Agladupols A–E, Triterpenoids from *Aglaia duperreana*

Bo-Jun Xie, Sheng-Ping Yang, Hua-Dong Chen, and Jian-Min Yue*

State Key Laboratory of Drug Research, Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, 555 Zu Chong Zhi Road, Zhangjiang Hi-Tech Park, Shanghai 201203, People's Republic of China

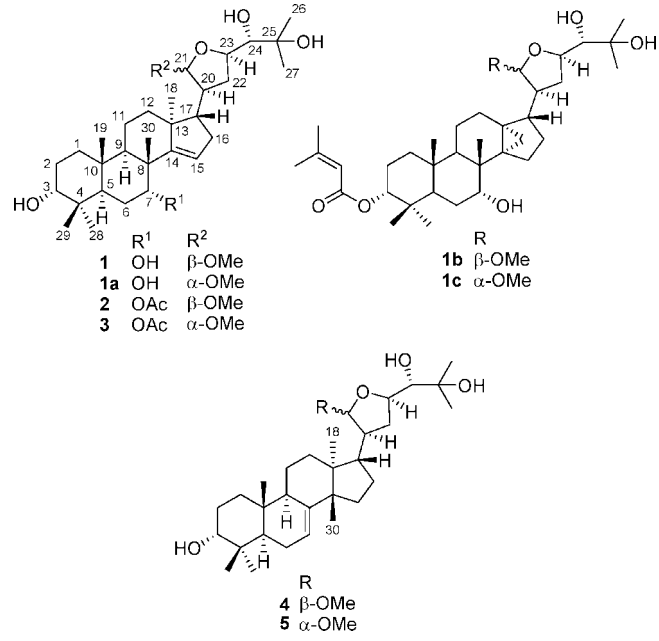
Received June 14, 2007

Three new apotirucallane-type triterpenoids, agladupols A–C (**1**–**3**), and two new tirucallane-type triterpenoids, agladupols D and E (**4** and **5**), along with four known compounds, were isolated from the leaves and stems of *Aglaia duperreana* (Meliaceae). The structures of compounds **1**–**5** were elucidated by spectroscopic data. A ^{13}C NMR-based general rule for assignment of the C-21 configuration in the side chain of apotirucallane- and tirucallane-type triterpenoids was proposed. According to this, the relative stereochemistry of 21-*O*-methyltoosendanpentol (**1a**), a known compound with the relative configurations of the stereocenters in the side chain undetermined, was completely assigned.

The genus *Aglaia* is composed of about 250–300 species distributed mainly in India, Malaysia, Australia, and Polynesia, of which seven species and one variety grow in the south of China.[1] Studies have revealed that plants of this genus are rich in apotirucallane- and tirucallane-type triterpenoids.[2] Investigation of flowers of *Aglaia duperreana* Pierre (Meliaceae) collected in Vietnam led to the isolation of 13 insecticidal cyclopentatetrahydrobenzofuran derivatives of rocaglamides.[3]

In the current study, five new triterpenoids (**1**–**5**) and four known compounds, 21-*O*-methyltoosendanpentol,[4] tricyclohumuladiol,[5] caryolane-1,9β-diol,[6] and 3,3a-dihydroxy-8a-(3-hydroxy-4-methoxy-phenyl)-4,6-dimethoxy-1-phenyl-2,3,3a,8a-tetrahydro-1*H*-8-oxa-cyclopenta[*a*]indene-2-carboxylic acid dimethylamide,[7] were isolated from the leaves and stems of *A. duperreana* that were collected in Xishuangbanna, China. A ^{13}C nuclear magnetic resonance (NMR)-based rule for assignment of the configuration at C-21 in the side chain of apotirucallane- and tirucallane-type triterpenoids was proposed. This allowed for the assignment of configuration to 21-*O*-methyltoosendanpentol (**1a**), a known compound.

