

Yuzurimine-Type Alkaloids from *Daphniphyllum yunnanense*

Ying-Tong Di,<sup>†,‡</sup> Hong-Ping He,<sup>†</sup> Chun-Shun Li,<sup>†</sup> Jun-Mian Tian,<sup>†</sup> Shu-Zhen Mu,<sup>§</sup> Shun-Lin Li,<sup>†</sup> Suo Gao,<sup>†</sup> and Xiao-Jiang Hao<sup>\*†</sup>

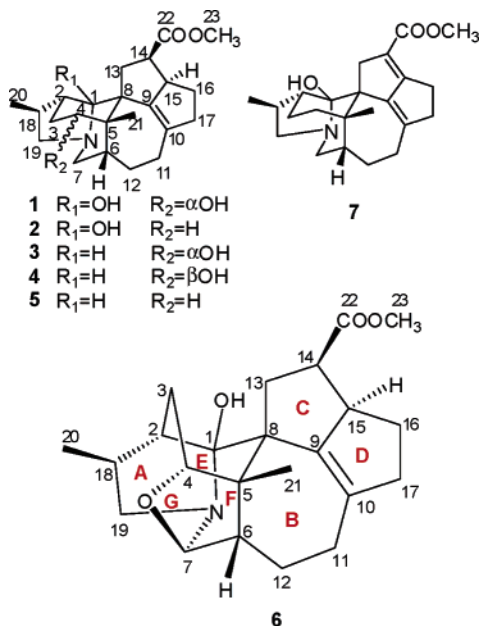
State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204, People's Republic of China, Graduate School of Chinese Academy of Sciences, Beijing 100039, People's Republic of China, and The Key Laboratory of Chemistry for Natural Product of Guizhou Province and Chinese Academy of Sciences, Guiyang 550002, People's Republic of China

Received July 19, 2006

Five new yuzurimine-type alkaloids, yunnandaphnines A–E (**2–6**), together with two known analogues, macrodaphniphyllamine (**1**) and calycinine A (**7**), have been isolated from the leaves and twigs of *Daphniphyllum yunnanense*. The structures of the new alkaloids were elucidated by spectroscopic methods. Yunnandaphnine E (**6**) is a novel heptacyclic yuzurimine-type alkaloid with an oxazine ring.

*Daphniphyllum* alkaloids are a structurally diverse group of nitrogen-containing polycyclic natural products isolated from plants of the genus *Daphniphyllum* (Daphniphyllaceae).<sup>1</sup> These ring systems have attracted great interest as challenging targets for total synthesis as well as biosynthetic studies.<sup>2–4</sup> Recently, a number of new *Daphniphyllum* alkaloids have been isolated from the genus.<sup>5–8</sup>

In our continuing search for structurally unique *Daphniphyllum* alkaloids,<sup>8</sup> five new yuzurimine-type alkaloids, yunnandaphnines A–E (**2–6**), along with two known analogues, macrodaphniphyllamine (**1**)<sup>9</sup> and calycinine A (**7**),<sup>8a</sup> were isolated from the leaves and twigs of *Daphniphyllum yunnanense*. Yunnandaphnine E (**6**) is a new heptacyclic yuzurimine-type alkaloid with an oxazine ring.



## Results and Discussion

Macrodaphniphyllamine (**1**) was first isolated in 1967; however only limited NMR data were reported.<sup>9</sup> To assist in the structure elucidation of the new alkaloids (**2–6**) through spectroscopic

comparison, we have made full <sup>1</sup>H and <sup>13</sup>C NMR assignments for **1** (Tables 1 and 2).

Yunnandaphnine A (**2**) was obtained as a white powder, and the molecular formula was established as C<sub>23</sub>H<sub>33</sub>NO<sub>3</sub> by HRESIMS [*m/z* 372.2544, (M + H)<sup>+</sup>] with eight degrees of unsaturation. The IR absorption bands at 3440 and 1737 cm<sup>-1</sup> suggested the presence of a hydroxyl and an ester carbonyl, respectively. The <sup>1</sup>H and <sup>13</sup>C NMR spectra of **2** (Tables 1 and 2) were closely related to those of the known compound macrodaphniphyllamine (**1**), with the exception of the loss of an oxymethine (δ<sub>C</sub> 75.4) in **1** and the addition of a methylene in **2**. All the NMR data implied that **2** was 4-deoxymacrodaphniphyllamine. This was further confirmed by 2D NMR experiments, and its planar structure and relative configuration are shown in Figures 1 and 2, respectively. In addition, the conformations of the cyclohexane (C-1–C-5 and C-8) and cycloheptene (C-5, C-6, and C-8–C-12) rings were all assigned as chairs from NOE correlations of H-4β/H-13β, H-2/H-13α, and H<sub>3</sub>-21/H-12β.

