Further *Daphniphyllum* Alkaloids from the Leaves of *Daphniphyllum macropodum* MIQ.

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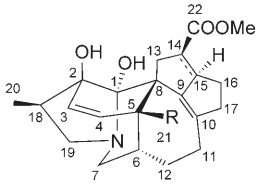
Five new polycyclic *Daphniphyllum* alkaloids, macropodumines F (**1**) and G (**2**), 17-oxoyuzurimine (**3**), and macropodumines H (**4**) and I (**5**), were isolated from the leaves of *D. macropodum* MIQ., collected in Sichuan Province, China. The structures and relative configurations of the new compounds – as well as of four known, related alkaloids – were elucidated on the basis of in-depth spectroscopic and mass-spectrometric analyses, by chemical derivatization, and by comparison of spectroscopic data with those of known compounds.

Introduction. – The plants of the genus *Daphniphyllum* are well-known to be able to produce structurally diverse, complex alkaloids with unique polycyclic skeletons [1]. These compounds have been challenging subjects in synthetic [2] as well as biosynthetic studies [3]. Recently, the discovery of a series of new *Daphniphyllum* alkaloids has significantly broadened the chemical diversity of this group of intriguing natural products [4].

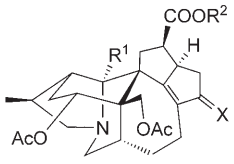
Daphniphyllum macropodum MIQ. is an evergreen tree widely distributed in the southern part of China. The extracts of the leaves and fruits of this plant have long been used as a folk medicine in China for the treatment of inflammation [5]. In our search for bioactive metabolites from Chinese medicinal plants [6], we previously investigated the chemical constituents of the stems of the *D. macropodum* collected from Guangxi Province, China, and three novel alkaloids, macropodumines A–C [4b], with either unprecedented carbon skeletons or a very rare zwitterionic moiety, were isolated. Very recently, we encountered the same plant in Emei Mountain, Sichuan Province, China. Chemical studies on the leaves and barks of this collection resulted in the isolation of two uncommon, new alkaloids, named macropodumines D and E [4a], both of which exhibit unprecedented carbon skeletons, quite different from the isolated alkaloidal constituents of the Guangxi sample.

The apparent chemical diversity of the constituents of *D. macropodum* stimulated us to carry out a systematic phytochemical study on different parts of this plant. First, the leaves of *D. macropodum* of the Sichuan sample were chemically investigated. In the course of this study, five new, minor alkaloids were obtained, macropodumine F (**1**), macropodumine G (**2**), 17-oxoyuzurimine (**3**), macropodumine H (**4**), and macro-

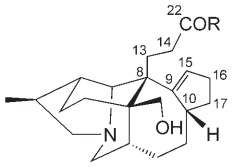
podumine I (**5**), together with four known, related alkaloids, macropodumine D [4a], yuzurimine (**6**) [7], deoxyyuzurimine (**7**) [8], and the zwitterionic alkaloid **8** [9]. This paper deals with the isolation and structural elucidation of the new compounds **1**–**5**, which are all structurally related to the most abundant compound, yuzurimine (**6**), but exhibiting either different oxidation patterns or ring openings.



1 R = CH_2OH
2 R = CH_2OH, $\Delta^{14(15)}$
9 R = CHO



	R^1	R^2	X
3	OH	Me	O
4	H	H	H_2
6	OH	Me	H_2
7	H	Me	H_2



5 R = NH_2
8 R = OH

Results and Discussion. – 1. *Structure Elucidation*. Classical workup [4b] of the $CHCl_3$-soluble material of the 95%-EtOH extract of the leaves of *D. macropodum* yielded the new compounds **1**–**5**, and the known alkaloids **6**, **7**, and macropodumine D; the known compound **8** was, in turn, obtained from the BuOH-soluble material. The known compounds were readily identified as macropodumine D [4a], yuzurimine (**6**) [7], deoxyyuzurimine (**7**) [8], and the zwitterionic alkaloid **8** [9] by analyses of their NMR spectra, and by comparison of spectroscopic and mass-spectrometric (MS) data with those reported in the literature. The new compounds **1**–**4** demonstrated considerable spectroscopic analogy with the co-occurring alkaloid yuzurimine (**6**), possessing a common yuzurimine-type [1] carbon skeleton. In contrast, compound **5**, like the co-occurring related known alkaloid **8**, displayed a 14,15-secoyuzurimine skeleton.

