Northalifoline, a New Isoquinolone Alkaloid from the Pedicels of Lindera megaphylla

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NORTHALIFOLINE, A NEW ISOQUINOLONE ALKALOID FROM THE PEDICELS OF *LINDERA MEGAPHYLLA*

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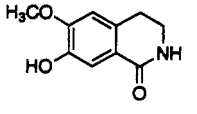
ABSTRACT.—A new isoquinolone alkaloid, northalifoline [**1**] was obtained from the pedicels of *Lindera megaphylla* along with six other alkaloids, namely, (+)-*O*-methylbulbocapnine [**2**], (+)-dicentrine [**3**], dicentrinone [**4**], (+)-*N*-methylnandigerine [**5**], (+)-*N*-methylhernovine [**6**], and (+)-reticuline [**7**]. Characterization of northalifoline [**1**] by physical methods and synthesis revealed its identity as 6-methoxy-7-hydroxy-1-oxo-1,2,3,4-tetrahydroisoquinoline.

Lindera megaphylla Hemsl. is a small deciduous tree of the Lauraceae family (1). The trunk and leaves of this plant are rich in alkaloids including members of the aporphine, oxoaporphine, benzyltetrahydroisoquinoline, and bisbenzylisoquinoline classes (2–4). The present work describes our study of the pedicel constituents of *L. megaphylla*. The EtOH extract of the pedicels was partitioned successively with Et_2O, *n*-BuOH, and H_2O. Chromatography of the *n*-BuOH portion gave seven alkaloids, including the novel alkaloid northalifoline [**1**], and six other alkaloids: (+)-*O*-methylbulbocapnine [**2**], (+)-



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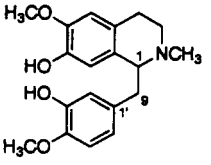

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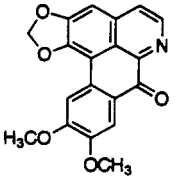

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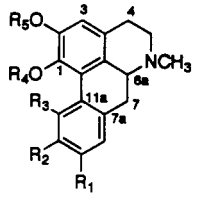


2 R_1=H, R_2=R_3=OCH_3, R_4=R_5=CH_2

3 R_1=R_2=OCH_3, R_3=H, R_4=R_5=CH_2

5 R_1=H, R_2=OH, R_3=OCH_3, R_4=R_5=CH_2

6 R_1=H, R_2=OH, R_3=OCH_3, R_4=CH_3, R_5=H

dicentrine [**3**], dicentrinone [**4**], (+)-*N*-methylnandigerine [**5**], (+)-*N*-methylhernovine [**6**], and (+)-reticuline [**7**].

RESULTS AND DISCUSSION

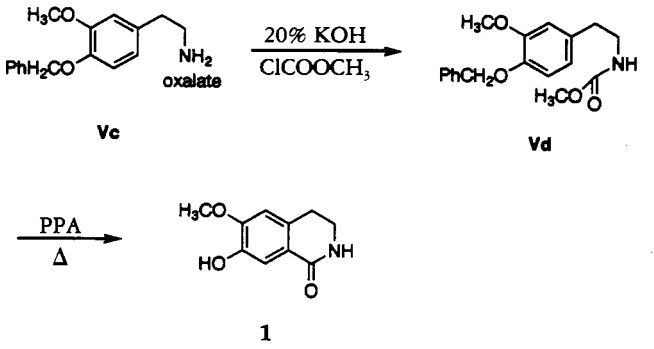
Northalifoline [**1**] crystallized as colorless rods from MeOH/Me_2CO, mp 222–224°. The ir spectrum of **1** showed a broad band centered at 3200 cm^{-1} (OH stretching), a strong and sharp band at 1640 cm^{-1} (-CO-, δ lactam), and characteristic absorptions for an aromatic ring. The mass spectrum of **1** showed a molecular ion peak at *m/z* 193 (measured *m/z* 193.0737 and calculated *m/z* 193.0735 for $C_{10}H_{11}NO_3$), an intense peak at *m/z* 164 (76%) indicating the loss of a CH_2=NH unit from the molecular ion, and a base peak at *m/z* 136 consistent with the further loss of a CO group. Analysis of the ^{1}H-nmr spectrum of **1** revealed a methoxy group resonating at δ 3.80, a hydroxyl group at δ 8.98, and two aromatic protons para to one another at δ 6.80 and 7.25, respectively. The coupling pattern of the remaining three sets of signals was analyzed and assigned. The N-H proton occurred at δ 7.52, and two methylene groups coupled to each other were at δ 3.30 and 2.76, respectively. These assignments were further confirmed by a ^{1}H-^{1}H COSY nmr experiment. Both ^{1}H- and ^{13}C-nmr assignments of **1** are depicted in Table 1. Furthermore, from an nOe experiment, a 6% enhancement of the signal intensity at δ 6.80 was observed when the signal at δ 3.80 was irradiated. This indicates that the methoxyl group is ortho to the aromatic proton H-5. Thus, the structure of **1** was elucidated as 6-methoxy-7-hydroxy-1-oxo-1,2,3,4-tetrahydroisoquinoline.