Yunnandaphnine B (**3**) was also isolated as a white powder. Its molecular formula, C<sub>23</sub>H<sub>33</sub>NO<sub>3</sub> obtained by HRESIMS, contained one less oxygen than **1**. The <sup>1</sup>H and <sup>13</sup>C NMR spectra in both compounds (Tables 1 and 2) matched closely, except that an α-nitrogen methine (δ<sub>C</sub> 65.7) in **3** replaced an amino ketal quaternary carbon (δ<sub>C</sub> 96.9) in **1**, supporting the fact that compound **3** has the same skeleton as **1** but lacking the hydroxyl at C-1. Data from the <sup>1</sup>H–<sup>1</sup>H COSY, HMQC, and HMBC spectra further justified the structure of **3**, as shown in Figure 1. The <sup>3</sup>J values (11.5, 6.0 between H-4 and H<sub>2</sub>-3) suggested H-4 took a β-axial orientation, which was confirmed by the observed correlations between H-4 and H-13α in the ROESY spectrum. In addition, the relative configuration at the remaining chiral centers of **3** would be analogous to those of **1** on the basis of <sup>13</sup>C NMR shifts and NOE data.

Yunnandaphnine C (**4**) had the same molecular formula of C<sub>23</sub>H<sub>33</sub>NO<sub>3</sub> as **3**, determined by HRESIMS [*m/z* 372.2544, (M + H)<sup>+</sup>]. The NMR features of **4** (Tables 1 and 2) closely resembled those of **3** except for the resonances in the vicinity of C-4. The correlation between H-4 (δ<sub>H</sub> 3.60) and H-6 (δ<sub>H</sub> 1.95) in its ROESY spectrum indicated that H-4 took an α-orientation. The structure of yunnandaphnine C was thus established as shown in Figure 1.

Yunnandaphnine D (**5**) was obtained as a white powder, whose molecular formula of C<sub>23</sub>H<sub>33</sub>NO<sub>2</sub> was determined by HRESIMS [*m/z* 356.2590, (M + H)<sup>+</sup>], indicating that it possessed two oxygen atoms less than **1**. The <sup>13</sup>C NMR and DEPT spectra (Table 2) revealed 23 carbons due to one ester carbonyl, one tetrasubstituted double bond, two quaternary carbons, six methines, nine methylenes, and three methyls. All the data implied that compound **5** has

\* Corresponding author. Tel: +86-871-5223263. Fax: +86-871-5219684. E-mail: haoxj@mail.kib.ac.cn.

<sup>†</sup> Kunming Institute of Botany.

<sup>‡</sup> Graduate School of Chinese Academy of Sciences.

<sup>§</sup> The Key Laboratory of Chemistry for Natural Product of Guizhou Province and Chinese Academy of Sciences.

**Table 1.**  $^1\text{H}$  [ $\delta_{\text{H}}$  (pattern,  $J$  (Hz))] NMR Data of Macrodaphniphyllamine (**1**) and Yunnandaphnines A–D (**2–5**) in  $\text{CDCl}_3$  at 300 K

