Triterpenoids from *Aglaia abbreviata* and Their Cytotoxic Activities

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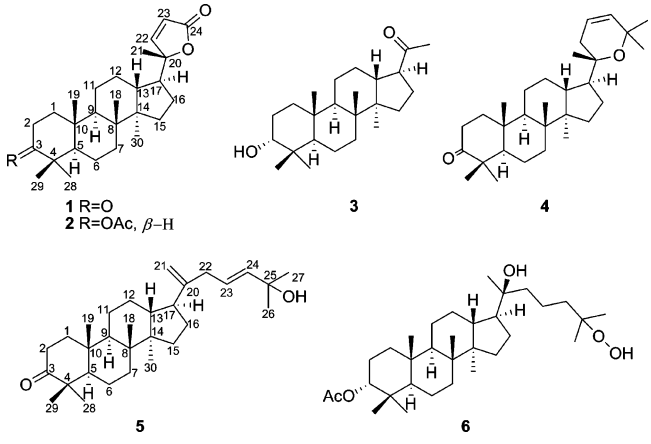
Six new triterpenoids (**1**−**6**), along with 10 known compounds, were isolated from the stems of *Aglaia abbreviata*. The structures of **1**−**6** were elucidated on the basis of their spectroscopic data. Compounds **1**−**6** were evaluated for their cytotoxic activities against a small panel of human tumor cell lines.

The genus *Aglaia* (Meliaceae) comprises more than 100 species distributed mainly in India, Malaysia, Indonesia, and Australia, but many more specific epithets appear in the literature due to the high number of synonyms.[1] Seven *Aglaia* species and one variety grow in the south of mainland China.[2] Various triterpenoids[3] (e.g., cycloartanes, dammaranes, and tirucallanes) and flavaglines[4] (e.g., cyclopenta[*b*]benzofurans, cyclopenta[*bc*]benzopyrans, and benzo[*b*]oxepines) have been isolated from this genus. In particular, some of the flavagline derivatives show interesting biological properties, such as antifungal,[5,6] antineoplastic,[7] antiviral,[8] cytotoxic,[9] and insecticidal.[10] In addition, potent anti-inflammatory activity was observed for certain triterpenes.[11] *Aglaia abbreviata* C. Y. Wu[2] is a wild shrub indigenous to Yunnan Province of the People's Republic of China, with no reports on its chemical constituents thus far.

In the present study, two new trinortriterpenoids (**1** and **2**), a new tetracyclic hexanortriterpene ketol (**3**), a new 20,25-epoxy-type dammarane triterpenoid (**4**), and two new dammarane-type triterpenoids (**5** and **6**), along with 10 known dammarane-type triterpenoids, were isolated from the stems of *A. abbreviata*. The structures of **1**−**6** were elucidated on the basis of spectroscopic data interpretation. We report herein the isolation and structure elucidation of these new compounds, along with their cytotoxic evaluation against a series of human tumor cell lines.



Results and Discussion

Aglaiabbreviatin A (**1**) was obtained as a white, amorphous powder. Its molecular formula was determined as $C_{27}H_{40}O_3$ from the HRESIMS ion at *m/z* 435.2875 $[M + Na]^+$ (calcd 435.2870). Its IR spectrum showed the presence of lactone (1767 cm^{-1}), carbonyl (1704 cm^{-1}), and carbon−carbon double-bond (1640 cm^{-1}) groups. The ^{13}C NMR spectrum showed 27 carbon resonances, which were classified by their chemical shifts and the HSQC spectrum as six methyls, eight methylenes, six methines (two olefinic), and seven quaternary carbons (one ester carbonyl and one ketone carbonyl). These functionalities accounted for three out of the total eight degrees of unsaturation. The remaining five degrees of unsaturation were consistent with the molecule containing five rings. In addition, the presence of six tertiary methyls (δ_H 0.88, 0.93, 0.94, 1.03, 1.07, and 1.46; each 3H) and two olefinic protons (δ_H 6.06, d, $J = 6.0$ Hz; 7.39, d, $J = 6.0$ Hz) was evident by analysis of the ^1H NMR data (Table 1).

