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MELOMORSINE, A NEW DIMERIC INDOLINE ALKALOID FROM *MELODINUS MORSEI*

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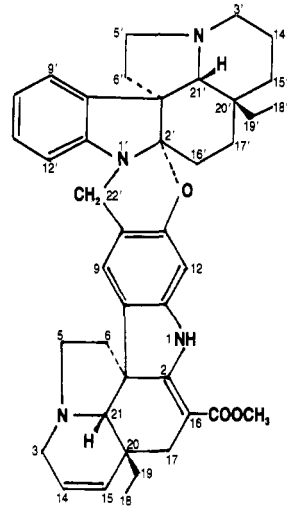
ABSTRACT.—A new dimeric indoline alkaloid, melomorsine [**1**], and six known alkaloids, 1,2-dehydroaspidospermidine, rhazidine, 11-hydroxytabersonine, aspidospermidine, geissoschizol, and vincoline have been isolated from the aerial parts of *Melodinus morsei*. The structure of **1** was established on the basis of spectral analysis.

Plants of the genus *Melodinus* are common in southwestern China. Some species, such as *M. suaveolens* and *M. henyri*, have been used in Chinese folk medicine for the treatment of meningitis in children and rheumatic heart diseases (1). They also have been reported to improve the circulation of blood (2). Many alkaloids have been isolated from a related species of this plant (3,4), but there has been no previous work on the chemical constituents of *M. morsei*. Recently, we have reported the isolation and structural determination of 15α-hydroxy-14,15-dihydrovindolinine and its 16-isomer, 15α-hydroxy-14,15-dihydro-16-*epi*-vindolinine from an EtOH extract of *M. morsei* (5). In a continuation of our research on the constituents of *M. morsei*, we have isolated a new dimeric indoline alkaloid along with six known compounds.

The new compound, melomorsine [**1**], was obtained as reddish crystals from aerial parts of *M. morsei*. The hrms contained a molecular ion at *m/z* 644.3750, indicating a molecular formula of $C_{41}H_{48}N_4O_3$ (calcd 644.3726). Its uv absorption characteristics, λ max 206 (4.6), 253 (4.3), 315 (4.2), and 327 (4.1) nm, were interpreted to be a composite of chromophores of aspidospermidine (6) and tabersonine (7). The ir spectrum revealed the presence of an NH group (3390 cm^{-1}) and a vinylogous amide unit reminiscent of tabersonine (1680 cm^{-1}). The mass spectrum showed a molecular peak at *m/z* 644 (13), a base peak at *m/z* 280, and also showed that [**1**] possessed fragments consistent with aspidospermidine (6) and tabersonine (7) shifted by 30 mass units. Thus, it was deduced that **1** could consist of aspidospermidine and tabersonine moieties. This conclusion was further supported by the ^1H-^{13}C-nmr and ^{13}C-^1H COSY nmr spectra of **1**.

In the aromatic region of the ^1H-nmr spectrum of **1**, two singlets were found at δ 6.42 and 6.93, in addition to two doublets at δ 6.41 (d, J=7.2 Hz) and 7.10 (d, J=7.2 Hz), and two triplets at δ



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6.70 (t, J=7.2 Hz) and 7.09 (t, J=7.2 Hz) (see Table 1). According to the multiplicity and coupling constants, it was deduced that, in one aromatic ring, two of the aromatic protons (δ 6.42 and 6.93) must be in the para- position, and that the other aromatic ring must be unsubstituted. Furthermore, the ^{1}H-nmr spectrum also indicated the presence of two methylene protons at δ 4.12 (1H, d, J=14.7 Hz) and 4.40 (1H, d, J=14.7 Hz). From the chemical shifts and coupling constants of the two methylene protons, it was also deduced that the methylene unit might link to the aromatic carbon and the indoline nitrogen. The DEPT spectrum of **1** exhibited 14 nonprotonated carbons, 10 methines, 14 methylenes, and 3 methyl groups, suggesting that one of the indoline nitrogens was substituted. Based on the above evidence and by comparing the ^{1}H-nmr spectra of **1** with those of aspidospermidine and tabersonine, it was concluded that **1** was a dimeric indoline alkaloid containing a methylene and an oxygen bridge, and that the centers of attachment were N(a) and C-2′ of the aspidospermidine moiety and two aromatic carbons (C-10, C-11) of the tabersonine moiety.