	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
1			2.97 (1H, m)	3.11 (1H, m)	2.73 (1H, br s)
2	2.19 (1H, m)	2.13 (1H, m)	2.31 (1H, m)	2.43 (1H, m)	2.23 (1H, m)
3 $\alpha$	1.36 (1H, m)	1.50 (2H, m)	1.43 (1H, m)	1.68 (1H, m)	1.48 (2H, m)
3 $\beta$	1.75 (1H, m)		1.92 (1H, m)	1.82 (1H, dd, 14.0, 4.0)	
4 $\alpha$		1.42 (1H, m)		3.60 (1H, m)	1.47 (1H, m)
4 $\beta$	3.73 (1H, dd, 11.5, 6.0)	1.65 (1H, dt, 13.5, 7.0)	3.73 (1H, dd, 11.5, 6.0)		1.58 (1H, m)
6	2.32 (1H, m)	1.90 (1H, m)	2.52 (1H, m)	1.95 (1H, m)	1.95 (1H, m)
7 $\alpha$	3.04 (1H, m)	3.19 (1H, dd, 12.5, 9.0)	3.05 (1H, dd, 12.0, 10.0)	2.95 (1H, m)	3.25 (1H, d, 12.5)
7 $\beta$	3.32 (1H, d, 10.5)	3.31 (1H, d, 12.5)	3.47 (1H, br d 12.0)	3.57 (1H, m)	3.03 (1H, dd, 12.5, 9.5)
11 $\alpha$	2.06 (1H, dd, 17.0, 5.5)	2.01 (1H, m)	2.12 (1H, dd, 18.0, 5.5)	2.20 (1H, m)	2.37 (1H, m)
11 $\beta$	2.40 (1H, m)	2.41 (1H, m)	2.52 (1H, m)	2.47 (1H, m)	2.04 (1H, m)
12 $\alpha$	1.42 (1H, m)	1.37 (1H, m)	1.54 (1H, m)	1.50 (1H, m)	1.40 (1H, m)
12 $\beta$	1.92 (1H, m)	2.08 (1H, m)	1.99 (1H, m)	2.05 (1H, m)	2.09 (1H, m)
13 $\alpha$	2.29 (1H, m)	2.42 (1H, dd, 14.5, 10.0)	1.88 (1H, dd, 14.0, 9.0)	2.05 (1H, m)	1.98 (1H, dd, 14.5, 9.0)
13 $\beta$	2.64 (1H, m)	2.62 (1H, dd, 14.5, 4.5)	2.69 (1H, dd, 14.0, 4.5)	2.88 (1H, dd, 15.0, 6.5)	2.61 (1H, dd, 14.5, 4.5)
14	43.1 (1H, m)	3.04 (1H, td, 10.5, 4.0)	2.92 (1H, m)	2.94 (1H, m)	2.91 (1H, dt, 9.5, 4.5)
15	3.51 (1H, m)	3.53 (1H, m)	3.58 (1H, m)	3.70 (1H, m)	3.54 (1H, m)
16 $\alpha$	1.85 (1H, m)	1.84 (1H, m)	1.92 (1H, m)	1.92 (1H, m)	1.86 (1H, td, 7.0, 11.5)
16 $\beta$	1.29 (1H, m)	1.35 (1H, m)	1.21 (1H, m)	1.18 (1H, m)	1.31 (1H, m)
17 $\alpha$	2.65 (1H, dd, 13.5, 4.0)	2.67 (1H, m)	2.83 (1H, m)	2.78 (1H, m)	2.68 (1H, m)
17 $\beta$	2.27 (1H, m)	2.31 (1H, dd, 15.0, 8.5)	2.27 (1H, m)	2.23 (1H, dd, 14.5, 8.0)	2.32 (1H, dd, 15.0, 9.0)
18	2.75 (1H, m)	2.77 (1H, m)	2.43 (1H, m)	2.40 (1H, m)	2.04 (1H, m)
19 $\alpha$	3.57 (1H, t, 10.5)	3.60 (1H, m)	3.86 (1H, m)	3.94 (1H, m)	2.23 (1H, m)
19 $\beta$	2.25 (1H, m)	2.26 (1H, dd, 11.5, 7.5)	2.37 (1H, m)	2.43 (1H, m)	3.43 (1H, m)
20	1.03 (3H, d, 7.5)	1.03 (3H, d, 7.5)	1.08 (3H, d, 6.5)	1.05 (3H, d, 5.5)	1.03 (3H, d, 6.5)
21	1.22 (3H, s)	1.12 (3H, s)	1.25 (3H, s)	1.26 (3H, s)	1.08 (3H, s)
23	3.62 (3H, s)	3.63 (3H, s)	3.64 (3H, s)	3.64 (3H, s)	3.64 (3H, s)

**Table 2.**  $^{13}\text{C}$  [ $\delta_{\text{C}}$ ] NMR Data of Macrodaphniphyllamine (**1**) and Yunnandaphnines A–D (**2–5**) in  $\text{CDCl}_3$  at 300 K

	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
1	96.9s	97.9s	65.7d	65.5d	67.1d
2	42.8d	43.4d	37.4d	35.0d	38.5d
3	30.5t	21.9t	30.8t	28.8t	22.4t
4	75.4d	38.7t	75.6d	77.2d	39.1t
5	44.1s	39.7s	39.9s	39.0s	35.0s
6	33.3d	42.8d	33.5d	39.5d	43.5d
7	58.1t	58.6t	57.3t	57.1t	58.7t
8	53.0s	52.6s	46.5s	44.9s	46.1s
9	143.8s	144.2s	142.5s	142.4s	145.0s
10	136.2s	135.8s	135.7s	135.1s	132.6s
11	25.5t	25.3t	25.3t	24.7t	25.3t
12	27.8t	28.8t	27.8t	27.3t	29.0t
13	36.8t	38.1t	37.9t	38.9t	39.2t
14	43.1d	43.0d	42.1d	41.9d	42.3d
15	57.1d	58.1d	53.5d	51.2d	54.2d
16	29.8t	29.5t	28.2t	28.2t	27.6t
17	43.0t	43.1t	42.7t	42.4t	42.6t
18	34.0d	34.4d	36.7d	37.1d	38.6d
19	64.6t	65.1t	65.0t	65.7t	65.5t
20	14.4q	14.5q	14.8q	13.9q	15.1q
21	21.1q	25.0q	20.5q	18.5q	24.7q
22	176.0s	176.5s	175.6s	175.8s	175.9s
23	51.0q	51.0q	51.3q	51.9q	51.1q