The aforementioned data indicated that compound **1** is based on a trinortriterpenoid skeleton similar to that of cabralealactone,[12] which was also isolated in this investigation. The gross structure of **1** was deduced from the HSQC and HMBC spectra (Figure 1a). In the HMBC spectrum, the correlations arising from the tertiary methyl protons to their neighboring carbons enabled the assignment of the five singlet methyls. The HMBC spectrum of **1** showed cross-peaks between two *gem*-dimethyl protons (δ_H 1.03 and 1.07) and the carbonyl carbon resonance at δ_C 217.8, which suggested the presence of a keto group at the C-3 position. The HMBC cross-peaks from Me-21 (δ_H 1.46) to the oxygenated quaternary C-20 (δ_C 92.3) and the olefinic C-22 (δ_C 159.4) carbons and the cross-peak between the olefinic proton at C-23 and the lactone carbon (δ_C 172.5) indicated the presence of an α,β-unsaturated-γ-lactone ring in the side chain of **1**, formed by oxidative degradation of two tertiary methyls from the side chain.

The relative configuration of **1** was established by a ROESY experiment (Figure 1b). Thus, the ROESY correlations of H-5/Me-28, H-5/H-9, H-9/Me-30, and Me-30/H-17 indicated that Me-28, H-5, H-9, Me-30, and H-17 are cofacial, and these were randomly assigned as being α-oriented. In turn, the ROESY correlations of Me-29/Me-19, Me-19/Me-18, Me-18/H-13, and Me-21/H-13 suggested that they are cofacial and β-oriented. The *S*-configuration was assigned to C-20, in common with most dammarane triterpenes, particularly those isolated from the genus *Aglaia*.[13] This was supported by the correlations of H-13 with Me-21 and of H-17 with Me-30 in the ROESY spectrum. Thus, the structure of **1** was assigned as depicted.

Aglaiabbreviatin B (**2**), a white, amorphous powder, exhibited a molecular formula of $C_{29}H_{44}O_4$, as indicated by the observed ion at *m/z* 479.3145 $[M + Na]^+$ (calcd 479.3132) in the HRESIMS, which was in agreement with the 1D NMR data (Table 1). The IR and NMR spectra of **2** were closely related to those of aglaiabbreviatin A (**1**). The major difference was that C-3 of **2** was found to be an oxymethine (δ_C 78.3) instead of a ketone carbonyl (δ_C 217.8) in **1**, which was confirmed by the HMBC correlations from H_2-2 (δ_H 1.58, 1.88) and two methyl signals (δ_H 0.83, 0.88) to C-3 (δ_C

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Table 1. ^{1}H and ^{13}C NMR Data of Compounds **1**−**3** in $CDCl_3$[a]

	1		**2**		**3**	
position	δ_H, mult. (*J* in Hz)	δ_C	δ_H, mult. (*J* in Hz)	δ_C	δ_H, mult. (*J* in Hz)	δ_C
1a	1.34, m	39.9	1.23, m	35.0	1.28, m	33.7
1b	1.89, m		1.57, m		1.42, m	
2a	2.41, dt (14.2, 3.6)	34.1	1.58, m	22.9	1.53, m	25.4
2b	2.52, dt (14.2, 5.6)		1.88, m		1.96, m	
3		217.8	4.62, t (3.0)	78.3	3.40, t (2.9)	76.2
4		47.4		36.8		37.6
5	1.26, m	55.4	1.19, m	50.7	1.27, m	49.6
6a	1.24, m	19.6	1.41, m	18.0	1.43, m	18.2
6b	1.55, m		1.41, m		1.28, m	
7a	1.37, m	34.5	1.14, m	34.3	1.44, m	35.5
7b	1.44, m		1.42, m		1.62, m	
8		40.3		40.5		40.7
9	1.52, m	49.9	1.39, m	50.3	1.42, m	50.5
10		36.9		37.2		37.3
11a	1.49, m	21.8	1.49, m	21.4	1.25, m	21.1
11b	2.05, m		2.05, m		1.55, m	
12a	1.34, m	26.7	1.34, m	25.2	1.21, m	25.6
12b	1.86, m		1.86, m		1.63, m	
13	2.08, m	47.4	2.08, m	47.5	1.92, m	45.2
14		50.2		50.3		50.2
15a	1.12, m	31.1	1.12, m	31.1	1.15, m	31.5
15b	1.46, m		1.46, m		1.65, m	
16a	1.25, m	25.2	1.25, m	27.0	1.72, m	26.0
16b	1.71, m		1.71, m		1.92, m	
17	1.44, m	43.6	1.44, m	43.4	2.58, td (14.7, 5.5)	54.3
18	0.88, s	16.0	0.92, s	16.4	0.99, s	15.6
19	0.93, s	15.2	0.85, s	16.0	0.86, s	16.0
20		92.3		92.3		212.4
21	1.46, s	23.8	1.46, s	23.7	2.12, s	30.3
22	7.39, d (6.0)	159.4	7.39, d (6.0)	159.4		
23	6.06, d (6.0)	121.3	6.06, d (6.0)	121.2		
24		172.5		172.5		
28	1.07, s	27.1	0.83, s	27.9	0.94, s	28.3
29	1.03, s	21.0	0.88, s	21.7	0.84, s	22.1
30	0.94, s	16.1	0.91, s	15.5	0.89, s	16.0
OAc-3			2.08, s	21.2		
				170.7		