Agladupol A (**1**) had molecular formula $C_{31}H_{52}O_6$ as deduced from the HRESIMS. The IR spectrum indicated the presence of OH (3440 cm^{-1}) and double bond (1637 cm^{-1}) groups. The ^1H NMR spectrum (Table 1) showed seven tertiary methyl groups (δ 0.86, 0.90, 0.96, 1.03, 1.05, 1.25, and 1.25), one methoxyl (δ 3.35), one olefinic proton (δ 5.46), and five protons bonded to carbons bearing oxygen (δ 3.18, 3.42, 3.92, 4.45, and 4.77). A total of 31 carbon resonances were observed in the ^{13}C NMR spectrum (Table 2). These were assigned, by distortionless enhancement by polarization transfer (DEPT) and heteronuclear single-quantum coherence (HSQC) experiments, to one trisubstituted double bond (δ 162.0 and 119.5), eight methyl, seven sp^3 methylene, nine sp^3 methine, and five sp^3 quaternary carbons. A comparison of the NMR data of **1** with those of 21-*O*-methyltoosendanpentol (**1a**),[4] indicated that **1** was an analogue of **1a**, an apotirucallane-type triterpenoid. The ^{13}C NMR data of **1** and **1a** suggested that two compounds shared the same tetracyclic system, and the major differences were in the side chain. This was confirmed by the 2D NMR data (Supporting Information). The heteronuclear multiple-bond correlations (HMBCs) of H-21/C-23 and OMe/C-21 revealed that the C-21 and C-23 were linked via an oxygen to form a tetrahydrofuran ring and the methoxyl was located C-21 to form a ketal group. In combination with the chemical shifts of the relevant protons and carbons, the HMBCs of H_2-22/C-24, H-24/C-25, H-24/C-26, H-24/C-27, H_3-26/C-25, and H_3-27/C-25 placed hydroxyls at C-24 and C-25. The structure of **1** was thus established as depicted.



The rotating-frame Overhauser enhancement spectroscopy (ROESY) spectrum showed that the relative configuration of the tetracyclic core in **1** was identical to that of **1a**. The ROESY cross-peaks of CH_3-18/H-21, H-21/H-12α, CH_3-18/H-20, and H-20/H-23 revealed that H-21, H-20, and H-23 were α-oriented. The rotation of C-23/C-24 seemed fairly fixed by the steric bulk or the hydrogen bond formed between 24-OH and the oxygen of the furan ring to give a favorable conformation in the solvent as judged from the small coupling constant ($J = 1.9$ Hz) between H-24 and H-23 and the ROESY correlations of H-24/H_2-22 and H-24/H-23. This indicated that H-24 was β-oriented. The small coupling constant ($J_{23,24} = 1.9$ Hz) indicated that they were in a *gauche* relationship. Furthermore, the ROESY correlations of MeO-21/H_3-26 and H-23/H_3-27 indicated that C-25 and H-23 were also in a *gauche* relationship, indicating that H-24 was β-oriented. Thus, the structure of agladupol A (**1**) was as indicated. In comparison to the known compound **1b**,[8] the highly similar ^{13}C NMR data (Table 2) of the side chain in both compounds **1** and **1b**, except for the C-20 of **1b**, were shifted downfield somewhat because of the deshielding effect of the 13,14,18-cyclopropyl group and further verified stereochemistry of the side chain of **1**.

* To whom correspondence should be addressed. Tel: +86-21-50806718. Fax: +86-21-50806718. E-mail: jmyue@mail.shcnc.ac.cn.