the same skeleton as **1**, but that it is without the hydroxyl groups at C-1 and C-4. Analysis of  $^1\text{H}$ – $^1\text{H}$  COSY, HMQC, HMBC, and TOCSY NMR data of **5** permitted establishing the structure of **5** as 1,4-dideoxymacrodaphniphyllamine (Figure 1). Furthermore, the relative configuration at the chiral carbons was elucidated to be same as those of **1** by ROESY data of **5** as well as by the similarity of the  $^{13}\text{C}$  NMR chemical shifts of **5** to those of **1**.

Yunnandaphnine E (**6**) was obtained as a white powder, and the molecular formula was established as  $\text{C}_{23}\text{H}_{31}\text{NO}_4$  by HRESIMS [ $m/z$  386.2338, ( $\text{M} + \text{H}$ ) $^+$ ] with nine sites of unsaturation. The  $^{13}\text{C}$  NMR spectra of **6** at 315 K in  $\text{CDCl}_3$  (Table 3) gave only 20 signals, including some partially broadened ones, which may be due to conformational exchange.<sup>5c,10</sup> Analysis of the 2D NMR data of **6** implied that it had the basic yuzurimine-type skeleton, although several key HMBC correlation signals related to quaternary carbons were not observed (Figure 3).

**Table 3.**  $^1\text{H}$  [ $\delta_{\text{H}}$  (pattern,  $J$  (Hz))] and  $^{13}\text{C}$  [ $\delta_{\text{C}}$ ] NMR Data of Yunnandaphnine E (**6**) and Its TFA Salt (**6a**) in  $\text{CDCl}_3$ 

	<b>6</b>		<b>6a</b>	
no.	$\delta_{\text{H}}^a$	$\delta_{\text{C}}^a$	$\delta_{\text{H}}^b$	$\delta_{\text{C}}^b$
1		c		109.9
2	2.27 (1H, m)	44.1	2.58 (1H, m)	44.4
3 $\alpha$	1.91 (1H, m)	24.3	2.13 (1H, dd, 15.5, 3.5)	23.0
3 $\beta$	1.72 (1H, m)		1.88 (1H, m)	
4	3.85 (1H, m)	84.7	4.21 (1H, d, 3.0)	87.6
5		47.8		47.0
6	2.02 (1H, m)	51.5	2.37 (1H, m)	49.8
7	4.20 (1H, br s)	93.8	4.89 (1H, br s)	95.5
8		c		53.9
9		c		137.5
10		141.9		146.5
11	2.09 (2H, m)	24.7	2.09 (2H, m)	24.4
12 $\alpha$	2.02 (1H, m)	26.0	2.25 (1H, m)	23.3
12 $\beta$	1.94 (1H, m)		2.06 (1H, m)	
13 $\alpha$	2.32 (1H, m) <sup>d</sup>	38.7	2.21 (1H, m)	38.6
13 $\beta$	2.47 (1H, m)		2.48 (1H, dd, 13.5, 10.0)	
14	3.15 (1H, m)	41.9	3.27 (1H, m)	41.8
15	3.46 (1H, m)	53.9	3.62 (1H, m)	52.7
16 $\alpha$	1.90 (1H, m)	28.8	1.98 (1H, m)	29.5
16 $\beta$	1.42 (1H, m)		1.29 (1H, m)	
17 $\alpha$	2.62 (1H, m)	40.6	2.60 (1H, m)	39.9
17 $\beta$	2.34 (1H, m)		2.30 (1H, m)	
18	2.71 (1H, m)	34.0	3.16 (1H, m)	32.7
19 $\alpha$	3.55 (1H, m)	58.2	4.07 (1H, m)	57.1
19 $\beta$	2.32 (1H, m) <sup>d</sup>		2.76 (1H, m)	
20	1.08 (3H, d, 7.0)	15.4	1.16 (3H, d, 7.0)	14.6
21	1.23 (3H, s)	22.4	1.34 (3H, s)	21.4
22		175.6		177.4
23	3.64 (3H, m)	51.2	3.71 (3H, s)	52.4

<sup>a</sup> Measured at 315 K. <sup>b</sup> Measured at 300 K. <sup>c</sup> Not observed. <sup>d</sup> Overlapped.