[a] Recorded at 500 MHz (^{1}H) and 125 MHz (^{13}C).

78.3). Additionally, a HMBC correlation was observed between H-3 (δ_H 4.62, t, J = 3.0 Hz) and an acetoxy carbonyl (δ_C 170.7), which indicated that OH-3 is acetylated and adopts an α-orientation. The relative configuration of **2** was established as being identical to that of **1** on the basis of a ROESY experiment. Therefore, the structure of aglaiabbreviatin B was established as **2**.

Aglaiabbreviatin C (**3**) gave a molecular formula of $C_{24}H_{40}O_2$, as determined from the HRESIMS ion at *m*/*z* 383.2935 $[M + Na]^+$ (calcd 383.2921). Proton signals for an oxygenated proton and six singlet methyls (one acetyl) in the ^{1}H NMR spectrum and 24 carbon signals in the ^{13}C NMR spectrum were observed. These, when combined with the overall unsaturation data, suggested that **3** is a hexanortriterpenoid. In the HMBC spectrum, the correlations from Me-19 (δ_H 0.86) to C-1, C-5, C-9, and C-10, Me-28 (δ_H 0.94) and Me-29 (δ_H 0.84) to C-3, C-4, and C-5, Me-18 (δ_H 0.99) to C-7, C-8, C-9, and C-14, and Me-30 (δ_H 0.89) to C-8, C-13, C-14, and C-15 enabled the assignments of the five singlet methyls and their neighboring carbons. A characteristic carbonyl carbon (δ_C 212.4, C-20) correlating with H-17 (δ_H 2.58, td, J = 14.7, 5.5 Hz) and an acetyl methyl (δ_H 2.12, s, H_3-21) allowed the placement of the keto group at C-17. These data suggested that **3** is a dammarane-type triterpenoid with the loss of a 2-methylpentyl moiety from the side chain. The HMBC cross-peaks from C-2 and C-4 to the oxygenated methine protons at δ_H 3.40 (t, J = 2.9 Hz) were used to place the hydroxy group at C-3, adopting an α-orientation. Comprehensive analysis of the 2D NMR (HSQC, HMBC, and ROESY) spectra confirmed the structure of **3**.