10.1021/np0702842 CCC: $37.00
Published on Web 08/22/2007

Table 1. ^{1}H NMR (400 MHz, $CDCl_3$) Spectroscopic Data for **1**–**4**

position	1	2	3	4	5
1α	1.34 m	1.36 m	1.32 m	1.45 m	1.46 m
1β	1.31 m	1.36 m	1.32 m	1.33 m	1.36 m
2α	1.55 m	1.57 m	1.51 m	1.58 m	1.58 m
2β	1.90 m	1.94 m	1.90 m	1.89 m	1.90 m
3	3.42 dd (2.9, 2.4)	3.42 br s	3.37 br s	3.47 br s	3.43 d (2.9)
5	1.94 m	1.83 m	1.78 m	1.73 m	1.76 m
6α	1.69 m	1.62 m	1.60 m	1.98 m	1.92 m
6β	1.69 m	1.74 m	1.70 m	1.91 m	2.02 m
7	3.92 dd (2.8, 2.6)	5.17 br s	5.11 br s	5.27 br s	5.23 br s
9	1.99 m	2.02 m	1.99 m	2.30 m	2.34 m
11α	1.48 m	1.71 m	1.68 m	1.55 m	1.50 m
11β	1.71 m	1.48 m	1.42 m	1.47 m	1.57 m
12α	1.58 m	1.58 m	1.41 m	1.27 m	1.51 m
12β	1.50 m	1.48 m	1.41 m	1.84 m	1.71 m
15α	5.46 br s	5.21 br s	5.15 br s	1.49 m	1.71 m
15β				1.49 m	1.92 m
16α	2.13 m	1.94 m	1.91 m	1.26 m	1.25 m
16β	2.13 m	2.05 m	2.05 m	1.84 m	1.90 m
17	1.97 m	1.91 m	1.62 m	1.98 m	1.74 m
18	1.03 s	1.00 s	0.98 s	0.85 s	0.86 s
19	0.90 s	0.90 s	0.86 s	0.78 s	0.77 s
20	2.16 m	2.14 m	2.25 m	1.96 m	2.15 m
21	4.77 d (4.1)	4.75 br d (4.2)	4.75 d (3.6)	4.71 br s	4.76 d (3.3)
22α	1.90 m	1.87 m	1.84 m	1.88 m	1.49 m
22β	1.95 m	1.87 m	1.73 m	1.88 m	1.49 m
23	4.45 ddd (1.9, 6.7, 8.9)	4.43 m	4.19 m	4.43 m	4.19 m
24	3.18 d (1.9)	3.16 d (8.1)	3.20 d (7.2)	3.18 br d (7.9)	3.22 d (5.4)
26	1.25 s[a]	1.26 s[a]	1.21 s[a]	1.28 s[a]	1.27 s[a]
27	1.25 s[a]	1.26 s[a]	1.25 s[a]	1.28 s[a]	1.30 s[a]
28	0.96 s	0.85 s	0.80 s	0.94 s	0.93 s
29	0.86 s	0.83 s	0.78 s	0.92 s	0.91 s
30	1.05 s	1.08 s	1.04 s	1.00 s	0.98 s
MeO	3.35 s	3.36 s	3.31 s	3.37 s	3.31 s
Ac		1.95 s	1.91 s		

[a] May be exchanged in the same column.

Agladupol B (**2**) had molecular formula $C_{33}H_{54}O_7$ as determined by HRESIMS. IR absorptions at 3436, 1739, and 1635 cm^{-1} indicated the presence of hydroxyl, ester carbonyl, and double bond functions, respectively. The ^{1}H and ^{13}C NMR spectra of **2** and **1** were similar, except for the presence of an additional acetyl group (δ_C 170.4, 21.3; δ_H 1.95) in **2**, suggesting that it was an acetylated derivative of **1**. The chemical shift of H-7 (δ 5.17) in **2** was downfield-shifted $\Delta\delta$ 1.25 from that of **1**, which indicated the presence of a 7-OAc; this was confirmed by the HMBC from H-7 to the carbonyl carbon signal of the acetyl. The acetoxyl at C-7 was assigned α orientation by the ROESY cross-peaks of H-7/H$_3$-30 (β). In comparison to the ^{13}C NMR data of **1**, the C-8 and C-14 of **2** were upfield-shifted $\Delta\delta$ 2.1 and 2.3, respectively, because of the shielding effect of 7-OAc, while its C-7 and C-9 were downfield-shifted $\Delta\delta$ 3.3 and 1.4, respectively, because of the deshielding effect of 7-OAc. The complete assignments of the ^{1}H and ^{13}C NMR of **2** were achieved by a comprehensive analysis of 2D NMR spectra including HSQC, HMBC, and ROESY (Supporting Information).