To further elucidate its structure, **6** was treated with  $\text{CF}_3\text{COOH}$  and converted to its TFA salt (**6a**). In the  $^{13}\text{C}$  NMR spectrum of **6a** (Table 3), all 23 resonances were observed corresponding to one ester carbonyl, one tetrasubstituted double bond, three  $\text{sp}^3$  quaternary carbons, seven  $\text{sp}^3$  methines, seven methylenes, and three methyls. The  $^{13}\text{C}$  NMR data suggested that the methylene at  $\delta_{\text{C}}$  57.1 (C-19) was linked to the nitrogen atom, and the methine at  $\delta_{\text{C}}$  87.6 (C-4) to an oxygen atom. The chemical shifts of the methine

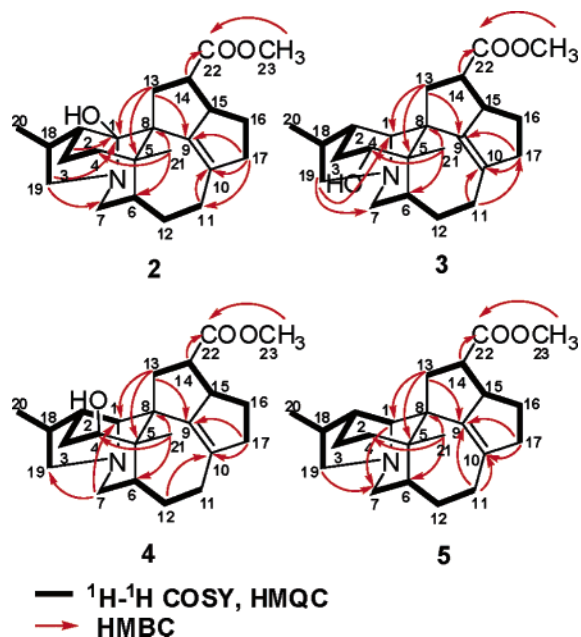


Figure 1. Selected 2D NMR data of yunnandaphnines A–D (2–5).

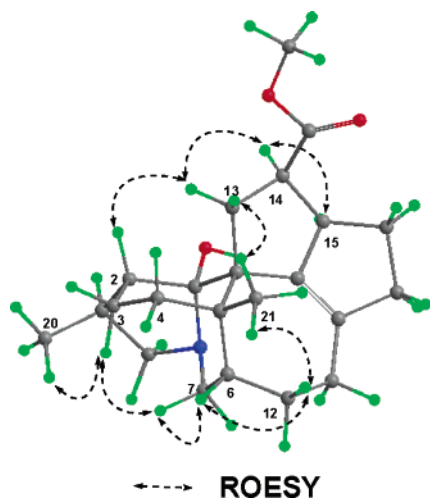


Figure 2. Energy-minimized model of 2 illustrating the major ROESY correlations used to define the relative configuration.

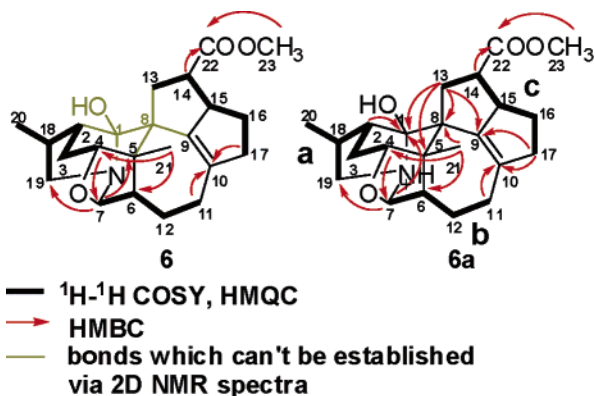


Figure 3. Selected 2D NMR data of yunnandaphnine E (6) and its TFA salt (6a).

carbon at  $\delta_C$  95.5 (C-7) and of the quaternary carbon at  $\delta_C$  109.9 (C-1) revealed that they were amino ketal carbons. The above data indicated that 6a possessed a heptacyclic structure. The  $^1\text{H}$ – $^1\text{H}$  COSY, HMQC, and HMBC spectra revealed three partial structures (a–c) as shown in Figure 3. The connectivity of the fragments

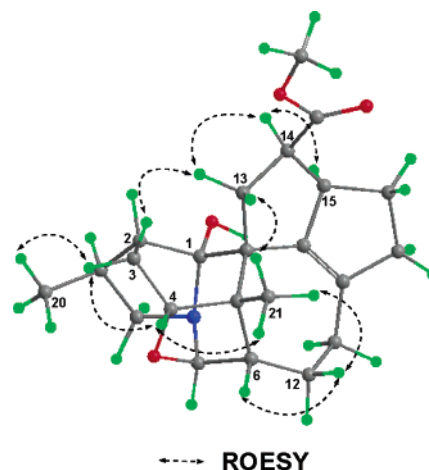


Figure 4. Energy-minimized model of 6 (MM2 followed by PM3) illustrating the major ROESY correlations used to define the relative configuration.