Comparison of the ^{13}C-nmr data of **[1]**, aspidospermidine and 11-hydroxytabersonine (see Table 2) showed that all carbons of the monomeric units were represented in the spectrum of the dimer, and the aromatic carbon (C-10, C-11) shifts and multiplicity of the tabersonine moiety and the C-2 shift and multiplicity of the aspidospermidine moiety were modified. The last observation indicates that N(a) and C-2 of the aspidospermidine

TABLE 1. 500 MHz ^{1}H-Nmr and 125 MHz ^{13}C-nmr Data of Melomorsine [**1**] (in $CDCl_3$, TMS as Internal Standard).

Position	^{13}C nmr	^{1}H nmr	Position	^{13}C nmr	^{1}H nmr
2	166.79		2′	96.96	
3	50.36	α-H 3.19 m β-H 3.45 m	3′	53.27	α-H 3.04 m β-H 3.14 m
5	51.08	α-H 2.70 m β-H 3.04 m	5′	53.32	α-H 2.05 m β-H 2.35 m
6	44.67	α-H 2.07 m β-H 1.80 m	6′	31.08	α-H 2.97 m β-H 1.16 m
7	54.84		7′	56.23	
8	130.90		8′	136.29	
9	119.56	6.93 s	9′	122.94	7.10 d (7.2 Hz)
10	110.45		10′	116.55	6.79 dd (7.2 Hz)
11	153.02		11′	127.57	7.09 dd (7.2 Hz)
12	99.89	6.42 s	12′	106.02	6.41 d (7.2 Hz)
13	143.09		13′	146.77	
14	124.71	5.79 ddd	14′	22.03	α-H 1.80 m β-H 1.60 m
15	133.17	5.72 dd	15′	35.18	α-H 1.60 m β-H 1.16 m
16	92.00		16′	24.38	α-H 1.60 m β-H 2.10 m
17	28.89	α-H 2.55 dd β-H 2.40 dd	17′	23.45	α-H 2.08 m β-H 1.76 m
18	7.14	0.62 t (7.4 Hz)	18′	7.52	0.68 t (7.4 Hz)
19	27.34	0.90 dq, 1.05 dq	19′	31.45	0.90 q, 1.30 d q
20	41.49		20′	35.22	
21	70.12	2.63 d (2Hz)	21′	73.37	2.12 b s
C=O	168.97		22′	40.56	4.40 d (14.7 Hz) 4.12 d (14.7 Hz)
OCH_3	50.78	3.76 s			

TABLE 2. ^{13}C-Nmr Spectral Data Comparison of Melomorsine [**1**], 11-Hydroxytabersonine, and Aspidospermidine.

Carbon No.	Chemical shifts (DEPT)[a]		Carbon No.	Chemical shifts (DEPT)[a]	
	1	Tabersonine		**1**	Aspidospermidine
2	166.79 (C)	166.7 (C)	2′	96.96 (C)	65.4 (CH)
3	50.36 (CH_2)	50.3 (CH_2)	3′	53.27 (CH_2)	53.7 (CH_2)
5	51.08 (CH_2)	50.8 (CH_2)	5′	53.32 (CH_2)	52.9 (CH_2)
6	44.67 (CH_2)	44.3 (CH_2)	6′	31.08 (CH_2)	38.7 (CH_2)
7	54.83 (C)	55.0 (C)	7′	56.23 (C)	52.9 (C)
8	130.90 (C)	130.4 (C)	8′	136.29 (C)	135.6 (C)
9	119.56 (CH)	122.0 (CH)	9′	122.94 (CH)	122.7 (CH)
10	110.45 (C)	105.0 (CH)	10′	116.55 (CH)	118.8 (CH)
11	153.02 (C)	159.9 (C)	11′	127.57 (CH)	127.0 (CH)
12	99.89 (CH)	96.9 (CH)	12′	106.02 (CH)	110.1 (CH)
13	143.09 (C)	144.0 (C)	13′	146.77 (C)	149.3 (C)
14	124.71 (CH)	124.8 (CH)	14′	22.03 (CH_2)	21.6 (CH_2)
15	133.17 (CH)	132.9 (CH)	15′	35.18 (CH_2)	34.3 (CH_2)
16	92.00 (C)	92.2 (C)	16′	24.38 (CH_2)	23.0 (CH_2)
17	28.89 (CH_2)	26.7 (CH_2)	17′	23.45 (CH_2)	28.1 (CH_2)
18	7.14 (CH_3)	7.3 (CH_3)	18′	7.16 (CH_3)	6.6 (CH_3)
19	27.34 (CH_2)	28.4 (CH_2)	19′	31.45 (CH_2)	29.8 (CH_2)
20	41.19 (C)	41.2 (C)	20′	35.22 (C)	35.5 (C)
21	70.12 (C)	69.9 (C)	21′	73.37 (C)	71.1 (C)
C=O	168.97 (C)	168.8 (C)	22″	40.56 (CH_2)	
OCH	50.78 (CH_3)	50.8 (CH_3)			