Aglaiabbreviatin D (**4**) was obtained as a white, amorphous powder. The HRESIMS displayed a pseudomolecular ion at *m*/*z* 441.3740 $[M + H]^+$ (calcd for $C_{30}H_{49}O_2$, 441.3727), consistent with a molecular formula of $C_{30}H_{48}O_2$. IR absorption bands revealed the presence of a carbonyl (1711 cm^{-1}) group and a carbon−carbon double bond (1644 cm^{-1}). The ^{1}H NMR data (Table 2) indicated the presence of eight tertiary methyls at δ_H 0.88, 0.94, 1.00, 1.04, 1.08, 1.13, 1.32, and 1.34 (each 3H, s) and two olefinic protons at δ_H 5.70 (2H, m). The ^{13}C NMR spectrum showed 30 carbon resonances, which were classified from the ^{1}H NMR and HSQC spectra as a ketone carbonyl (δ_C 218.0), double-bond carbons (δ_C 126.2 and 133.0), eight methyls, nine sp^3 methylenes, four sp^3 methines, and six sp^3 quaternary carbons. A comparison of the NMR data of **4** with those of 20*S*,25-epoxy-24*R*-hydroxy-3-dammarane,[1] previously isolated from the same genus, revealed that the structures of the two compounds are closely related, with the main differences occurring through the formation of a double bond between C-23 and C-24 in **4**. This conclusion was confirmed by HMBC correlations (Figure 3a) from Me-26 and Me-27 to C-25, H-24 to C-25, and H-23 to C-22. Compound **4** shares the same relative configuration as those of other dammarane-type compounds. The ROESY correlations of Me-29/Me-19, Me-19/Me-18, Me-18/H-13, and H-13/Me-21 indicated that they are cofacial, and these were randomly assigned as being β-oriented. Subsequently, the ROESY (Figure 3b) correlations of H-5/Me-28, H-5/H-9, H-9/Me-30, and Me-30/H-17 suggested that they are α-oriented. The structure of **4** was thus defined as shown.

Aglaiabbreviatin E (**5**) gave a molecular formula of $C_{30}H_{48}O_2$, as deduced from the HRESIMS at *m*/*z* 441.3734 $[M + H]^+$ (calcd for $C_{30}H_{49}O_2$, 441.3727). The IR absorption bands implied the presence of hydroxy (3431 cm^{-1}), carbonyl (1725 cm^{-1}), and carbon−carbon double-bond (1642 cm^{-1}) functionalities. The ^{1}H NMR spectrum of **5** showed the presence of seven tertiary methyls at δ_H 0.87, 0.94, 1.01, 1.04, 1.08, 1.33, and 1.33 (each 3H, s) and four olefinic protons at δ_H 5.64 (2H, m), 4.88 (1H, s), and 4.95 (1H, s). The ^{13}C NMR spectrum showed 30 carbon resonances, which were classified by ^{1}H NMR and HSQC experiments as seven methyls, nine sp^3 methylenes, four sp^3 methines, five sp^3 quaternary carbons, one ketone carbonyl (δ_C 218.1), and two double bonds (δ_C 151.3, 109.3; 139.5, 125.6). Comparison of the NMR data of **5** with those of **4** revealed the carbon framework of the two compounds to be similar, with the only differences occurring in the side chain. In the HMBC experiment, correlations from two olefinic protons at C-21 to C-20, C-22, and C-17 were used to assign the terminal double bond ($\Delta^{20,21}$). HMBC correlations from two methyls (Me-26 and Me-27) to an oxygenated carbon (δ_C 70.7) were used to assign the hydroxy group at C-25. The HMBC correlations from the olefinic proton at C-24 (δ_H 5.64, m) to the C-25 and H_2-22 to C-23 (δ_C 125.6) and C-20 showed the presence of another double bond and the side chain at the C-17 of **5** and also permitted the connectivity of C-22 and C-25 to be proposed via a double bond at C-23 and C-24. The relative configuration of **5** was established by the ROESY spectrum as being the same as that of **4**.

Aglaiabbreviatin F (**6**) gave a molecular formula of $C_{32}H_{54}O_5$, as established on the basis of the HRESIMS at *m*/*z* 541.3877 $[M + Na]^+$ (calcd 541.3863). The IR absorption bands implied the presence of hydroxy (3432 cm^{-1}), ester carbonyl (1738 cm^{-1}), and carbon−carbon double-bond (1639 cm^{-1}) functionalities. Comparison of the ^{1}H and ^{13}C NMR data of **6** with those of **2** revealed these two compounds to possess the same tetracyclic core. In the HMBC spectrum, correlations from Me-21 and H-17 to an oxygenated carbon (δ_C 75.2) were used to assign a hydroxy group at C-20. In addition, two extra oxygen atoms in the molecular formula and a downfield shifted oxygenated quaternary carbon signal at δ_C 81.8[14] correlated with two tertiary methyls (Me-26 and Me-27) in the HMBC spectrum, consistent with a hydroperoxy