(a–c), heteroatoms, and quaternary carbons was furnished by the HMBC experiment. In the HMBC spectrum, cross-peaks for H<sub>2</sub>–19 to C-1 and C-7 indicated that C-1, C-7, and C-19 were all connected to the nitrogen atom. The connectivities of C-21 ( $\delta_C$  21.4) to C-4, C-6 ( $\delta_C$  49.8) and C-8 ( $\delta_C$  53.9) via C-5 ( $\delta_C$  47.0) were shown by HMBC correlations from H<sub>3</sub>–21 to C-4, C-5, C-6, and C-8. The HMBC correlations from H-13 $\alpha$  to C-1 and C-8 and from H-2 to C-1 indicated that substructures a and c were connected through C-1 and C-8. The critical correlation between H-7 ( $\delta_H$  4.89) and C-4 created one tetrahydrofuran ring G and one oxazine ring: C1–C8–C5–C4–O–C7–N. The additional correlations of H<sub>2</sub>–11/C-10, H<sub>2</sub>–17/C-10, H<sub>2</sub>–13/C-9, H-14/C-22, and H<sub>3</sub>–23/C-22 clearly indicated the other linkages of 6a. Thus, the planar structure of 6a, the TFA salt of 6, was unambiguously established.

The relative configuration of 6 was deduced from ROESY correlations, as shown in the computer-generated 3D drawing (Figure 4). The ROESY correlations of H-4/H-13 $\beta$  and H-3 $\beta$ /H-13 $\alpha$  indicated the relative configurations at C-4 and the boat conformation of ring E (C-1–C-5 and C-8).

## Experimental Section

**General Experimental Procedures.** Optical rotations were recorded on a Perkin-Elmer model 241 polarimeter. IR spectra were measured in a Bio-Rad FTS-135 spectrometer with KBr pellets. ESI and high-resolution mass spectra were recorded using a Finnigan MAT 90 instrument and VG Auto Spec-3000 spectrometer, respectively.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were measured on a Bruker DRX-500 instrument, while  $^{13}\text{C}$  NMR spectra were recorded on a Bruker AM-400 spectrometer. Chemical shifts were reported using residual  $\text{CHCl}_3$  ( $\delta_H$  7.26 and  $\delta_C$  77.0) as internal standard. Column chromatography was performed on silica gel H (10–40  $\mu\text{m}$ ; Qingdao Marine Chemical Inc.), amino silica gel (75–100  $\mu\text{m}$ , Fuji Silysia Chemical LTD, Japan), Sephadex LH-20 (40–70  $\mu\text{m}$ , Amersham Pharmacia Biotech AB, Uppsala, Sweden), and Lichroprep RP-18 gel (40–63  $\mu\text{m}$ , Merck, Darmstadt, Germany). Precoated silica gel GF254 and HF254 plates (Qingdao Haiyang Chemical Plant, Qingdao, People's Republic of China) were used for TLC.

**Plant Material.** The leaves and twigs of *Daphniphyllum yunnanense* were collected in Xishuangbanna of Yunnan Province, People's Republic of China, in April 2005. The sample was identified by Prof. Shun-Cheng Zhang, Xishuangbanna Tropical Botanical Garden, Chinese Academy of Sciences, and a voucher specimen (KIB 05050217) was deposited at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences.

**Extraction and Isolation.** Air-dried and powdered leaves and twigs of *D. yunnanense* (7 kg) were extracted with 95% EtOH, and the extract was partitioned between EtOAc and 0.001 N HCl. The aqueous layer was alkalinized to pH 10 with 2 N NaOH followed by exhaustive

