Myricananone and Myricananadiol: Two New Cyclic 'Diarylheptanoids' from the Roots of *Myrica nana*

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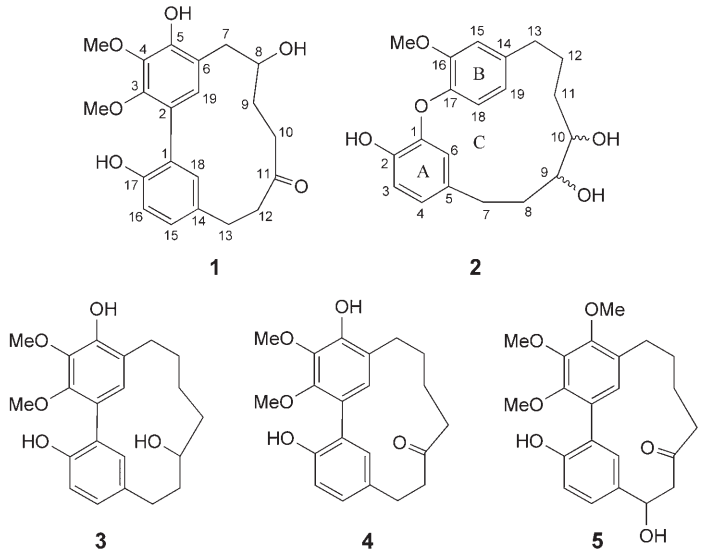
Two new cyclic 'diarylheptanoids', myricananone (**1**) and myricananadiol (**2**), were isolated from the roots of *Myrica nana*, together with the known compounds myricanol (**3**), myricanone (**4**), and porson (**5**). Their structures were determined by spectroscopic methods, including 1D- and 2D-NMR as well as HR-ESI-MS analyses.

Introduction. – *Myrica nana* CHEVAL. (Myricaceae) is an evergreen shrub native to Yunnan and Guizhou Provinces of mainland China [1]. Its fruits are edible and beneficial for dyspepsia. Its roots are used as a Chinese folk medicine for the treatment of bleeding, diarrhea, stomach pain, burns, and skin diseases [2]. Several triterpenoids, flavonoids, tannins and 'diarylheptanoids' have been isolated from other Myricaceae plants [3–11], and some phenolic compounds were previously reported from the fresh leaves of *M. nana* [12]. However, the information on the chemical constituents of the roots of this plant is still scarce.

Herein, we report on the constituents of the 95% EtOH extract of the roots of *M. nana*, from which the cyclic compounds **1**–**5** were isolated. Compounds **1** and **2**, named myricananone and myricananandiol, respectively, are new natural products, and the known compounds **3**–**5** were isolated for the first time from this plant. In this paper, we describe the isolation and structural elucidation of these isolates.

Results and Discussion. – Compound **1** was obtained as a colorless, optically inactive powder. Its HR-ESI mass spectrum showed the quasi-molecular $[M+Na]^+$ ion peak at *m*/*z* 395.1467 (calc. 395.1471), corresponding to the molecular formula $C_{21}H_{24}O_6$, with ten degrees of unsaturation. Analysis of the ^{1}H- and ^{13}C-NMR data of **1** (*Table*) indicated a cyclic 'diarylheptanoid' closely related to the known compounds **3**–**5**. The high similarity of the ^{13}C-NMR signals of **1** and **3** in the aromatic region indicated that they shared the same diphenyl substitution pattern.

The positions of the OH and C=O groups were determined by ^{1}H,^{1}H-COSY and HMBC experiments (*Fig. 1*). Two spin systems were readily identified as H–C(7)/H–C(8)/H–C(9)/H–C(10) and as H–C(12)/H–C(13) by the ^{1}H,^{1}H-COSY inter-



actions[1]). The connection of C(10) and C(12) *via* a C=O group in 11-position was established by the HMBC correlations of CH_2(9), CH_2(10), CH_2(12), and CH_2(13) with C(11). The linkage of the aliphatic chain with the diphenyl moiety was assembled with the aid of HMBC correlations between CH_2(7) and C(5), C(6), and C(19); between CH_2(12) and C(14); between CH_2(13) and both C(14) and C(15), and between C(13) and both H–C(15) and H–C(18).

