

2-*N*-Methylexcentricine, a New Alkaloid from Roots of *Stephania excentrica*

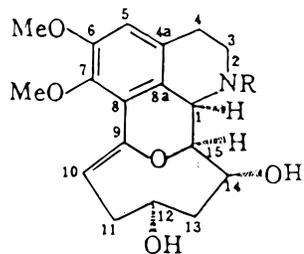
Jing-Zhen Deng* and Shou-Xun Zhao

Department of Phytochemistry, China Pharmaceutical University, Nanjing, Jiangsu 210009, People's Republic of China

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2-*N*-methylexcentricine (**2**), a new alkaloid related to excentricine, was isolated together with 10 other known alkaloids from the roots of *Stephania excentrica*. The structure of **2** was elucidated by spectroscopic analysis.

In the previous paper,¹ we reported that excentricine (**1**), a new alkaloid with a novel tetrahydroisoquinoline skeleton possessing an eight-membered oxygen-heterocyclic ring, was isolated from the roots of *Stephania excentrica* H. S. Lo (Menispermaceae), along with eight known alkaloids: roemerine, 4-demethylhasubanonine, oxoputerine, oxoanolobine, isoboldine, homoaromoline, (+)-coclaurine, and sinococuline. The structure of excentricine was established as **1**. Our continuous phytochemical investigation of the roots of *S. excentrica* afforded 2-*N*-methylexcentricine (**2**), a new alkaloid with the same skeleton as **1**, and a known alkaloid 2-*N*-methylcoclaurine. This paper deals with the isolation of excentricine (**1**), 2-*N*-methylexcentricine (**2**), and nine other known alkaloids, and with the structural elucidation of **2**.



- 1 R = H
2 R = Me

2-*N*-methylexcentricine (**2**) was obtained as needles from the alkaloidal fraction of the roots of *S. excentrica* by chromatography on Si gel. Its HRMS gave the molecular formula C₁₉H₂₅O₅N. The IR, ¹H- and ¹³C-NMR spectra were similar to those of excentricine (**1**), suggesting that **1** and **2** had the same skeleton. The ¹H-NMR spectrum of **2** showed an additional *N*-methyl group at δ 2.58 (3H, s) and an upfield proton at δ 4.08 (d, J = 6.0 Hz, H-1) as compared with **1** (Table 1). The ¹³C-DEPT spectrum of **2** displayed a methyl carbon at δ 36.83 (q) and a downfield carbon at δ 61.51 (d, C-1) in contrast to **1**. On the basis of this evidence, there is an *N*-methyl group in **2**, instead of the NH found in **1**. The CD spectrum of **2** resembled that of **1**, showing the same configuration as **1**. All of the other known alkaloids were identified by comparison of their mp, $[\alpha]_D$ (and CD), IR, UV, ¹H NMR, and ¹³C NMR with literature data.^{2–7}

Table 1. ¹H- (400 MHz) and ¹³C- (100 MHz) NMR Data (CDCl₃, δ) for **1** and **2**

position	1		2		
	δ_H (J, Hz)	δ_C	δ_H (J, Hz)	δ_C	
1	4.90 (d, J = 6.2)	54.99 d	4.08 (d, J = 6.0)	61.51 d	
3	3.75 (m)	44.64 t	3.84 (m)	46.71 t	
4	3.45 (ddd, J = 12.5, 12.5, 6.8)	26.21 t	3.47 (ddd, J = 11.8, 11.8, 6.0)	27.05 t	
	3.22 (ddd, J = 12.5, 12.5, 6.8)		3.21 (ddd, J = 11.8, 11.8, 6.0)		
	3.08 (ddd, J = 12.5, 6.8, 1.5)		3.11 (ddd, J = 11.8, 6.0, 2.1)		
4a		130.44 s		130.55 s	
5	6.86 (s)	114.07 d	6.84 (s)	115.01 d	
6		155.37 s		155.40 s	
7		145.66 s		146.05 s	
8		125.82 s		125.21 s	
8a		118.07 s		119.22 s	
9		147.72 s		147.83 s	
10	6.14 (t, J = 7.8)	116.75 d	6.16 (t, J = 7.9)	116.12 d	
11	2.82 (ddd, J = 11.4, 11.4, 7.8)	35.97 t	2.80 (ddd, J = 11.2, 11.2, 7.9)	35.04 t	
	2.16 (m)		2.18 (m)		
12	3.57 (m)	71.55 d	3.41 (m)	72.35 d	
13	2.21 (m, 2H)	52.13 t	2.34 (m, 2H)	51.41 t	
14	4.00 (br t, J = 9.6)	67.75 d	4.09 (br t, J = 9.2)	68.32 d	
15	4.13 (dd, J = 9.6, 6.2)	79.65 d	4.22 (dd, J = 9.2, 6.0)	80.56 d	
	MeO-6		3.85 (s)		57.26 q
	MeO-7	3.74 (s)	61.45 q	3.73 (s)	62.11 q
	2- <i>N</i> -CH ₃		2.58 (s)		36.83 q