A synthetic approach toward **1** (Scheme 1) has been accomplished. The synthesis started with the conversion of vanillin to 3-methoxy-4-benzyloxy-β-phenethylamine (**Vc**) oxalate via *O*-benzylvanillin (**Va**) (5) (yield 84.5%) and 3-methoxy-4-benzyloxy-β-nitrostyrene (**Vb**) (6) (yield 60.3%) intermediates by known methods. Reduction of β-nitrostyrene (**Vb**) with LAH in THF was carried out according to a known procedure (7) to afford 3-methoxy-4-benzyloxy-β-phenethylamine which was then converted to

TABLE 1. ^{1}H- and ^{13}C-Nmr Chemical Shift Assignments of Compounds **1** and **7**.

Position	Compound					
	1 (DMSO-d_6)			**7** (CD_3OD)		
	δ ^{13}C	δ ^{1}H	COLOC (^2J and ^3J)	δ ^{13}C	δ ^{1}H	COLOC (^2J and ^3J)
1	164.63 (s)		H-8	65.72 (d)	3.63	H_3-NCH_3, Hb-3, H-8
3	39.50 (t)	3.30		47.51 (t)	2.67~2.52a, 3.10~3.02b	H_3-NCH_3
4	27.27 (t)	2.76	H-5	25.93 (t)	2.67~2.52a, 2.80~2.7b	H-5
4a	131.01 (s)		H-8	125.31 (s)		Ha-3, H-8
5	110.46 (d)	6.80		112.49 (d)	6.56	Ha-4
6	150.51 (s)		OCH_3-6, H-8, OH-7	147.71 (s)		OCH_3-6, H-8
7	144.96 (s)		H-5	145.01 (s)		H-8, H-5
8	113.71 (d)	7.25	OH-7	115.62 (d)	6.14	
8a	121.80 (s)		H-5, H-NH	130.59 (s)		Hb-9, H-1, H-5
9				40.97 (t)	2.67~2.52a, 2.97b	H-2′
1′				133.75 (s)		Hb-9, H-5′
2′				117.55 (d)	6.60	Hb-9
3′				147.23 (s)		H-5′
4′				147.36 (s)		OCH_3-4′, H-2′
5′				112.61 (d)	6.72	H-6′
6′				121.78 (d)	6.47	Hb-9, H-2′
OCH_3 (6)	55.55 (q)	3.80		56.36 (q)	3.73	
OCH_3 (4′)				56.25 (q)	3.75	
NCH_3				42.53 (q)	2.38	
NH		7.52				
OH		8.98				

[a]Assignments were based on ^{13}C-DEPT, ^{13}C-^{1}H COSY, ^{1}H-^{1}H COSY, and COLOC spectra.



SCHEME 1

oxalate salt (**Vc**) in 41.3% isolated yield. The preparation of 3-methoxy-4-benzyloxy-β-phenethylmethylcarbamate (**Vd**) in 88.4% yield and cyclization of **Vd** to the desired product [**1**] (6.6%) with PPA was carried out by the method of Brossi *et al.* (8). The spectral data (ir, ^{1}H-nmr, and eims) of synthetic **1** were indistinguishable from those of the natural product **1**.