[a]Chemical shifts are in δ values (ppm) from TMS in $CDCl_3$.

unit are attached to the C-10 and C-11 of the tabersonine unit by a methylene unit and by oxygen. Thus, the structure of **1** was tentatively assigned as shown in Figure 1.

The relative configuration of **1** was further confirmed by nOe experiments. Irradiation of Hα-22′ (4.40 ppm) caused enhancements of the H-12′ (6.41 ppm) and the H-9 (6.93 ppm) signals. Irradiation of Hα-16′ (2.10 ppm) caused an enhancement of the Hβ-22′ (4.12 ppm) signal. These results indicate that the C-22′ methylene must link N(a) of the aspidospermidine unit and C-11 of the tabersonine unit.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mps were determined on a Boetius apparatus and are uncorrected. Optical rotations were determined on a Perkin-Elmer 241 polarimeter. Ir spectra were recorded in a KBr pellet on a Perkin-Elmer Model 683 spectrometer. Uv spectra were taken in EtOH on a Shimadzu Model 240 spectrophotometer. Nmr spectra were recorded on an AM-500 spectrometer with $CDCl_3$ as solvent and TMS as internal standard. Eims (70 eV) were recorded on a ZAB-2F mass spectrometer, and hreims were recorded with a MAT-711 mass spectrometer.

PLANT MATERIAL.—The aerial parts of *M. morsei* Tsiang were collected in southern Guangxi Province, People's Republic of China, in August 1989. The botanical identification of this plant was made by Professor Yu-Heng Chen, Department of Medicinal Plants, Institute of Materia Medica, Chinese Academy of Medical Sciences. A voucher specimen is deposited in the Herbarium of Guangxi Institute of Botany, Guilin, People's Republic of China.

EXTRACTION AND ISOLATION.—The air-dried plant material of *M. morsei* (20 kg) was extracted with 95% EtOH 3 times. The EtOH solution was combined and concentrated under reduced pressure to yield a gum, which was dissolved in 1% HCl and filtered. The filtrate was passed through a cation-exchange resin column. The exchanged air-dried cation-exchange resin was then treated with 10% NH_4OH and refluxed with Et_2O for 20 h. The combined Et_2O extracts were evaporated at reduced pressure to give 80 g (0.4%) of crude alkaloids. Dry-column chromatography on Si gel

(80–120 mesh, 2.5 kg), eluting with $CHCl_3$-MeOH (9:1) separated the crude alkaloids (70 g) into 5 fractions (A–E). Repeated cc on Si gel eluting with a $CHCl_3$/MeOH gradient as solvent and followed by prep. tlc of each fraction, respectively, afforded seven compounds: melomorsine [**1**] (20 mg), 1,2-dehydroaspidospermidine (20 mg) rhazidine (27 mg), 11-hydroxytabersonine (34 mg), aspidospermidine (21 mg), geissoschizol (22 mg), and vincoline (23 mg). The known alkaloids were identified by comparison of their physical and spectroscopic properties with literature data.

Melomorsine [**1**].—mp 70–71°, $[\alpha]^{20}D$ −197.64° (*c*=0.635, $CHCl_3$), uv λ max (EtOH) (log ε) 206 (4.6), 253 (4.3), 315 (4.2), 327 (4.2) nm; ir ν max (KBr) 3390 (NH), 1680, 1610, 1475, 1460, 1380, 1335, 1260, 1105, 750 cm^{-1}; eims *m/z* 644 [M^+] (13), 365 (22), 364 (8), 294 (3), 282 (23), 280 (100), 265 (8), 251 (45), 222 (10), 210 (80), 194 (24), 182 (14), 168 (11), 156 (12), 144 (6), 143 (7), 135 (50), 124 (88), 122 (27), 121 (20), 107 (31); hrms *m/z* 644.3750 (calcd for $C_{41}H_{48}N_4O_3$, 644.3726); ^1H nmr and ^{13}C nmr see Tables 1 and 2.

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