Experimental Section

General Experimental Procedures. Melting points were determined on a Microscopic apparatus and are uncorrected. The optical rotation was measured on a JASCO DIP-181 autopolarimeter. The UV spectra were registered on a Shimadzu UV-300 spectrophotometer, and IR spectra, on a Shimadzu IR-400. ¹H- and ¹³C-NMR spectra were recorded on a JNM-GX 400 instrument. The CD spectra were obtained on a JASCO J-500A instrument, using MeOH as solvent.

Plant Material. The roots of *Stephania excentrica* H. S. Lo were collected in July 1989, from the southwest of Jiangxi Province, People's Republic of China. The plant was authenticated by Professor H-S. Lo, South China Institute of Botany, Academia Sinica, Guangzhou, where a voucher specimen is deposited.

Extraction and Isolation. The roots of *S. excentrica* were air-dried for 2 weeks and ground into a powder. The powder (8 kg) was extracted by percolation with EtOH at room temperature. The EtOH extract was evaporated under reduced pressure and the residue treated with 2.0% HCl. The mixture was filtered and the filtrate extracted with CHCl₃ to give part A. The filtrate was then basified with NH₄OH and extracted with CHCl₃ to yield Part B, and then with *n*-BuOH to

* To whom correspondence should be addressed: Department of Chemistry, University of Virginia, Charlottesville, VA 22901.

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afford part C. Part A (50 g) was subjected to chromatography on Si gel and eluted with petroleum–EtOAc (100:1–50:100) to provide roemerine (25 mg, 0.000 31%), 4-demethylhasubanonine (25 g, 0.31%), oxoputerine (8 mg, 0.0001%), oxoanolobine (15 mg, 0.000 19%), and isoboldine (12 mg, 0.000 15%). Part B (25 g) and part C (20 g) were separately placed on Si gel columns, and both were eluted with CHCl₃ gradually enriched with MeOH, and consequently, part B furnished homoaromoline (1.2 g, 0.015%), 2-*N*-methylexcentricine (**2**) (15 mg, 0.000 15%), and excentricine (**1**) (45 mg, 0.000 56%), while part C gave 2-*N*-methylcoclaurine (9 mg, 0.000 11%), (+)-coclaurine (38 mg, 0.000 48%), and sinococuline (125 mg, 0.0016%).

Excentricine (1): obtained as needles (45 mg) from Me₂CO–MeOH; mp 195–196 °C; [α]²²_D +261° (*c* 0.03, MeOH); UV (MeOH) λ_{max} (log ε) 228 (4.31), 263 (4.02), 302 (3.23) nm; IR (dry film) ν_{max} 3350, 3300, 1650, 1600, 1500, 1380, 1360, 1300, 1080, 1045, 1100, 840 cm⁻¹; EIMS *m/z* [M]⁺ 333 (42), 332 (19), 316 (20), 302 (46), 274 (35), 260 (100), 230 (69), 192 (15); CD (MeOH) Δε (nm) +19.2 (220), +14.4 (260), +0.8 (306).

2-*N*-Methylexcentricine (2): obtained as needles (15 mg) from CHCl₃; mp 215–217 °C; [α]¹⁸_D +266° (*c*

0.02, MeOH); UV (MeOH) λ_{max} (log ε) 228 (4.42), 264 (4.02), 305 (3.51) nm; IR ν_{max} 3350, 1650, 1600, 1480, 1390, 1365, 1300, 1145, 1080, 1050, 1100, 850 cm⁻¹; HRMS *m/z* C₁₉H₂₅O₅N (obsd 347.1782, calcd for C₁₉H₂₅O₅N 347.1733), EIMS *m/z* [M]⁺ 347 (48) (C₁₉H₂₅O₅N), 346 (25), 330 (23), 329 (56), 274 (100), 244 (58), 206 (35); ¹H- and ¹³C-NMR data, see Table 1; CD Δε (nm) +18.4 (221), +14.8 (262), +1.0 (306).

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