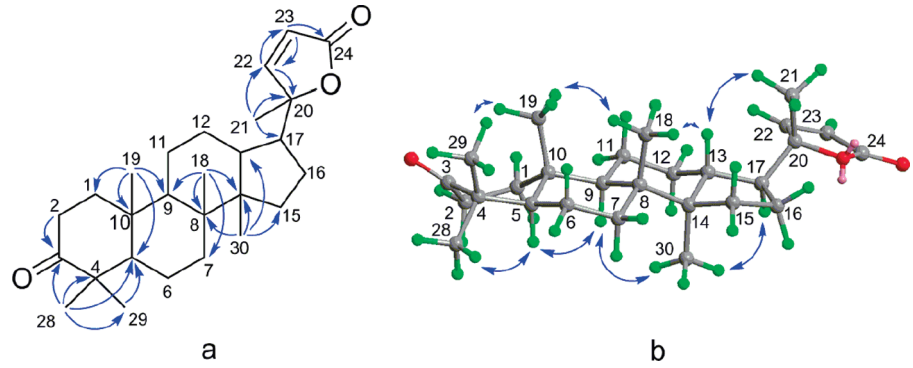

Figure 1. Selected HMBC (H → C) (a) and ROESY (⟷) correlations (b) of **1**.

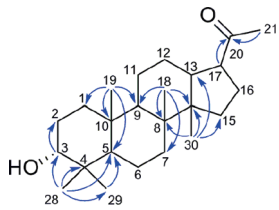

Figure 2. Key HMBC (H → C) correlations of **3**.

group occurring at C-25. The placement of the double bond at C-23 and C-24 was verified by the HMBC correlations of H-20/C-23 and H-24/C-26 and C-27. The relative configuration of **6** was established as being the same as that of **2** on the basis of the ROESY correlations. The structure of **6** was therefore established as shown.

The known compounds cabralealactone,[15] cabraleahydroxylactone,[15] cabraleahydroxylactone acetate,[15] cabraleone,[15] ocotillone,[15] cabraleadiol,[15] cabraleadiol monoacetate,[15] 20*S*,24*S*-dihydroxydammer-25-en-3-one,[16] 24,25-dihydroxydammar-20-en-3-one,[17] and dammarenediol[18] were identified by comparison of their spectroscopic data with reported values.

Compounds **1**−**6** were evaluated for their cytotoxicity against the K562 (leukemia), SMMC-7721 (hepatocellular carcinoma), MCF-7 (breast cancer), and KB (oral epithelial cancer) human cell lines, as well as multi-drug-resistant MCF-7/ADM and KB/VCR cells (Table 3). Compounds **3**−**6** were found to show cytotoxicity against several of the tumor cell lines used, with compound **6** showing the greatest potency.

Experimental Section

General Experimental Procedures. Optical rotations were measured with a JASCO P-1020 polarimeter. IR spectra (KBr disks) were recorded on a Bruker Tensor 27 spectrometer. NMR spectra were recorded on a Bruker ACF-500 NMR instrument (^{1}H: 500 MHz, ^{13}C: 125 MHz), with TMS as internal standard. Mass spectra were obtained on a MS Agilent 1100 Series LC/MSD ion-trap mass spectrometer (ESIMS) and a Mariner ESITOF spectrometer (HRESIMS). All solvents used were of analytical grade (Jiangsu Hanbang Science and Technology. Co., Ltd.). Silica gel (Qingdao Haiyang Chemical Co., Ltd.), Sephadex LH-20 (Pharmacia), and RP-C_{18} (40−63 μm, FuJi) were used for column chromatography. Preparative HPLC was carried out using an Agilent 1100 Series instrument with a Shim-Pak RP-C_{18} column (20 × 200 mm) and a 1100 Series multiple wavelength detector.

Plant Material. The air-dried stems of *Aglaia abbreviata* were collected from Xishuangbanna, Yunnan Province, People's Republic of China, in May 2008, and were authenticated by Professor Jing-Yun Cui, Xishuangbanna Botanical Garden, Chinese Academy of Sciences, People's Republic of China. A voucher specimen has been deposited in the Department of Natural Medicinal Chemistry, China Pharmaceutical University (accession number AA200805).