Agladupol C (**3**) had the same molecular formula ($C_{33}H_{54}O_7$) as **2**. The NMR data (Tables 1 and 2) of **3** revealed that it was a stereoisomer of **2**. The only difference between compounds **2** and **3** was at C-21. The carbon resonance of **3** was severely downfield-shifted ($\Delta\delta$ 4.7) compared to that of **2**, suggesting that the 21-OMe of **3** was α-oriented. This was supported by the downfield-shifted resonance of C-17 (δ 57.4). For a 21β-OMe, such as the cases of **1** and **2**, the C-17 usually upfield resonates because of the γ-gauche effect of 21β-OMe.[9] The side chain assigned for **3** was identical to that of the known compound **1c**.[8] The ^{13}C NMR of the side chain in compounds **3** and **1c** were similar, except that C-20 of **3** was slightly upfield because of the presence of a 18-Me instead of the 13,14,18-cyclopropyl group of **1c**. The structure of **3** was further confirmed by 2D NMR experiments, including HSQC, HMBC, and ROESY spectra.

Agladupol D (**4**) had molecular formula $C_{31}H_{52}O_5$. Its IR spectrum indicated the presence of hydroxyl(s) (3446 cm^{-1}) and a double bond (1637 cm^{-1}). The ^{13}C NMR data, along with the DEPT and HSQC experiments, classified the functionalities as eight methyl, eight sp^3 methylene, eight sp^3 methine, five sp^3 quaternary carbons, and a trisubstituted double bond (δ 118.1 and 145.7). The ^{1}H NMR spectrum indicated eight methyl groups; seven were tertiary ones (δ 0.78, 0.85, 0.92, 0.94, 1.00, 1.28, and 1.28), and one was a methoxyl group (δ 3.37). The data suggested that **4** was a tirucallane-type triterpenoid. Extensive analysis of its HMBC spectrum afforded the planar structure of **4**. The relative configuration of **4** was established by the ROESY experiment. The structure of **4** was thus elucidated.

Compound **4** shared the same tetracyclic core with a known compound sapelin A,[10] and their corresponding carbon resonances in the tetracyclic core were very similar, except for C-18 and C-19, with a similarity coefficient of $R^2 = 0.99092$. If the assignments for C-18 and C-19 of sapelin A were reversed, the similarity coefficient of the tetracyclic core between two compounds **4** and sapelin A becomes $R^2 = 0.99972$. This suggested that the assignments for C-18 and C-19 of sapelin A could be reversed.

The ^{13}C NMR data of agladupol E (**5**) were very similar to those of **4**, except for differences of the carbons close to C-21. This observation implied that compound **5** was probably the 21-epimer of **4**. The chemical shift of C-21 (δ 108.9) was very close to that (δ 109.4) of **3**, which had a 21α-OMe, indicating that the 21-OMe of **5** was also α-oriented. Further, as compared with compound **4**, the signals of C-17 and C-22 of **5** were downfield-shifted ca. $\Delta\delta$ 5.3 and 2.2, respectively, largely because of the absence of the γ-gauche effects from 21-OMe,[9] supporting the stereochemistry of C-21 as assigned for **5**, The structure of agladupol E was thus elucidated to be **5**.

The side chains of compounds **1**–**5** shared the same planar structure, but there were differences in the orientation of MeO-21.