Macropodumine F (**1**)[1]), an optically active, colorless oil ($[\alpha]_D^{23} = -13.8$), showed a pseudo-molecular ion peak at *m*/*z* 402 ($[M+H]^+$) in the ESI mass spectrum, in accord with the molecular formula $C_{23}H_{31}NO_5$, as established by HR-ESI-MS (*m*/*z* 402.2272 ($[M+H]^+$; calc. 402.2280)), indicating nine degrees of unsaturation. In the IR spectrum of **1**, OH (3433 cm^{-1}) and ester C=O (1732 cm^{-1}) bands were evident. The ^{1}H-NMR spectrum of **1** (*Table 1*) exhibited two sharp *doublet*s at δ(H) 5.80 and 5.87 ($J = 10.3$ Hz, 1 H each), indicating the presence of a disubstituted, (*Z*)-configured C=C bond. The ^{13}C-NMR (DEPT) spectrum (*Table 2*) revealed signals due to one ester C=O group, a tetrasubstituted C=C bond, and a disubstituted C=C bond, which accounted for three degrees of unsaturation. The remaining six degrees of unsaturation were, thus, attributed to a hexacyclic ring system. Two oxygenated tertiary C-atoms (δ(C) 94.5, 80.2) were assigned as C(1) and C(2), respectively, based on the HMBC correlations for H_a–C(7), H_b–C(13), and CH_2(19) to C(1); and for H–C(18),

[1]) For systematic names, see the *Exper. Part*.

H_b–C(19), and Me(20) to C(2), respectively (*Fig.*[2])). The location of the disubstituted C=C bond, *i.e.*, $\Delta^{3(4)}$, was determined by the HMBC cross-peaks of H–C(3)/C(1), H–C(3)/C(5), H–C(4)/C(2), H–C(4)/C(5), and H–C(4)/C(8).

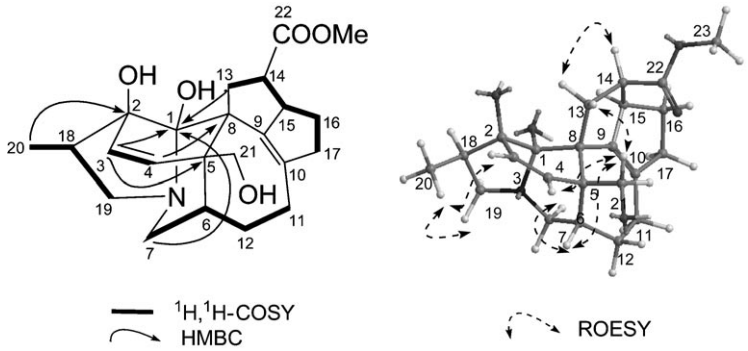


Figure. *Selected 2D-NMR correlations for* **1**

The above-mentioned structural features of **1** were strongly reminiscent of those of yuzurimine C (**9**) [10]. Careful comparison of the NMR data of **1** with those of **9** revealed that **1** differs from **9** only by the substituents at C(5), the aldehyde function in **9** being reduced to a primary alcohol in **1**, as supported by a pair of *AB*-type NMR signals at δ(H) 3.76, 4.10 (2*d*, $J = 11.9$ Hz, 1 H each) (δ(C) 66.3), in agreement with a difference of two mass units in the corresponding mass spectra. This conclusion was further supported by the strong HMBC cross-peaks for CH_2(21) to C(4), C(5), C(6), and C(8) (*Figure*). Moreover, ROESY correlations (*Figure*) of Me(20)/H–C(3), H_b–C(21)/H–C(4), H_b–C(21)/H–C(6), H_b–C(21)/H_b–C(13), H–C(4)/H–C(6), H_a–C(13)/H–C(14), and H–C(14)/H–C(15) suggested that the relative configuration of the stereogenic C-atoms in **1** were the same as those in **9**, based on the known configuration of macropodumine F, a C(21)-reduced derivative of yuzurimine C (**9**).