extraction with  $\text{CHCl}_3$ .  $\text{CHCl}_3$ -soluble materials were roughly separated by amino silica gel column chromatography, using  $\text{CHCl}_3/\text{MeOH}$  (from 0:1 to 1:0) as eluent, to give five fractions (A1–A5). A2 was subjected to a  $\text{C}_{18}$  column ( $\text{MeOH}/0.1\% \text{ TFA}$ , 1:9 → 8:2), in which a fraction that eluted with 50%  $\text{MeOH}/0.1\% \text{ TFA}$  was purified further by Sephadex LH-20 ( $\text{CHCl}_3/\text{MeOH}$ , 1:1) to afford two major fractions, B1 and B2. Fraction B1 was chromatographed over a normal silica gel column eluting with petroleum ether/ $\text{Et}_2\text{NH}$  (30:1 → 10:1) to afford **1** (20 mg), **2** (8 mg), **5** (7 mg), and **7** (12 mg). Fraction B2 was chromatographed over a silica gel column eluted with petroleum ether/ $\text{EtOAc}$  (5:1) to yield **6** (4 mg). Fraction A4 was subjected to a  $\text{C}_{18}$  column ( $\text{MeOH}/0.1\% \text{ TFA}$ , 1:9 → 7:3), in which a fraction that eluted with 40%  $\text{MeOH}/0.1\% \text{ TFA}$  was further purified by Sephadex LH-20 ( $\text{MeOH}$ ) and then chromatographed over a normal silica gel column eluted with petroleum ether– $\text{Et}_2\text{NH}$  (15:1) to yield **3** (8 mg) and **4** (3 mg).

**Preparation for 6a.** **6** in  $\text{CDCl}_3$  was treated with 1.2 equiv of  $\text{CF}_3\text{-COOH}$  and stirred for 2 min.

**Macrocephalophyllamine (1):** needles ( $\text{MeOH}$ );  $^1\text{H}$  and  $^{13}\text{C}$  NMR data, see Tables 1 and 2; ESIMS  $m/z$  386  $[\text{M} + \text{H}]^+$ .

**Yunnandaphnine A (2):** white powder;  $[\alpha]_D^{25} -56.0$  ( $c$  0.20,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  3400, 2923, 2853, 1737, and 1631  $\text{cm}^{-1}$ ;  $^1\text{H}$  and  $^{13}\text{C}$  NMR data, see Tables 1 and 2; ESIMS  $m/z$  372  $[\text{M} + \text{H}]^+$ ; HRESIMS  $m/z$  372.2544 (calcd for  $\text{C}_{23}\text{H}_{34}\text{NO}_3$ , 372.2538).

**Yunnandaphnine B (3):** white powder;  $[\alpha]_D^{25} +0.79$  ( $c$  0.21,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  3424, 2953, 2858, 1732, 1630, and 1435  $\text{cm}^{-1}$ ;  $^1\text{H}$  and  $^{13}\text{C}$  NMR, see Tables 1 and 2; ESIMS  $m/z$  372  $[\text{M} + \text{H}]^+$ ; HRESIMS  $m/z$  372.2547 (calcd for  $\text{C}_{23}\text{H}_{34}\text{NO}_3$ , 372.2538).

**Yunnandaphnine C (4):** white powder;  $[\alpha]_D^{25} -24.0$  ( $c$  0.22,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  3386, 2951, 2859, 1731, 1631, and 1444  $\text{cm}^{-1}$ ;  $^1\text{H}$  and  $^{13}\text{C}$  NMR, see Tables 1 and 2; ESIMS  $m/z$  372  $[\text{M} + \text{H}]^+$ ; HRESIMS  $m/z$  372.2544 (calcd for  $\text{C}_{23}\text{H}_{34}\text{NO}_3$ , 372.2538).

**Yunnandaphnine D (5):** white powder;  $[\alpha]_D^{25} -45.2$  ( $c$  0.21,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  2927, 2869, 1738, 1458, 1436, 1367, and 1317  $\text{cm}^{-1}$ ;  $^1\text{H}$  and  $^{13}\text{C}$  NMR, see Tables 1 and 2; ESIMS  $m/z$  356  $[\text{M} + \text{H}]^+$ ; HRESIMS  $m/z$  356.2590 (calcd for  $\text{C}_{23}\text{H}_{34}\text{NO}_3$ , 356.2589).

**Yunnandaphnine E (6):** white powder;  $[\alpha]_D^{25} -88.0$  ( $c$  0.16,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  3433, 2949, 2855, 1735, 1632, and 1451  $\text{cm}^{-1}$ ;  $^1\text{H}$  and  $^{13}\text{C}$  NMR, see Table 3; ESIMS  $m/z$  386  $[\text{M} + \text{H}]^+$ ; HRESIMS  $m/z$  386.2338 (calcd for  $\text{C}_{23}\text{H}_{34}\text{NO}_3$ , 386.2331).

**Acknowledgment.** The authors thank Prof. Shun-Cheng Zhang, Xishuangbanna Tropical Botanical Garden, Chinese Academy of Sciences, for collection and identification of the plant material.

**Supporting Information Available:** 1D, 2D NMR spectra for yunnandaphnines A–E (**2–6**) and yunnandaphnine E's TFA salt (**6a**). This material is available free of charge via the Internet at <http://pubs.acs.org>.