In the NOESY spectrum of **1** (*Fig. 1*), key NOEs were observed between H–C(19) and H–C(7), H–C(8), H_a–C(9), and H–C(18); between H–C(8) and H_a–C(10); between H_b–C(9) and H_b–C(10); between H–C(18) and H_a–C(9), H–C(12), and

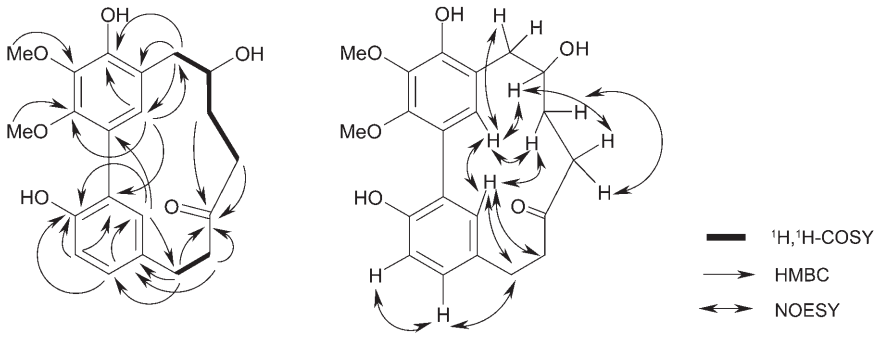


Fig. 1. *Key ^{1}H,^{1}H-COSY, HMBC, and NOESY interactions of* **1**

[1]) Arbitrary atom numbering.

Table. *^{1}H- and ^{13}C-NMR Data of* **1** *and* **2**. At 400 and 100 MHz, resp., δ in ppm, J in Hz.

Position[1])	**1**[a])		Position[1])	**2**[b])	
	δ(H)	δ(C)		δ(H)	δ(C)
1		126.8	1		144.8
2		124.1	2		149.3
3		149.0	3	6.73 (*d*, *J* = 8.0)	116.5
4		141.1	4	6.57 (*dd*, *J* = 8.0, 1.9)	122.8
5		150.2	5		133.8
6		123.4	6	5.72 (*d*, *J* = 1.9)	114.5
7a	2.90–3.04 (*m*)	36.9	7	2.48–2.62 (*m*)	29.4
7b	2.64–2.75 (*m*)				
8	4.24 (*m*)	71.0	8	1.50–1.54 (*m*)	35.2
9a	2.14–2.18 (*m*)	32.3	9	2.87–2.92 (*m*)	74.9
9b	1.61–1.65 (*m*)				
10a	2.64–2.75 (*m*)	42.2	10	2.48–2.62 (*m*)	76.6
10b	2.90–3.04 (*m*)				
11		216.0	11a	1.22–1.24 (*m*)	32.9
			11b	1.38–1.47 (*m*)	
12a	2.90–3.04 (*m*)	43.4	12a	1.63–1.73 (*m*)	27.5
12b	2.75–2.81 (*m*)		12b	1.90–1.95 (*m*)	
13	2.90–3.04 (*m*)	29.0	13a	2.48–2.62 (*m*)	36.0
			13b	2.87–2.92 (*m*)	
14		133.0	14		141.5
15	6.98 (br. *d*, *J* = 8.0)	129.6	15	6.98 (*d*, *J* = 1.7)	117.7
16	6.74 (*d*, *J* = 8.0)	117.3	16		152.7
17		152.9	17		144.6
18	6.56 (br. *s*)	134.2	18	7.08 (*d*, *J* = 7.8)	125.2
19	6.40 (*s*)	130.8	19	6.94 (*dd*, *J* = 7.8, 1.7)	122.2
OMe	3.78 (*s*)	61.6	OMe	3.64 (*s*)	56.4
OMe	3.88 (*s*)	61.5	OMe	7.67 (*s*)	
			9-OH	3.24 (br. *s*)	
			10-OH	3.18 (br. *s*)	

[a]) In CD_3OD. [b]) In (D_6)Acetone.

H–C(13); and between H–C(13) and H–C(15). Since the compound showed no optical activity, it was most likely present as a racemic mixture.

From the above data, the structure of the new compound **1** was, thus, deduced as 3,12,15-trihydroxy-16,17-dimethoxytricyclo[12.3.1.1^{2,6}]nonadeca-1(18),2(19),3,5,14,16-hexaen-9-one, and given the trivial name *myricananone*.

Compound **2** was obtained as a colorless, optically active powder ($[\alpha]_D^{23.6} = -71.4$). The molecular formula $C_{20}H_{24}O_5$ was derived by HR-ESI-MS (*m*/*z* 367.1517 ($[M + Na]^+$; calc. 367.1521), requiring nine degrees of unsaturation. The ^{13}C-NMR spectrum of **2** (*Table*) exhibited 20 signals, which were ascribable to two benzene rings, five CH_2 and two oxygenated CH groups, as well as one MeO function.