Macropodumine G (**2**), obtained as an optically active, colorless oil ($[\alpha]_D^{23} = +73.8$), had the molecular formula $C_{23}H_{29}NO_5$ according to HR-ESI-MS, with a molecular weight two mass units lower than that of **1**. Careful comparison of the ^{13}C-NMR data of **2** and **1** (*Table 2*) revealed that **2** exhibited an additional tetrasubstituted C=C bond (δ(C) 118.6, 170.7)), $\Delta^{14(15)}$, conjugated with the $\Delta^{9(10)}$ C=C bond. Significant HMBC correlations of H_b–C(13)/C(14) (δ(C) 118.6), H_b–C(13)/C(15) (δ(C) 170.7), and H_α–C(16)/C(15) supported this assignment, as further confirmed by marked NMR downfield shifts for C(9), C(10), and C(22) with respect to those of **1**. Accordingly, macropodumine G (**2**) was identified as the 14,15-dedydro derivative of **1**.

Both compounds **1** and **2** possess a yuzurimine skeleton, but with a $\Delta^{3(4)}$ C=C bond. To our knowledge, this type of *Daphniphyllum* alkaloids was isolated from a natural source for the second time. In addition, although the C(4) atom of yuzurimine-type alkaloids often carries an OH or AcO group [1], the corresponding 3,4-dehydrated products are rarely encountered.

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[2]) Arbitrary atom numbering.

Table 1. *^{1}H-NMR Data of* **1**–**5**. Recorded at 400 MHz in $CDCl_3$ (**1**–**4**) or CD_3OD (**5**); δ in ppm, J in Hz.