Table 2. ^{13}C NMR (100 MHz, $CDCl_3$) Spectroscopic Data for **1–4**

position	**1**	**1a**[a]	**1b**[b]	**1c**[b]	**2**	**3**	**4**	**5**
1	32.5	32.83	34.0	33.9	32.5	32.5	31.1	31.6
2	25.0	25.05	22.9	22.8	25.0	25.0	25.3	25.3
3	76.2	76.20	77.0	77.1	75.9	75.8	76.1	76.1
4	37.0	37.07	36.3	36.3	36.9	36.8	37.3	37.3
5	40.4	40.51	41.3	41.3	41.8	41.7	44.5	44.5
6	23.6	23.74	24.2	24.2	23.2	23.1	23.8	23.8
7	72.2	72.30	74.3	74.2	75.5	75.4	118.1	118.1
8	44.3	44.44	39.1	39.1	42.2	42.1	145.7	145.6
9	41.6	41.71	44.0	43.9	43.0	43.0	48.4	48.3
10	37.6	37.72	37.3	37.3	37.4	37.3	34.7	34.7
11	16.3	16.27	16.3	16.1	16.4	16.3	17.4	17.4
12	32.8	32.62	25.4	25.6	33.2	33.2	31.1	31.1
13	46.6	46.98	28.9	28.5	46.4	46.6	43.4	43.5
14	162.0	162.43	37.1	36.3	159.7	159.9	50.7	50.9
15	119.5	119.20	26.3	25.9	118.2	117.8	34.1	34.3
16	34.9	34.71	27.6	26.3	35.0	34.6	27.2	27.3
17	52.3	57.54	44.6	48.4	52.2	57.4	44.9	50.2
18	19.8	19.32	13.6	13.6	19.9	19.3	23.1	22.5
19	15.2	15.24	15.7	15.7	15.3	15.3	12.9	12.9
20	44.6	45.90	48.6	49.1	44.7	45.8	46.2	47.7
21	104.6	109.55	105.3	109.2	104.7	109.4	104.8	108.9
22	31.4	33.80	31.0	32.2	31.3	33.6	31.5	33.7
23	78.7	76.90	78.9	77.0	78.7	76.7	78.7	76.6
24	76.6	75.59	76.6	75.5	76.5	75.4	76.5	75.4
25	72.9	73.07	72.9	73.1	72.9	72.9	72.9	73.0
26	26.3[c]	26.37[c]	26.4	26.4	26.4[c]	26.3[c]	26.3[c]	26.4[c]
27	26.3[c]	26.49[c]	26.4	26.5	26.3[c]	26.2[c]	26.2[c]	26.3[c]
28	28.0	28.07	27.8	27.8	28.0	27.9	27.7	27.7
29	22.1	22.15	21.9	21.9	21.9	21.8	21.7	21.7
30	27.7	27.73	19.5	19.5	27.5	27.4	27.2	27.1
OCH_3	55.1	55.60	55.2	55.7	55.1	55.5	55.1	55.6
$OCO\underline{C}H_3$					21.3	21.2		
$O\underline{C}OCH_3$					170.4	170.4		

[a] Literature data, see ref 4. [b] Literature data, see ref 8. [c] May be exchanged in the same column.

Observation of the ^{13}C NMR data of the side chains of these compounds (Table 2), the chemical shifts of C-21, allowed us to distinguish between the α and β orientation of MeO-21. For the compounds having MeO-21β, the C-21 carbon resonances normally appeared at δ 105.0 ± 0.5, while for the ones with a MeO-21α, the chemical shifts of C-21 usually resonated at δ 109.0 ± 0.5.[8,9] According to this rule, the stereochemistry of 21-*O*-methyltoosendanpentol (**1a**),[4] a known compound reported with the unassigned configuration of the side chain, could be assigned to have a MeO-21α on the basis of the chemical shift of C-21 (δ 109.55). The relative stereochemistry of C-20, C-23, and C-24 of **1a** was then assigned as depicted by comparing the corresponding ^{13}C NMR data with those of **3**.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a Perkin-Elmer 341 polarimeter (Na filter, λ = 589 nm). IR spectra were recorded on a Perkin-Elmer 577 spectrometer with KBr disks. NMR spectra were measured on a Bruker AM-400 spectrometer. EIMS and HREIMS (70 eV) were carried out on a Finnigan MAT 95 mass spectrometer. Electrospray ionization mass spectrometry (ESIMS) spectra were carried out on a Bruker Esquire 3000plus instrument, and HRESIMS spectra were carried out on a Waters-Micromass Q-TOF mass spectrometer. All solvents used were of analytical grade (Shanghai Chemical Reagents Company Ltd.). Silica gel (200–300 mesh), silica gel H (Qingdao Haiyang Chemical Co. Ltd., People's Republic of China), C18 reversed-phase silica gel (150–200 mesh, Merck), and MCI gel (CHP20P, 75–150 μm, Mitsubishi Chemical Industries Ltd., Japan) were used for column chromatography. Precoated thin-layer chromatography (TLC) plates with silica gel GF254 (Qingdao Haiyang Chemical Co. Ltd., People's Republic of China) were used for TLC.