^{13}C-Nmr data of **3** have been reported in the literature (9), but they are both not fully assigned and have partial ambiguities. Through our integrated ^{1}H-, ^{13}C-, DEPT, heteronuclear COSY, and COLOC nmr experiments, the assignment of all carbon signals of **3** was carried out (Table 2). The analysis of the ^{1}H-nmr spectra of compounds **2**, **5**, **6**, and **7** did not allow a straightforward assignment of all signals due to overlapping. As to the ^{13}C-nmr spectra, most resonances of the protonated carbons could

TABLE 2. ^{1}H- and ^{13}C-Nmr Chemical Shift Assignments[a] of Compounds **2** and **3**.

Position	Compound					
	2 ($CDCl_3$)			**3** (DMSO-d_6)		
	δ ^{13}C	δ ^{1}H	COLOC (^2J and ^3J)	δ ^{13}C	δ ^{1}H	COLOC (^2J and ^3J)
1	143.06 (s)		Ha, Hb-1-OCH_2O-2, H-3	141.25 (s)		Ha, Hb-1-OCH_2O-2, H-3
2	146.76 (s)		Ha, Hb-1-OCH_2O-2, H-3	146.12 (s)		Ha, Hb-1-OCH_2O-2, H-3
3	107.25 (d)	6.58	Ha-4	106.52 (d)	6.57	Ha-4
3a	125.68 (s)		Ha-4, Hb-5	126.64 (s)		Ha-4
4	29.16 (t)	3.11a, 2.61b	Hb-5, H-3	28.72 (t)	2.53a, 2.97～2.86b	H-3
5	53.01 (t)	2.48a, 3.00b	H_3-NCH_3	52.92 (t)	2.33a, 2.97～2.86b	H_3-NCH_3
6a	62.92 (d)	2.93	Ha, Hb-7, H_3-NCH_3, Hb-5	61.94 (d)	2.97～2.86	H_3-NCH_3, Hb-7
7	35.32 (t)	2.39a, 3.03b	H-8	33.73 (t)	2.38a, 3.14b	H-8
7a	130.20 (s)		H-9	128.43 (s)		Ha, Hb-7, H-11
8	122.21 (d)	6.94	Ha, Hb-7	112.03 (d)	6.96	Ha, Hb-7
9	111.50 (d)	6.82		148.26 (s)		OCH_3-9, H-11
10	152.03 (s)		OCH_3-10, H-8	147.26 (s)		OCH_3-10, H-8
11	146.76 (s)		OCH_3-11, H-9	110.68 (d)	7.58	
11a	124.11 (s)		Ha, Hb-7, H-8	122.68 (s)		Ha, Hb-7, H-8
11b	113.85 (s)			115.86 (s)		H-11
11c	128.70 (s)		Ha, Hb-7, Ha-4, H-3	126.33 (s)		Ha, Hb-7, H-3
OCH_3 (1)						
OCH_3 (9)				55.42 (q)	3.79	
OCH_3 (10)	55.91 (q)	3.84		55.70 (q)	3.75	
NCH_3 (11)	60.78 (q)	3.73				
1-OCH_2O-2	100.43 (t)	6.02a, 5.85b		100.52 (t)	6.10a, 5.96b	
N-CH_3	44.03 (q)	2.50		53.57 (q)	2.41	

[a]Assignments were based on ^{13}C-DEPT, ^{13}C-^{1}H COSY, ^{1}H-^{1}H COSY, and COLOC spectra.

TABLE 3. ^{1}H- and ^{13}C-Nmr Chemical Shift Assignments[a] of Compounds **5** and **6**.