The ^{1}H-NMR spectrum of **2** showed two *ABX*-type spin systems in the aromatic region, resonating at δ(H) 7.08 (*d*, *J* = 7.8 Hz, 1 H), 7.04 (br. *d*, *J* = 7.8 Hz, 1 H), and 7.06 (br. *s*, 1 H); and at 6.73 (*d*, *J* = 8.0 Hz, 1 H), 6.57 (*dd*, *J* = 8.0, 1.9 Hz, 1 H), and

5.72 (*d*, $J = 1.9$ Hz, 1 H), respectively. The unusual upfield-shifted aromatic signal at δ(H) 5.71 was assumed to be caused by the anisotropy of the neighboring benzene *B*-ring; similar phenomena were observed before in the related structures of galeon and acerogenin B [13][14].

The above data suggested that **2** was a diphenyl-ether analogue of a 'diarylheptanoid'. The substitution patterns of the two benzene rings were resolved on the basis of HMBC correlations (*Fig. 2*) between H–C(3) and both C(4) and C(5); between H–C(6) and C(1), C(2), and C(4); between 2-OH and both C(2) and C(3); between H–C(15) and C(16); between H–C(18) and C(16), C(17), and C(19); between H–C(19) and C(15); and between 16-MeO and C(16). The positions of the two OH groups in the aliphatic chain were determined as C(9) and C(10), respectively, as derived from the ^{1}H,^{1}H-COSY interactions for CH_2(7)/CH_2(8)/H–C(9)/H–C(10)/CH_2(11)/CH_2(12)/CH_2(13), for HO–C(9)/H–C(9), and for HO–C(10)/H–C(10), as well as based on the HMBC correlations between H–C(4) and C(7); between H–C(6) and C(7); between H–C(7) and C(4), C(5), and C(6); between H–C(8) and C(5); between H–C(12) and C(14); and between H–C(13) and C(14), C(15), and C(19).

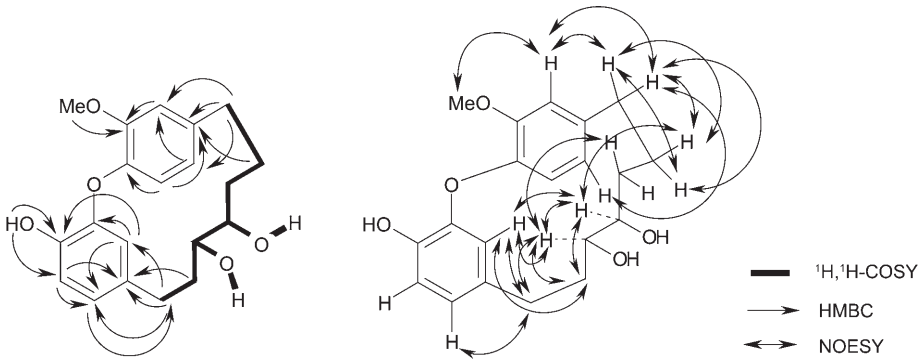


Fig. 2. *Key ^{1}H,^{1}H-COSY, HMBC, and NOESY interactions of* **2**

The unusual upfield shifts of H–C(9) (δ(H) 2.87–2.92) and H–C(10) (δ(H) 2.48–2.62) indicated that these two H-atoms were somewhat shielded by the aromatic *B*-ring, which can happen when rings *A* and *B* are almost perpendicular to one another. In addition, key NOEs were observed in the ROESY spectrum of **2** (*Fig. 2*) between CH_2(7) and H–C(4), H–C(6), and H–C(9); between CH_2(8) and H–C(6), H–C(9), and H–C(10); between H–C(6) and both H–C(9) and H–C(10); between H_a–C(11) and H–C(9); between H_a–C(12) and H–C(10); and between H–C(19) and H_b–C(13). This indicated that the flexible ring *C* adopts a preferential conformation in solution, in which free rotation about the single bonds is restricted.

Thus, from the above data, the structure of the new compound **2** was deduced as 17-methoxy-2-oxatricyclo[13.2.2.1^{3,7}]icosa-1(17),3(20),4,6,15,18-hexaene-4,10,11-triol, and given the trivial name *myricananadiol*. The relative and absolute configurations at the two stereogenic centers, C(9) and C(10), remain to be determined.

The three known cyclic 'diarylheptanoids' were identified as myricanol (**3**) [9], myricanone (**4**) [9], and porson (**5**) [15], respectively, by comparison of their spectroscopic data with literature values. These compounds were all isolated for the first time from *M. nana*.