Atom[2])	**1**	**2**	**3**	**4**	**5**
H–C(1)				3.26 (*s*)	3.38 (br. *s*)
H–C(2)			2.28–2.32 (*m*)	2.37–2.41 (*m*)	2.33–2.37 (*m*)
H_α–C(3)	5.80 (*d*, *J* = 10.3)	5.95 (*d*, *J* = 10.3)	1.52–1.56 (*m*)	1.38–1.43 (*m*)	1.49–1.52 (*m*)
H_β–C(3)			2.00–2.05 (*m*)	2.02–2.05 (*m*)	1.67–1.72 (*m*)
H_α–C(4)	5.87 (*d*, *J* = 10.3)	5.88 (*d*, *J* = 10.3)			1.97–2.00 (*m*)
H_β–C(4)			5.35 (*dd*, *J* = 12.0, 7.5)	5.27 (*dd*, *J* = 11.5, 6.4)	2.05–2.09 (*m*)
H–C(6)	1.82–1.85 (*m*)	2.00–2.03 (*m*)	2.68–2.72 (*m*)	2.68 (*t*, *J* = 7.9)	2.41–2.45 (*m*)
H_a–C(7)	3.11–3.15 (*m*)	2.97–3.03 (*m*)	3.40–3.44 (*m*)	3.62 (*d*, *J* = 13.8)	3.29–3.32 (*m*)
H_b–C(7)	2.84–2.86 (*m*)	2.96–2.99 (*m*)	3.32–3.36 (*m*)	3.00 (*dd*, *J* = 13.8, 4.2)	3.21–3.25 (*m*)
H–C(10)					2.96–2.99 (*m*)
H_a–C(11)	2.43–2.47 (*m*)	2.96–2.99 (*m*)	1.75–1.79 (*m*)	1.94–1.97 (*m*)	1.69–1.72 (*m*)
H_b–C(11)	2.05–2.08 (*m*)	2.04–2.07 (*m*)	1.63–1.66 (*m*)	2.40–2.43 (*m*)	1.57–1.62 (*m*)
H_a–C(12)	1.98–2.02 (*m*)	1.90–1.93 (*m*)	2.60–2.65 (*m*)	1.53–1.57 (*m*)	2.01–2.05 (*m*)
H_b–C(12)	1.49–1.53 (*m*)	1.68–1.71 (*m*)	2.41–2.45 (*m*)	1.83–1.87 (*m*)	1.41–1.47 (*m*)
H_a–C(13)	3.04–3.06 (*m*)	3.70–3.74 (*m*)	2.91–2.96 (*m*)	1.87–1.91 (*m*)	2.12–2.16 (*m*)
H_b–C(13)	2.51 (*dd*, *J* = 14.0, 2.3)	2.68–2.73 (*m*)	2.72–2.76 (*m*)	2.98–3.03 (*m*)	1.79–1.83 (*m*)
H_a–C(14)	3.00–3.04 (*m*)		3.18 (*t*, *J* = 9.0)	2.75–2.79 (*m*)	2.13–2.17 (*m*)
H_b–C(14)					2.13–2.17 (*m*)
H–C(15)	3.66–3.69 (*m*)		3.46–3.49 (*m*)	3.40–3.45 (*m*)	5.72 (br. *s*)
H_α–C(16)	1.86–1.90 (*m*)	2.65–2.69 (*m*)	2.49 (*d*, *J* = 5.1)	1.80–1.85 (*m*)	2.25–2.27 (*m*)
H_β–C(16)	1.25–1.28 (*m*)	2.71–2.75 (*m*)	2.49 (*d*, *J* = 5.1)	1.45–1.48 (*m*)	2.46–2.49 (*m*)
H_α–C(17)	2.67–2.72 (*m*)	2.90–2.95 (*m*)		2.51–2.57 (*m*)	1.58–1.62 (*m*)
H_β–C(17)	2.30–2.33 (*m*)	3.00–3.06 (*m*)		2.16 (*dd*, *J* = 14.7, 8.1)	2.13–2.17 (*m*)
H–C(18)	2.27–2.32 (*m*)	2.34–2.38 (*m*)	2.88–2.93 (*m*)	2.46–2.51 (*m*)	2.47–2.53 (*m*)
H_a–C(19)	3.44–3.46 (*m*)	3.63–3.68 (*m*)	3.72–3.77 (*m*)	3.85 (*t*, *J* = 11.3)	3.67–3.71 (*m*)
H_b–C(19)	2.08–2.12 (*m*)	2.13–2.17 (*m*)	2.31–2.37 (*m*)	2.30 (*dd*, *J* = 12.4, 8.2)	2.51–2.55 (*m*)
Me(20)	1.16 (*d*, *J* = 7.5)	1.25 (*d*, *J* = 6.0)	1.08 (*d*, *J* = 7.2)	1.00 (*d*, *J* = 6.6)	1.09 (*d*, *J* = 6.8)
H_a–C(21)	4.10 (*d*, *J* = 11.9)	3.76 (*d*, *J* = 10.8)	4.33 (*d*, *J* = 11.4)	4.35 (*d*, *J* = 11.5)	4.21 (*d*, *J* = 10.7)
H_b–C(21)	3.76 (*d*, *J* = 11.9)	3.71 (*d*, *J* = 10.8)	3.98 (*d*, *J* = 11.4)	4.47 (*d*, *J* = 11.5)	3.58 (*d*, *J* = 10.7)
Me(23)	3.65 (*s*)	3.67 (*s*)	3.60 (*s*)		

Compound **3** was assigned the molecular formula $C_{27}H_{35}NO_8$ by HR-ESI-MS (*m*/*z* 524.2255 ($[M+Na]^+$)), indicating eleven degrees of unsaturation. The ^{13}C-NMR (DEPT) spectra (*Table 2*) revealed the presence of an α,β-unsaturated ketone (δ(C) 139.2, 178.0, 209.2). Further analysis of spectroscopic data (*Tables 1* and *2*) and comparison with those of yuzurimine (**6**) revealed that the structures of compounds **3** and **6** are closely related. In fact, the only difference between them occurred at C(17) (oxo *vs.* methylene group). This difference was in accord with the appearance of a C=O signal at δ(C) 209.2 in the ^{13}C-NMR spectrum of **3**, as well as with a strong UV absorption at λ_{max} 248 nm ($\log \varepsilon = 3.39$). The presence of a C(17)=O group was further confirmed by the significant HMBC correlation of CH_2(16)/C(17). Finally, the ROESY cross-peaks between H–C(2)/Me(20), H–C(4)/H_a–C(13), H_a–C(21)/H–C(6),

Table 2. *^{13}C-NMR Data of* **1**–**8**. At 100 MHz in $CDCl_3$ (**1**–**4**, **6**, **7**), CD_3OD (**5**), or D_2O (**8**); δ in ppm.