Position	Compound					
	5 (CD_3OD)			**6** (CD_3OD)		
	δ ^{13}C	δ ^{1}H	COLOC (^2J and ^3J)	δ ^{13}C	δ ^{1}H	COLOC (^2J and ^3J)
1	144.28 (s)		Ha, Hb-1-OCH_2O-2, H-3	145.51 (s)		OCH_3-1, H-3
2	148.48 (s)		Ha, Hb-1-OCH_2O-2, H-3	150.10 (s)		H-3
3	108.12 (d)	6.55	Ha-4	115.68 (d)	6.64	Ha-4
3a	126.85 (s)		Ha-4, Hb-5	128.84 (s)		Ha-4, H-6a
4	29.54 (t)	2.58a, 3.08～2.91b	H-3	29.01 (t)	2.63a, 3.07～2.99b	H-3
5	53.94 (t)	2.41a, 3.08～2.91b	H_3-NCH_3	53.96 (t)	2.49a, 3.07～2.99b	H_3-NCH_3
6a	64.38 (d)	2.88	Ha-5, H_3-NCH_3	64.61 (d)	2.84	H_3-NCH_3
7	35.77 (t)	2.30a, 3.08～2.91b	H-8	36.09 (t)	2.30a, 3.07～2.99	H-8
7a	129.61 (s)		H-9	125.95 (s)		H-6a, H-9
8	123.87 (d)	6.82	Ha, Hb-7	123.52 (d)	6.87	Ha, Hb-7
9	116.50 (d)	6.75		115.99 (d)	6.76	
10	150.53 (s)		H-8	150.19 (s)		H-8
11	146.59 (s)		OCH_3-11, H-9	147.03 (s)		OCH_3-11, H-9
11a	124.62 (s)		Hb-7, H-8	125.59 (s)		Ha, Hb-7, H-8
11b	115.26 (s)			125.59 (s)		H-6a
11c	129.16 (s)		Ha-7, Ha-4, H-3	128.39 (s)		Ha-7, Ha-4, H-3
OCH_3 (1)				60.82 (q)	3.43	
OCH_3 (9)						
NCH_3 (10)						
OCH_3 (11)	60.69 (q)	3.60		60.72 (q)	3.47	
1-OCH_2O-2	101.69 (t)	5.94a, 5.77b				
N-CH_3	43.98 (q)	2.45	Ha-5, H-6a	43.97 (q)	2.49	

[a]Assignments were based on ^{13}C-DEPT, ^{13}C-^{1}H COSY, ^{1}H-^{1}H COSY, and COLOC spectra.

be assigned by means of DEPT and 2D-C,H correlation techniques. The assignments of the quaternary carbons were obtained by COLOC (^2J and ^3J) nmr experiments. The ^{13}C-nmr data of these compounds (**2**, **5**, **6**, and **7**) are shown in Tables 1, 2, and 3, respectively.

Isoquinolone alkaloids have been found in species of the Ranunculaceae, Menispermaceae, Berberidaceae, Papaveraceae, Hernandiaceae, Lauraceae, and Monimiaceae (10). Five other substances closely related to **1** reported before are corydaline, *N*-methylcorydaline, noroxyhydrastinine, oxyhydrastinine, and thalifoline (11). Compound **1** may originate in nature from the oxidation of the bisbenzyltetrahydroisoquinoline alkaloid, lindoldhamine, which is known to occur in the same plant (3). This is in accordance with the hypothesis of Krane and Shamma (10). One of the isolated alkaloids, (+)-dicentrine [**3**], has been reported to possess antiplatelet aggregation, vasorelaxant, and antiarrhythmic activities (12). Compound **1** is an isoquinolone derivative and represents a new addition to the structural classes of alkaloids obtained from plants in the genus *Lindera*.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mps were determined with a Yanagimoto micro melting point apparatus and are uncorrected. Optical rotations were measured using a Jasco DIP-370 polarimeter in $CHCl_3$. Ir spectra were taken on a Perkin-Elmer 781 ir spectrometer. The uv spectrum was obtained on a Hitachi U-3200 spectrophotometer in MeOH. Eims spectra were recorded on a JEOL JMS-SX 102A spectrometer. The hreims spectrum was recorded on a JEOL JMX-HX 110 spectrometer. ^{1}H-, ^{13}C-, and 2D nmr measurements were recorded on a Bruker ACP-300 spectrometer with deuterated solvents as internal standard.

PLANT MATERIAL.—The pedicels of *Lindera megaphylla* were collected at Shin-Dian, Taipei Hsien,

Taiwan, in July 1991. A voucher specimen has been deposited in the herbarium of the Department of Botany, National Taiwan University.

