_{12}H_{18}N_2O$, calc. 194.1419), 177 $[M-OH]^+$ (12), 166 $[M-CH_2CH_2]^+$ (25), 151 $[M-Ac]^+$ (100), 123 (69); IR $\nu_{max}^{CHCl_3}$: 2930, 2870 (C-H), 1640 (C=O), 1410 (C-N); ^{13}C NMR: see Table 1; ^1H NMR (270 MHz, $CDCl_3$): δ7.22 and 6.63 (1H, *s*, H-6), 3.58 (3H, *m*, H-2 and H-5′ (eq)), 3.06 (1H, *m*, H-2′), 2.92 (1H, *m*, H-5′ (ax)), 2.17 and 2.14 (3H, *s*, -Ac).

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