Position	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
1	94.5 (*s*)	94.7 (*s*)	96.7 (*s*)	64.6 (*d*)	75.1 (*d*)	96.9 (*s*)	67.1 (*d*)	73.2 (*d*)
2	80.2 (*s*)	80.3 (*s*)	42.4 (*d*)	37.0 (*d*)	39.3 (*d*)	42.1 (*d*)	37.5 (*d*)	36.7 (*d*)
3	126.6 (*d*)	129.7 (*d*)	27.5 (*t*)	27.7 (*t*)	21.7 (*t*)	27.3 (*t*)	27.2 (*t*)	19.7 (*t*)
4	135.6 (*d*)	132.0 (*d*)	71.6 (*d*)	73.6 (*d*)	34.6 (*t*)	72.9 (*d*)	73.3 (*d*)	33.9 (*t*)
5	45.9 (*s*)	45.7 (*s*)	44.8 (*s*)	41.1 (*s*)	43.2 (*s*)	45.1 (*s*)	41.2 (*s*)	41.2 (*s*)
6	35.5 (*d*)	33.0 (*d*)	34.7 (*d*)	33.6 (*d*)	40.4 (*d*)	34.4 (*d*)	35.0 (*d*)	38.1 (*d*)
7	53.2 (*t*)	55.5 (*t*)	58.6 (*t*)	56.3 (*t*)	60.3 (*t*)	58.6 (*t*)	58.0 (*t*)	58.2 (*t*)
8	50.3 (*s*)	49.8 (*s*)	54.7 (*s*)	45.6 (*s*)	43.2 (*s*)	52.1 (*s*)	46.4 (*s*)	41.3 (*s*)
9	143.9 (*s*)	150.1 (*s*)	178.0 (*s*)	143.3 (*s*)	152.9 (*s*)	144.0 (*s*)	144.4 (*s*)	150.7 (*s*)
10	136.5 (*s*)	152.5 (*s*)	139.2 (*s*)	133.9 (*s*)	49.5 (*d*)	136.7 (*s*)	133.6 (*s*)	47.8 (*d*)
11	26.0 (*t*)	26.4 (*t*)	18.9 (*t*)	24.8 (*t*)	34.4 (*t*)	25.3 (*t*)	25.3 (*t*)	33.0 (*t*)
12	25.7 (*t*)	27.8 (*t*)	26.4 (*t*)	26.6 (*t*)	32.4 (*t*)	27.1 (*t*)	26.9 (*t*)	30.4 (*t*)
13	33.6 (*t*)	38.8 (*t*)	36.1 (*t*)	39.4 (*t*)	34.2 (*t*)	37.5 (*t*)	39.1 (*t*)	32.6 (*t*)
14	43.0 (*d*)	118.6 (*s*)	42.5 (*d*)	44.3 (*d*)	33.2 (*t*)	43.1 (*d*)	42.7 (*d*)	32.3 (*t*)
15	57.6 (*d*)	170.7 (*s*)	47.4 (*d*)	53.3 (*d*)	130.6 (*d*)	57.5 (*d*)	54.0 (*d*)	130.7 (*d*)
16	29.7 (*t*)	25.1 (*t*)	38.4 (*t*)	28.3 (*t*)	30.9 (*t*)	28.7 (*t*)	28.2 (*t*)	29.6 (*t*)
17	42.9 (*t*)	42.5 (*t*)	209.2 (*s*)	42.5 (*t*)	33.7 (*t*)	43.2 (*t*)	42.8 (*t*)	32.4 (*t*)
18	44.1 (*d*)	46.4 (*d*)	33.9 (*d*)	36.0 (*d*)	38.8 (*d*)	34.4 (*d*)	38.2 (*d*)	36.2 (*d*)
19	58.3 (*t*)	58.7 (*t*)	64.4 (*t*)	64.7 (*t*)	65.9 (*t*)	64.5 (*t*)	64.8 (*t*)	64.3 (*t*)
20	15.5 (*q*)	18.0 (*q*)	14.7 (*q*)	14.4 (*q*)	14.4 (*q*)	14.7 (*q*)	15.5 (*q*)	13.0 (*q*)
21	66.3 (*t*)	63.2 (*t*)	66.0 (*t*)	66.7 (*t*)	68.0 (*t*)	67.0 (*t*)	67.0 (*t*)	66.5 (*t*)
22	177.6 (*s*)	166.7 (*s*)	173.9 (*s*)	179.5 (*s*)	179.2 (*s*)	175.3 (*s*)	175.0 (*s*)	183.1 (*s*)
23	51.4 (*q*)	50.9 (*q*)	51.5 (*q*)			51.1 (*q*)	51.1 (*q*)	