EXTRACTION AND ISOLATION.—The dried pedicels (4 kg) were extracted with 95% EtOH (20 liters×3) and the EtOH extract was evaporated under reduced pressure. The residue obtained was diluted with H_2O (2 liters) and then partitioned successively with Et_2O (1 liter×3) and *n*-BuOH (1 liter×4). The *n*-BuOH extract (290 g) was subjected to cc on Celite (500 g) and eluted successively with C_6H_6 (3 liters), $CHCl_3$ (3 liters), and 50% MeOH/$CHCl_3$ (4 liters) to give three extracts. The C_6H_6 part was combined with the Et_2O extract. The $CHCl_3$ extract (90 g) was further subjected to cc on Si gel (500 g) with a gradient of MeOH in $CHCl_3$ and six fractions (1–6) were collected. Compounds **1** (42 mg) and **4** (120 mg) were isolated from fractions 3 and 4, respectively. The precipitate obtained from fraction 2 was recrystallized from Me_2CO to give compound **3** (810 mg). Fraction 1 and the filtrate of fraction 2 were combined and concentrated, and the residue (20 g) was then rechromatographed on Si gel (600 g) and eluted with C_6H_6-Me_2CO-$CHCl_3$ (4:1:0.5) to give compounds **2** (310 mg) and **3** (4 g). Sequential chromatography of the 50% MeOH/$CHCl_3$ extract on Si gel (EtOAc/MeOH gradient) and Sephadex LH-20 (MeOH) afforded compounds **5–7**.

Northalifoline (6-methoxy-7-hydroxy-1-oxo-1,2,3,4-tetrahydroisoquinoline) [**1**].—Colorless rod crystals from MeOH/Me_2CO, mp 222–224°; ir ν max (KBr) 3200, 1640, 1580, 1510 cm^{-1}; uv λ max (log ϵ) 302 (3.84), 259 (3.95), 225 (4.27) nm; eims *m/z* [M^+] 193 (82), 164 (76), 136 (100), 121 (14), 93 (10); hreims *m/z* [M^+] 193.0737 ($C_{10}H_{11}NO_3$ requires 193.0735); ^1H nmr (DMSO-d_6) δ 2.76 (2H, t, J=6.6 Hz, H_2-4), 3.30 (2H, dt, J=2.8 and 6.6 Hz, H_2-3), 3.80 (3H, s, -OCH_3-6), 6.80 (1H, s, H-5), 7.25 (1H, s, H-8), 7.52 (1H, br s, NH-2), 8.98 (1H, br s, OH-7); ^{13}C nmr, see Table 1.

Synthesis of northalifoline [**1**].—3-Methoxy-4-benzyloxy-β-phenethylamine (**Vc**) oxalate (10 g) was dissolved in 16 ml of H_2O, and made alkaline (pH 10) with aqueous 20% KOH. Methylchloroformate (5.6 g) was added dropwise to the alkaline solution while stirring and the reaction mixture was maintained at pH 10 during the course of the reaction (8). The resulting mixture was extracted with $CHCl_3$, and the organic portion was washed with H_2O and evaporated under reduced pressure to afford a residue, which was subjected to chromatography on Si gel. Elution with 25% EtOAc in *n*-hexane gave **Vd** (Scheme 1, yield 88.4%) as needles, mp 77–77.5°; ir ν max (KBr) 3380, 3340, 1680 cm^{-1}; ^1H nmr ($CDCl_3$) δ 2.71 (2H, t, J=7.2 Hz, H_2-β), 3.38 (2H, m, H_2-α), 3.64 (3H, s, -$COOCH_3$), 3.85 (3H, s, -OCH_3), 4.70 (1H, br s, -$HNCOOCH_3$), 5.10 (2H, s, -OCH_2-Ph), 6.63 (1H, dd, J=1.9 and 8.0 Hz, H-6), 6.70 (1H, d, J=1.9 Hz, H-2), 6.79 (1H, d, J=8.0 Hz, H-5), 7.43–7.24 (5H, m, benzylic-H).

To a warmed (120°) quantity of polyphosphoric acid (4.5 g) was added 3-methoxy-4-benzyloxy-β-phenylethylmethylcarbonate (**Vd**) (500 mg) in one vessel. After addition, the reaction mixture was stirred at 120° for 40 min. The reaction mixture was then poured into ice H_2O, and made alkaline by adding $NaHCO_3$. The resulting solution was washed with EtOAc and then readjusted to weak acidity with NH_4Cl. The acidic solution was extracted with EtOAc again and the organic portion was concentrated *in vacuo*. Purification of the residue via chromatography on Si gel by eluting with 3% MeOH/$CHCl_3$ afforded product **1** (20.2 mg, yield 6.6%), mp 214–215°. The analytical data of synthetic **1**, indicated ir, ^1H-nmr, and eims spectra identical to that of natural **1**.