Plant Material. The plant material of *A. duperreana* was collected from Xishuangbanna, China, and was authenticated by Professor You-Kai Xu of Xishuangbanna Tropical Botanical Garden, Chinese Academy of Sciences. A voucher specimen (accession number AD-X-lsze2Y) has been deposited in the Shanghai Institute of Materia Medica.

Extraction and Isolation. The dried and powdered leaves and stems of *A. duperreana* (5 kg) were percolated with 95% EtOH for 3 times. After removal of the solvent under reduced pressure, the EtOH extract (290 g) was partitioned between H_2O and EtOAc to give an EtOAc-soluble fraction (58 g), which was subjected to a MCI column [MeOH/H_2O, 50:50 → 90:10 (v/v)] to obtain five fractions (1–5). Fraction 2 was separated on a silica gel column [petroleum ether/EtOAc (1:2) and petroleum ether/acetone (3:1)], to give tricyclohumuladiol (19 mg), caryolane-1, 9β-diol (12 mg), and 3,3a-dihydroxy-8a-(3-hydroxy-4-methoxy-phenyl)-4,6-dimethoxy-1-phenyl-2,3,3a,8a-tetrahydro-1*H*-8-oxa-cyclopenta[*a*]indene-2-carboxylic acid dimethylamide (24 mg). Fraction 3 was subjected to a silica gel column and gradient elution with petroleum ether/acetone (from 20:1 to 0:1) to afford three fractions (3a–3c). Fraction 3b (1.3 g) was separated on a silica gel column (petroleum ether/EtOAc, 2:1; $CHCl_3$/MeOH, 200:1) to yield two major parts, and each of them was purified on a reversed-phase column (MeOH/H_2O, 80:20 → 85:15) to give **3** (122 mg) and **2** (28 mg), respectively. Fraction 3c (1.6 g) was separated on a silica gel column ($CHCl_3$/MeOH, 50:1) to afford subfractions 3c.1–3c.2. Purification of subfraction 3c.1 (0.5 g) using a silica gel column (petroleum ether/EtOAc, 1:1; $CHCl_3$/MeOH, 20:1) and then a reversed-phase silica gel column (MeOH/H_2O, 76:24 → 78:22) gave 21-*O*-methyltoosendanpentol (30 mg) and **1** (24 mg). In a similar purification procedure, subfraction 3c.2 (0.35 g) afforded compounds **4** (53 mg) and **5** (69 mg).

Agladupol A (1): white amorphous powder. $[\alpha]_D^{20}$ −35.6 (*c* 0.8500, $CHCl_3$). IR (KBr, disc) ν_{max}: 3440, 2937, 1637, 1460, 1385, 1061, 1036 cm^{-1}. ^1H NMR: see Table 1. ^{13}C NMR: see Table 2. EIMS *m/z*: 399 (9), 330 (100), 312 (30), 297 (10), 235 (7), 160 (25). HRESIMS *m/z*: 543.3678 ($[M + Na]^+$, calcd for $C_{31}H_{52}O_6Na$, 543.3662).

Agladupol B (2): white amorphous powder. $[\alpha]_D^{20}$ −28.1 (*c* 1.3500, $CHCl_3$). IR (KBr, disc) ν_{max}: 3442, 2933, 1730, 1637, 1458, 1377, 1254, 1028 cm^{-1}. ^1H NMR: see Table 1. ^{13}C NMR: see Table 2. EIMS *m/z*: 441 (4), 372 (90), 312 (100), 297 (19), 279 (12), 160 (46). HRESIMS *m/z*: 585.3782 ($[M + Na]^+$, calcd for $C_{33}H_{54}O_7Na$, 585.3767).

Agladupol C (3): white amorphous powder. $[\alpha]_D^{20}$ −98.7 (*c* 4.2150, $CHCl_3$). IR (KBr, disc) ν_{max}: 3437, 2976, 1740, 1635, 1458, 1377, 1246, 1097, 1030 cm^{-1}. ^1H NMR: see Table 1. ^{13}C NMR: see Table 2. EIMS *m/z*: 441 (5), 372 (100), 312 (68), 297 (13), 160 (27). HRESIMS *m/z*: 585.3716 ($[M + Na]^+$, calcd for $C_{33}H_{54}O_7Na$, 585.3767).