H_b–C(13)/H–C(14), and H–C(14)/H–C(15) helped us to assign the relative configurations at all stereogenic centers of **3**, which are identical as those in **6**. From the above data, the structure of **3** was, thus, elucidated as 17-oxoyuzurimine.

Macropodumine H (**4**) was obtained as an optically active, colorless, amorphous powder ($[\alpha]_D^{23} = +14.5$). HR-ESI-MS showed the $[M+H]^+$ ion at m/z 458.2530, suggesting the molecular formula $C_{26}H_{35}NO_6$, the molecular weight being 14 mass units lower than that of deoxyyuzurimine (**7**). The IR spectrum of **4** showed the presence of ester C=O (1736 cm^{-1}) and carboxylate (1572 cm^{-1}) functions. The NMR data of **4** (*Tables 1* and *2*) were similar to those of **7**, except for the absence of a MeO group (δ(H) 3.60, δ(C) 51.1) in **7**, suggesting that **4** was the free-acid analogue of **7**. This was confirmed by methylation of **4** with diazomethane, which afforded the expected methyl ester, whose spectroscopic data (and $[\alpha]_D$ value) were identical to those of **7**. Thus, macropodumine H (**4**) was identified as the demethylated, free-acid form of deoxyyuzurimine (**7**).

Macropodumine I (**5**) showed a pseudo-molecular ion peak at m/z 359 ($[M+H]^+$) in the ESI mass spectrum. The even mass unit of **5** indicated the presence of a second N-atom, which was unambiguously confirmed by HR-ESI-MS, providing the molecular formula $C_{22}H_{34}N_2O_2$ (m/z 359.2681 ($[M+H]^+$; calc. 359.2699). The ^{13}C-NMR data of **5** (*Table 2*) showed great similarity to those of the co-occurring alkaloid **8**, except for C(22) (δ(C) 179.2 *vs.* 183.1). However, the polarities of **5** and **8** were quite different, the later being much more polar than the former according to TLC (SiO_2; $CHCl_3$/MeOH

8:2): R_f 0.75 (**5**) *vs.* 0.11 (**8**). The less polar nature of **5**, bearing in mind the molecular formula $C_{22}H_{34}N_2O_2$, indicated that the COOH group of **8** was changed to a primary amide in **5**, in accord with a mass difference of one atomic unit. IR Absorption bands of a primary amide (3523, 3501, 1701 cm^{-1}) for **5** further supported this assumption. Detailed analysis of the 2D-NMR (^1H,^1H-COSY, HSQC, HMBC) spectra justified the planar structure of **5**. The β-orientation of H–C(6), H–C(10), Me(20), and CH_2(21) in **5**, deduced from the ROESY spectrum, were the same as those in **8**.