(+)-O-Methylbulbocapnine [**2**].—Colorless prism crystals from Me_2CO, mp 127–129° [lit. (2) 129–130°]; [α]D +225° (*c*=0.12); uv λ max 308, 267, 224 nm; eims *m/z* [M^+] 339 (100), 338 (44), 324 (68), 309 (32), 296 (20), 294 (30), 280 (13), 265 (11), 252 (10), 238 (11), 152 (11), 139 (4); ^1H nmr ($CDCl_3$) δ 2.39 (1H, Ha-7), 2.48 (1H, Ha-5), 2.50 (3H, s, N-CH_3), 2.61 (1H, Ha-4), 2.93 (1H, H-6a), 3.00 (1H, Hb-5), 3.03 (1H, Hb-7), 3.11 (1H, Hb-4), 3.73 (3H, s, -OCH_3-11), 3.84 (3H, s, -OCH_3-10), 5.85 (1H, d, J=1.4 Hz, Ha-methylenedioxy), 6.02 (1H, d, J=1.4 Hz, Hb-methylenedioxy), 6.58 (1H, s, H-3), 6.82 (1H, d, J=8.1 Hz, H-9), 6.94 (1H, d, J=8.1 Hz, H-10); ^{13}C nmr, see Table 2.

(+)-Dicentrine [**3**].—Colorless prisms from MeOH, mp 169–170° [lit (2) 168–169°] ; [α]D +69° (*c*=0.68); uv λ max 389, 305, 281 nm; eims *m/z* [M^+] 339 (75), 338 (100), 324 (13), 296 (31), 294 (7), 280 (10), 265 (31), 252 (5), 238 (14), 152 (16), 139 (4); ^1H nmr (DMSO-d_6) δ 2.33 (1H, Ha-5), 2.38 (1H, Ha-7), 2.41 (3H, s, N-CH_3), 2.53 (1H, Ha-4), 2.97–2.86 (3H, m, Hb-4, Hb-5, H-6a), 3.14 (1H, Hb-7), 3.75 (3H, s, OCH_3-10), 3.79 (3H, s, OCH_3-9), 5.96 (1H, d, J=1.2 Hz, Ha-methylenedioxy), 6.10 (1H, d, J=1.2 Hz, Hb-methylendioxy), 6.57 (1H, s, H-3), 6.96 (1H, s, H-8), 7.58 (1H, s, H-11); ^{13}C nmr see Table 2.

Dicentrinone [**4**].—Orange fine needle crystals from MeOH, mp >300° [lit. (2) 282–283°, dec]; uv λ max 389, 351, 271, 249, 211 nm; ir (KBr) ν max 1640 (conjugated C=0), 1054, 963 (methylenedioxy) cm^{-1}; eims *m/z* [M^+] 335 (100), 320 (19), 304 (15), 292 (13), 289 (9), 264 (11), 249 (10), 163 (8); ^1H nmr (TFA-d_1) δ 9.31 (1H, d, J=6.4 Hz), 9.16 (1H, d, J=6.4 Hz), 8.92 (1H, s), 8.62 (1H, s), 7.22 (2H, s), 4.72 (3H, s, -OCH_3), 4.76 (3H, s, -OCH_3).

(+)-N-Methylnandigerine [**5**].—Colorless prisms from Me_2CO: mp 175–176° [lit. (2) 169–170°]; [α]D +412° (*c*=0.78); uv λ max 309, 268, 222 nm; eims *m/z* [M^+] 325 (100), 324 (58), 295 (41), 294 (25),

280 (61), 252 (17) 181 (12), 152 (24), 139 (8); ^{1}H nmr (CD_3OD) δ 2.30 (1H, Ha-7), 2.41 (1H, Ha-5), 2.45 (3H, s, N-CH_3), 2.58 (1H, Ha-4), 2.88 (1H, H-6a), 3.08–2.91 (3H, Hb-4, Hb-5, Hb-7), 3.60 (3H, s, OCH_3-11), 5.77 (1H, d, J=1.1 Hz, Ha-methylenedioxy), 5.94 (1H, d, J=1.1 Hz, Hb-methylenedioxy), 6.55 (1H, H-3), 6.75 (1H, d, J=8.0 Hz, H-9), 6.82 (1H, d, J=8.0 Hz, H-8); ^{13}C nmr, see Table 3.