Agladupol D (4): white amorphous powder. $[\alpha]_D^{20}$ +11.0 (*c* 0.0950, $CHCl_3$). IR (KBr, disc) ν_{max}: 3446, 2949, 2872, 1637, 1460, 1385, 1367, 1094, 982, 905 cm^{-1}. ^1H NMR: see Table 1. ^{13}C NMR: see Table 2. EIMS *m/z*: 504 (20), 489 (9), 457 (65), 439 (61), 415 (60), 393 (22), 381 (32), 367 (100), 349 (21), 314 (20), 299 (43). HREIMS *m/z*: 504.3835 ($[M]^+$, calcd for $C_{31}H_{52}O_5$, 504.3815).

Agladupol E (5): white amorphous powder. $[\alpha]_D^{20}$ −46.0 (*c* 0.1400, $CHCl_3$). IR (KBr, disc) ν_{max}: 3444, 2949, 2885, 1637, 1462, 1385, 1365, 1099, 1038, 982 cm^{-1}. ^1H NMR: see Table 1. ^{13}C NMR: see Table 2. EIMS *m/z*: 504 (58), 457 (86), 439 (72), 415 (83), 393 (40), 367 (100), 349 (24), 314 (24), 299 (78). HREIMS *m/z*: 504.3816 ($[M]^+$, calcd for $C_{31}H_{52}O_5$, 504.3815).

Acknowledgment. Financial support from the Key Project of the National Natural Science Foundation (Grant 30630072) and the Shanghai Municipal Scientific Foundation (Grant 06DZ22028) of the People's Republic of China is gratefully acknowledged. We thank Professor Y.-K. Xu for the collection and identification of the plant material.

Supporting Information Available: Selected HMBC and ROESY correlations of agladupols A–D (**1–4**) and IR, ESIMS (EIMS for **4** and **5**), ^1H, ^{13}C, and 2D NMR spectra of agladupols A–E (**1–5**). This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Chen, S. K.; Li, H.; Chen, P. Y. In *Chinese Flora (Zhongguo Zhiwu Zhi)*; Science Press: Beijing, China, 1997; Vol. 43 (3), pp 69–74.

(2) (a) Omobuwajo, O. R.; Martin, M.-T.; Perromat, G.; Sévenet, T.; Païs, M.; Awang, K. *J. Nat. Prod.* **1996**, *59*, 614–617. (b) Benosman, A.; Richomme, P.; Sevenet, T.; Perromat, G.; Hadi, A. H. A.; Bruneton, J. *Phytochemistry* **1995**, *40*, 1485–1487.

(3) Chaidir; Hiort, J.; Nugroho, B. W.; Bohnenstengel, F. I.; Wray, V.; Witte, L.; Hung, P. D.; Kiet, L. C.; Sumaryono, W.; Proksch, P. *Phytochemistry* **1999**, *52*, 837–842.
(4) Inada, A.; Konishi, M.; Nakanishi, T. *Heterocycles* **1989**, *28*, 383–387.
(5) Naya, Y.; Kotake, M. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 2405.
(6) Heymann, H.; Tezuka, Y.; Kikuchi, T.; Supriyatna, S. *Chem. Pharm. Bull.* **1994**, *42*, 138–146.
(7) Nugroho, B. W.; Edrada, R. A.; Güssregen, B.; Wray, V.; Witte, L.; Proksch, P. *Phytochemistry* **1997**, *44*, 1455–1461.
(8) Mitsui, K.; Maejima, M.; Saito, H.; Fukaya, H.; Hitotsuyanagi, Y.; Takeya, K. *Tetrahedron* **2005**, *61*, 10569–10582.
(9) Biavatti, M. W.; Vieira, P. C.; Da Silva, M. F. G. F.; Fernandes, J. B.; Albuquerque, S. *J. Nat. Prod.* **2002**, *65*, 562–565.
(10) Jolad, S. D.; Hoffmann, J. J.; Schram, K. H.; Cole, J. R.; Tempesta, M. S.; Bates, R. B. *J. Org. Chem.* **1981**, *46*, 4085–4088.

NP0702842