2. *Biological Studies.* All the new and known compounds were tested for their inhibitory properties against human protein tyrosine phosphatase 1B (hPTP1B), a key target for the treatment of type-II diabetes and obesity [11]. However, none of them showed an inhibitory effect. Other bioassays, including cytotoxicity and anti-inflammation tests, are currently underway.

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Experimental Part

General. Column chromatography (CC) was performed on silica gel (200–300 mesh; *Qingdao Haiyang*), *LiChroprep NH_2* (40–63 μm; *Merck*), and *Sephadex LH-20* (*Amersham Biosciences*). Thin-layer chromatography (TLC) was performed on precoated *G60 F-254* silica-gel plates (*Yantai*). UV Spectra: *756 CRT* spectrophotometer (Shanghai); λ_{max} (log ε) in nm. Optical rotation: *Perkin-Elmer 341* polarimeter. IR Spectra: *Nicolet Magna FT-IR-750* spectrophotometer; in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Varian Mercury-400* apparatus, at 400/100 MHz for ^1H and ^{13}C, resp.; chemical shifts δ in ppm rel. to residual solvent peaks [$CDCl_3$: δ(H) 7.26, δ(C) 77.0; CD_3OD: δ(H) 3.30, δ(C) 49.5], coupling constant *J* in Hz. ESI- and HR-ESI-MS: *Q-TOF Micro* LC-MS/MS mass spectrometer; in *m*/*z*.

Plant Material. Daphniphyllum macropodum MIQ. was collected in Emei Mountain, Sichuan Province, P. R. China, in April 2005, and identified by Prof. *Hong-Gui Xu*, Hong Kong Baptist University, China. A voucher specimen (No. 05P-18) is available for inspection at the Herbarium of the Institute of Materia Medica, Chinese Academy of Science, Shanghai.

Extraction and Isolation. The air-dried, powdered leaves (1.1 kg) of *D. macropodum* were repeatedly extracted with 95% EtOH (3 × 7 d) at r.t. Evaporation of the solvent gave a residue, which was suspended in H_2O (1000 ml), and adjusted to pH 4–5 by addition of 2N aq. H_2SO_4. The acidified mixture was defatted with AcOEt (3 × 1000 ml), and the aq. layer was adjusted to pH 9–10 with sat. aq. Na_2CO_3 soln., and then extracted with $CHCl_3$ (3 × 1000 ml) and BuOH (3 × 1000 ml). The $CHCl_3$-soluble part was subjected to CC (SiO_2; $CHCl_3$/MeOH/Et_2NH 50:1:0.1 → 1:1:0.1). The fraction eluted with $CHCl_3$/MeOH/Et_2NH 25:1:0.1 was further purified by CC (*LiChroprep NH_2*; 1. petroleum ether/AcOEt 4:1; 2. $CHCl_3$/MeOH 95:5) to afford pure **1** (8.6 mg), **2** (13.8 mg), **3** (4.2 mg), **4** (23.5 mg), **5** (6.1 mg), **6** (802 mg), **7** (21.1 mg), and macropodumine D (6.1 mg). The above BuOH-soluble material was also subjected to CC (SiO_2; $CHCl_3$/MeOH/Et_2NH 50:1:0.1 → 1:1:0.1) to afford four major fractions (*Fr. 1–Fr. 4*). *Fr. 4* was further purified by CC (*Sephadex LH-20*; $CHCl_3$/MeOH 1:1) to afford **8** (20.5 mg).

Macropodumine F (= *Methyl (3*R**,3a*S**,5a*R**,6*S**,10a*R**,11*R**,12aS*,12b*S**)-2,3,3a,5a,6,8,9,10,10a,11,12,12b-Dodecahydro-3a,12b-dihydroxy-5a-(hydroxymethyl)-3-methyl-7*H*-1,6-methanocyclopent[1,8]-azuleno[4,3a-g]indole-11-carboxylate*; **1**). Colorless oil. $[\alpha]_D^{23} = -13.8$ ($c = 0.53$, $CHCl_3$). IR (KBr): 3433, 2950, 2925, 1732, 1436, 1170. ^1H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. ESI-MS: 402 ($[M+H]^+$), 825 ($[2M+Na]^+$). HR-ESI-MS: 402.2272 ($[M+H]^+$, $C_{23}H_{32}NO_5^+$; calc. 402.2280).