Extraction and Isolation. The air-dried stems (10 kg) were extracted with 95% ethanol under reflux three times. After removal of the solvent under vacuum, the viscous concentrate was first suspended in H_2O and then partitioned with $CHCl_3$ and EtOAc, successively. The $CHCl_3$-soluble partition (130 g) was fractionated by column chromatography over D101 porous resin using gradient aqueous ethanol to give fractions A−F, combined according to TLC results. Fraction D (16 g) was chromatographed on a column of silica gel, eluted successively with a gradient of petroleum ether−ethyl acetate (20:1 to 1:2), to give seven subfractions (D1−D7). Subfraction D2 was chromatographed on a column of reversed-phase C_{18} silica gel, eluted with MeOH−H_2O (5:5

Table 2. ^{1}H and ^{13}C NMR Data of Compounds **4**−**6** in $CDCl_3$[a]

	4		**5**		**6**	
position	δ_H, mult. (*J* in Hz)	δ_C	δ_H, mult. (*J* in Hz)	δ_C	δ_H, mult. (*J* in Hz)	δ_C
1a	1.46, m	39.8	1.43, m	40.0	1.17, m	34.3
1b	1.92, m		1.92, m		1.45, m	
2a	2.47, dt (14.4, 4.6)	34.0	2.45, dt (14.2, 3.6)	34.1	1.57, m	22.9
2b	2.72, dt (14.2, 5.6)		2.73, dt (14.2, 5.6)		1.87, m	
3		218.0		218.1	4.63, t (2.5)	78.4
4		47.3		47.5		36.7
5	1.38, m	55.3	1.38, m	55.4	1.23, m	50.7
6a	1.46, m	19.6	1.46, m	19.7	1.45, m	18.0
6b	1.56, m		1.55, m		1.56, m	
7a	1.32, m	34.5	1.68, m	34.9	1.26, m	35.0
7b	1.56, m		1.88, m		1.57, m	
8		40.2		40.4		40.6
9	1.74, m	49.8	1.43, m	50.3	1.45, m	50.4
10		36.8		36.9		37.1
11a	1.26, m	21.9	1.42, m	21.9	1.19, m	22.4
11b	1.51, m		1.52, m		1.53, m	
12a	1.28, m	27.4	1.07, m	25.0	1.25, m	27.4
12b	1.88, m		1.59, m		1.80, m	
13	1.68, m	42.5	2.23, m	47.5	1.65, m	42.4
14		50.2		49.4		50.0
15a	1.09, m	31.0	1.59, m	31.4	1.08, m	31.1
15b	1.47, m		1.61, m		1.48, m	
16a	1.53, m	24.7	1.41, m	28.9	1.75, m	24.9
16b	1.73, m		1.91, m		1.92, m	
17	1.43, m	49.9	1.70, dd (10.4, 3.0)	45.4	1.87, m	50
18	1.00, s	15.1	1.01, s	15.8	0.97, s	15.5
19	0.94, s	15.9	1.08, s	15.4	0.87, s	16.0
20		74.9		151.3		75.2
21	1.13, s	25.6	a 4.88, s b 4.95, s	109.3	1.14, s	25.5
22a	2.19, m	43.3	2.66, d (4.0)	37.2	2.23, m	43.4
22b	2.67, m		2.70, d (4.0)		2.24, m	
23	5.70, m	126.2	5.64,m	125.6	5.76, m	126.8
24	5.70, m	133.0	5.64,m	139.5	5.63, m	137.6
25		70.6		70.7		81.8
26	1.32, s	29.9	1.33, s	29.9	1.35, s	24.1
27	1.34, s	29.8	1.33, s	29.9	1.33, s	24.5
28	1.08, s	26.7	0.94, s	26.8	0.84, s	27.9
29	1.04, s	20.9	1.04, s	21.0	0.89, s	21.3
30	0.88, s	16.3	0.87, s	16.1	0.92, s	16.6
OAc-3					2.08, s	21.7
						170.8

[a] Recorded at 500 MHz (^{1}H) and 125 MHz (^{13}C).