(+)-N-Methylhernovine [**6**].—A brownish yellow amorphous powder from Me_2CO: mp 161–162° [lit. (4) 162–163°]; [α]D +243° (*c*=0.23); uv λ max 389, 305, 272 nm; eims *m/z* [M^+] 327 (86), 326 (23), 312 (54), 296 (100), 281 (45), 252 (11), 224 (6), 181 (7), 152 (9), 147 (7); ^{1}H nmr (CD_3OD) δ 2.30 (1H, Ha-7), 2.49 (1H, Ha-5), 2.49 (3H, s, N-CH_3), 2.63 (1H, Ha-4), 2.84 (1H, H-6a), 3.07–2.99 (3H, Hb-4, Hb-5, Hb-7), 3.43 (3H, s, OCH_3-1), 3.47 (3H, s, OCH_3-11), 6.64 (1H, s, H-3), 6.76 (1H, d, J=8.0 Hz, H-9), 6.87 (1H, d, J=8.0 Hz, H-8); ^{13}C nmr, see Table 3.

(+)-Reticuline [**7**].—A brownish yellow oil; [α]D +43° (*c*=0.76); uv λ max 283 nm; eims *m/z* [M^+] 329 (1), 192 (47), 177 (26), 148 (100); ^{1}H nmr (CD_3OD) δ 2.38 (3H, s, N-CH_3) 2.67–2.52 (3H, Ha-3, Ha-4, Ha-9), 2.80–2.72 (1H, Hb-4), 2.97 (1H, Hb-9), 3.10–3.02 (1H, Hb-3), 3.63 (1H, H-1), 3.73 (3H, s, OCH_3-6), 3.75 (3H, s, OCH_3-4′), 6.14 (1H, s, H-8), 6.47 (1H, dd, J=1.4 and 8.1 Hz, H-6′), 6.56 (1H, s, H-5), 6.60 (1H, d, J=1.4 Hz, H-2′), 6.72 (1H, d, J=8.1 Hz, H-5′); ^{13}C nmr, see Table 1.

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LITERATURE CITED

1. C.E. Chang, in: "Flora of Taiwan." Ed. by H.L. Li, Epoch Publishing Co., Ltd., Taipei, Taiwan, 1976, Vol. II, pp. 430–431.
2. S.T. Lu, S.Y. Wang, P.H. Lai, C.M. Lin, and L.C. Lin, *Yakugaku Zasshi*, **92**, 910 (1972).
3. S.T. Lu and I.S. Chen, *Heterocycles*, **4**, 1073 (1976).
4. S.T. Lu and T.C. Wang, *J. Taiwan Pharm. Assoc.*, **37**, 131 (1985).
5. R. Dickinson, I.M. Heilbron, and F. Irving, *J. Chem. Soc.*, 1888 (1927).
6. C.B. Gairand and G.R. Lappin, *J. Org. Chem.*, **18**, 1 (1953).
7. J. Finkelstein, *J. Am. Chem. Soc.*, **73**, 550 (1951).
8. A. Brossi, F. Schenker, and W. Leimgruber, *Helv. Chim. Acta*, **47**, 2089 (1964).
9. T.A. Broadbent and E.G. Paul, *Heterocycles*, **20**, 863 (1983).
10. B.D. Krane and M. Shamma, *J. Nat. Prod.*, **45**, 377 (1982).
11. J. Lundstrom, in: "The Chemistry and Biology of Isoquinoline Alkaloids." Ed. by J.D. Phillipson, M.F. Roberts, and M.H. Zenk, Springer-Verlag, Berlin, 1985, pp. 47–61.
12. C.C. Chen, Y.L. Huang, J.C. Ou, M.L. Su, S.M. Yu, and C.M. Teng, *Planta Med.*, **57**, 406 (1991).

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