Macropodumine G (= *Methyl (3*R**,3a*S**,5a*R**,6*S**,10a*R**,11*R**,12aS*,12b*S**)-2,3,3a,5a,6,8,9,10,12,12b-Decahydro-3a,12b-dihydroxy-5a-(hydroxymethyl)-3-methyl-7*H*-1,6-methanocyclopent[1,8]azuleno[4,3a-g]indole-11-carboxylate*; **2**). Colorless oil. UV (MeOH): 303 (3.76). $[\alpha]_D^{23} = +73.8$ ($c = 0.42$, $CHCl_3$). IR (KBr): 3433, 2922, 1697, 1629, 1267, 1116. ^1H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. ESI-MS: 400 ($[M+H]^+$), 821 ($[2M+Na]^+$). HR-ESI-MS: 400.2104 ($[M+H]^+$, $C_{23}H_{30}NO_5^+$; calc. 400.2124).

17-Oxoyuzurimine (= *Methyl (3*S*,3a*R*,5*R*,5a*S*,6*S*,10a*R*,11*R*,12a*S*,12b*R*)-5-Acetoxy-5a-(acetoxymethyl)-2,3,3a,5,5a,6,7,8,9,10,10a,11,12,12b-tetradecahydro-12b-hydroxy-3-methyl-9-oxo-4*H*-1,6-methanocyclopent[1,8]azuleno[4,3a-g]indole-11-carboxylate*; **3**). Colorless oil. $[\alpha]_D^{23} = +14$ ($c = 0.26$, $CHCl_3$). UV (MeOH): 248 (3.39). IR (KBr): 2924, 1741, 1702, 1658, 1247, 1037. ^{1}H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. ESI-MS: 502 ($[M+H]^+$), 524 ($[M+Na]^+$). HR-ESI-MS: 524.2255 ($[M+Na]^+$, $C_{27}H_{35}NNaO_8^+$; calc. 524.2260).

Macropodumine H (= *(3*S*,3a*R*,5*R*,5a*S*,6*S*,10a*R*,11*R*,12a*S*,12b*S*)-5-Acetoxy-5a-(acetoxymethyl)-2,3,3a,5,5a,6,7,8,9,10,10a,11,12,12b-tetradecahydro-3-methyl-4*H*-1,6-methanocyclopent[1,8]azuleno[4,3a-g]indole-11-carboxylic Acid*; **4**). Amorphous powder. $[\alpha]_D^{23} = +14.5$ ($c = 0.47$, $CHCl_3$). IR (KBr): 3427, 2923, 1736, 1572, 1259. ^{1}H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. ESI-MS: 458 ($[M+H]^+$), 937 ($[2M+Na]^+$). HR-ESI-MS: 458.2530 ($[M+H]^+$, $C_{26}H_{36}NO_6^+$; calc. 458.2543).

Macropodumine I (= *(3S*,3aR*,5aR*,6S*,8aR*,11bS*,11cS*)-2,3,3a,5,5a,6,7,8,8a,9,10,11c-Dodecahydro-5a-(hydroxymethyl)-3-methyl-1,6-methano-1*H*-azuleno[5,4-g]indole-11b(4*H*)-propanamide*; **5**). Colorless oil. $[\alpha]_D^{23} = -22.1$ ($c = 0.38$, MeOH). IR (KBr): 3523, 3501, 3369, 2919, 1701, 1662, 1631, 1109. ^{1}H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. ESI-MS: 359 ($[M+H]^+$), 739 ($[2M+Na]^+$). HR-ESI-MS: 359.2681 ($[M+H]^+$, $C_{22}H_{35}N_2O_2^+$; calc. 359.2699).

Methylation of **4**. An etheral soln. of diazomethane (0.5 ml) was added to a stirred soln. of **4** (1.5 mg) in MeOH (0.5 ml) at r.t. The mixture was stirred for 20 min and concentrated *in vacuo* to afford the expected Me ester **7**.

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