## References and Notes

- (1) For a review of *Daphniphyllum* alkaloids: Kobayashi, J.; Morita, H. In *The Alkaloids*; Cordell, G. A., Ed.; Academic Press: New York, 2003; Vol. 60, pp 165–205, and references therein.
- (2) (a) Niwa, H.; Hirata, Y.; Suzuki, K. T.; Yamamura, S. *Tetrahedron Lett.* **1973**, *14*, 2129–2132. (b) Suzuki, K. T.; Okuda, S.; Niwa, H.; Toda, M.; Hirata, Y.; Yamamura, S. *Tetrahedron Lett.* **1973**, *14*, 799–802.
- (3) (a) Denmark, S. E.; Baiazitov, R. Y. *J. Org. Chem.* **2006**, *71*, 593–605. (b) Solé, D.; Urbaneja, X.; Bonjoch, J. *Org. Lett.* **2005**, *7*, 5461–5464.
- (4) (a) Wallace, G. A.; Heathcock, C. H. *J. Org. Chem.* **2001**, *66*, 450–454. (b) Heathcock, C. H. *Proc. Natl. Acad. Sci. U.S.A.* **1996**, *93*, 14323–14327. (c) Heathcock, C. H.; Joe, D. *J. Org. Chem.* **1995**, *60*, 1131–1142. (d) Heathcock, C. H.; Kath, J. C.; Ruggeri, R. B. *J. Org. Chem.* **1995**, *60*, 1120–1130. (e) Heathcock, C. H. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 665–681, and references therein.
- (5) (a) Kubota, T.; Matsuno, Y.; Morita, H.; Shinzato, T.; Sekiguchi, M.; Kobayashi, J. *Tetrahedron* **2006**, *62*, 4743–4748. (b) Morita, H.; Ishioka, N.; Takatsu, H.; Iizuka, T.; Kobayashi, J. *J. Nat. Prod.* **2006**, *69*, 418–420. (c) Morita, H.; Ishioka, N.; Takatsu, H.; Kobayashi, J. *Org. Lett.* **2005**, *7*, 459–462.
- (6) (a) Zhang, H.; Yang, S. P.; Fan, C. Q.; Ding, J.; Yue, J. M. *J. Nat. Prod.* **2006**, *69*, 553–557. (b) Yang, S. P.; Zhang, H.; Yue, J. M. *J. Nat. Prod.* **2006**, *69*, 79–82. (c) Zhang, Z. J.; Zhang, C. R.; Yue, J. M. *Tetrahedron* **2005**, *61*, 11038–11045. (d) Chen, X.; Zhan, Z. J.; Yue, J. M. *Helv. Chim. Acta* **2005**, *88*, 854–860.
- (7) Zhang, W.; Guo, Y. W.; Krohn, K. *Chem. Eur. J.* **2006**, *12*, 5122–5127.
- (8) (a) Hao, X. J.; Zhou, J.; Node, M.; Fuji, K. *Yunnan Zhiwu Yanjiu* **1993**, *15*, 203–207. (b) Di, Y. T.; He, H. P.; Liu, H. Y.; Du, Z. Z.; Tian, J. M.; Yang, X. W.; Wang, Y. H.; Hao, X. J. *Tetrahedron Lett.* **2006**, *47*, 5329–5331. (c) Di, Y. T.; He, H. P.; Lu, Y.; Yi, P.; Li, L.; Wu, L.; Hao, X. J. *J. Nat. Prod.* **2006**, *69*, 1074–1076. (d) Mu, S. Z.; Wang, Y.; He, H. P.; Yang, X. W.; Wang, Y. H.; Di, Y. T.; Lu, Y.; Chang, Y.; Hao, X. J. *J. Nat. Prod.* **2006**, *69*, 1065–1069. (e) Li, L.; He, H. P.; Di, Y. T.; Tian, J. M.; Hao, X. J. *Helv. Chim. Acta* **2006**, *89*, 1457–1462. (f) Li, L.; He, H. P.; Di, Y. T.; Gao, S.; Hao, X. J. *Tetrahedron Lett.* **2006**, *47*, 6259–6262.
- (9) Nakano, T.; Seaki, Y. *Tetrahedron Lett.* **1967**, *8*, 4791–4797.
- (10) Broad signals of C-3, C-4, C-6, C-11, C-12, C-19, and C-21 located at or near the 2-oxa-8-azatetracyclo[6.3.0<sup>1,5</sup>.0<sup>3,8</sup>.0<sup>7,11</sup>]dodecane at 300 K only slightly coalesced on heating to 315 K. In addition, all the “missing” carbons were quaternary ones, which might be located at position C-1, C-8, and C-9.

NP060350K