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Experimental Part

General. Column chromatography (CC): silica gel (200–300 mesh, 10–40 μm; *Qingdao Marine Chemical Factory*, China), C_{18} reverse-phase (RP) silica gel (40–63 μm; *Daiso Co.*, Japan), and *Sephadex LH-20* (*Amersham Pharmacia Biotech*, Sweden). Thin-layer chromatography (TLC): silica gel GF_{254} (10–40 μm; *Qingdao*). All solvents were distilled before use. UV/VIS Spectra: *Shimadzu UV-2401PC* spectrophotometer; λ_{max} in nm. Optical rotations: *JASCO-20C* digital polarimeter. ^{1}H- and ^{13}C-NMR Spectra: *Bruker AM-400* spectrometer, at 400 and 100 MHz, resp; chemical shifts δ in ppm rel. to Me_4Si, *J* in Hz. ^{1}H,^{1}H-COSY, HMQC, HMBC, and NOESY Spectra: *Bruker DRX-500* spectrometer. MS: *VG AutoSpec-3000* mass spectrometer; in *m/z*. HR-ESI-MS: *API QSTAR Pulsar-1* mass spectrometer.

Plant Material. The roots of *Myrica nana* CHEVAL. were collected from Songhua dam, a Kunming suburb in Yunnan Province, China, in July 2005, and were identified by Dr. *Y. M. Shui*, Kunming Institute of Botany. A voucher specimen (CHYX0391) was deposited at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming, P. R. China.

Extraction and Isolation. The dried and powdered roots of *M. nana* (7.0 kg) were extracted with 95% EtOH at reflux (3×). The combined extracts were concentrated *in vacuo*. The residue was suspended in H_2O, and then extracted with AcOEt. The resulting AcOEt-soluble extract (276 g) was subjected to CC (SiO_2; $CHCl_3$/MeOH 5:1) to afford four fractions (*Fr. 1 – Fr. 4*). *Fr. 1* (67 g) was purified by CC (SiO_2; $CHCl_3$/AcOEt 4:1) to yield *Fr. 1.1 – Fr. 1.3. Fr. 1.1* (52 g) was further purified by CC (SiO_2; petroleum ether (PE)/AcOEt 2:1) to yield *Fr. 1.1.1 – Fr. 1.1.4. Fr. 1.1.1* (29 g) was purified by CC (SiO_2; $CHCl_3$/Me_2CO 6:1) to provide *Fr. 1.1.1.1 – Fr. 1.1.1.3. Fr. 1.1.1.1* (500 mg) was repeatedly subjected to RP-CC (1. C_{18}, MeOH/H_2O 50:50 → 100:0; 2. *Sephadex LH-20*, $CHCl_3$/MeOH 6:4) to afford **1** (13 mg) and **2** (6 mg). *Fr. 1.1.1.2* (1.2 g) was subjected to repeated vacuum liquid chromatography (VLC) (SiO_2; $CHCl_3$/i-PrOH 15:1) to yield **3** (107 mg). *Fr. 1.1.1.3* (300 mg) was also purified by VLC (SiO_2; PE/i-PrOH 15:1) and then by RP-CC (*Sephadex LH-20*; $CHCl_3$/MeOH 6:4) to yield **4** (26 mg) and **5** (22 mg).

3,12,15-Trihydroxy-16,17-dimethoxytricyclo[12.3.1.1^{2,6}]nonadeca-1(18),2(19),3,5,14,16-hexaen-9-one (**1**). Colorless powder. UV (MeOH): 295, 258. $[\alpha]_D^{23.5} = 0$ ($c = 0.12$, acetone). ^{1}H- and ^{13}C-NMR: see *Table*. EI-MS: 372 (M^+). HR-ESI-MS: 395.1467 ($[M+Na]^+$, $C_{21}H_{24}NaO_6^+$; calc. 395.1471).

17-Methoxy-2-oxatricyclo[13.2.2.1^{3,7}]icosa-1(17),3(20),4,6,15,18-hexaene-4,10,11-triol (**2**). Colorless powder. UV (MeOH): 279. $[\alpha]_D^{23.6} = -71.4$ ($c = 0.07$, acetone). ^{1}H- and ^{13}C-NMR: see *Table*. EI-MS: 344 (M^+). HR-ESI-MS: 367.1517 ($[M+Na]^+$, $C_{20}H_{24}NaO_5^+$; calc. 367.1521).

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