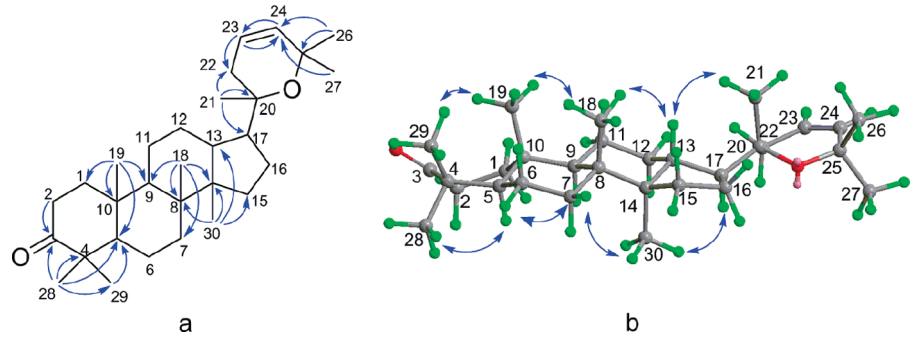

Figure 3. Selected HMBC (H → C) (a) and ROESY (⟷) correlations (b) of **4**.

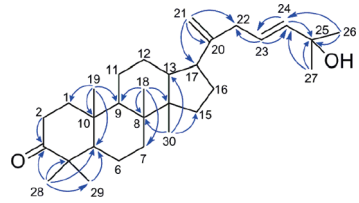

Figure 4. Key HMBC (H → C) correlations of **5**.

Table 3. Cytotoxicity of Compounds **1**−**6** for Six Cancer Cell Lines[a]

compound	MCF-7	MCF-7/ ADR	KB	KB/ VCR	SMMC-7721	K562
3	>10	>10	>10	1.1	>10	>10
4	>10	>10	1.2	0.96	2.1	1.2
5	>10	>10	2.7	0.83	4.2	1.8
6	>10	5.5	0.60	0.31	1.4	0.46
doxorubicin	0.54	>10	0.012	0.45	0.37	0.17

[a] Results are expressed as IC_{50} values in μM. Compounds **1** and **2** were inactive for all cell lines (IC_{50} > 10 μM).

to 9:1), to give three subfractions (D2a−D2c). Subfraction D2a was separated over ODS, using MeOH−H_2O (75:25) as the mobile phase, to give **1** (5 mg), cabralealactone (200 mg), and **3** (12 mg). Subfraction D3 was chromatographed on a column of reversed-phase C_{18} silica gel, eluted with MeOH−H_2O (5:5 to 9:1), to give four subfractions (D3a−D3d). Of these, subfraction D3c was separated by preparative HPLC, using MeOH−H_2O (85:15, 10 mL/min) as the mobile phase, to give **2** (8 mg), cabraleahydroxylactone (230 mg), cabraleahydroxylactone acetate (20 mg), and **4** (4 mg). Subfraction D3d was separated by preparative HPLC, using MeOH−H_2O (85:15, 10 mL/min) as the mobile phase, to give **5** (5 mg), cabraleone (9 mg), and ocotillone (6 mg). Subfraction D6 was chromatographed on a column of reversed-phase C_{18} silica gel, eluted with MeOH−H_2O (5:5 to 9:1), to give five subfractions (D6a−D6e). Subfraction D6b was separated by preparative HPLC, using CH_3OH−H_2O (85:15, 10 mL/min) as the mobile phase, to give **6** (8 mg), cabraleadiol (6 mg), and a mixture, and then the mixture was purified, using CH_3CN−H_2O (75:25, 10 mL/min) as the mobile phase, to afford 20*S*,24*S*-dihydroxydammer-25-en-3-one (15 mg) and 24,25-dihydroxydammar-20-en-3-one (12 mg). Subfraction D6d was separated by preparative HPLC, using CH_3OH−H_2O (85:15, 10 mL/min) as the mobile phase, to yield cabraleadiol monoacetate (18 mg) and dammarenediol (9 mg).

Aglaiabbreviatin A (1): white, amorphous powder; $[\alpha]^{25}_D$ −0.6 (*c* 0.11, CH_3OH); IR (KBr) ν_{max} 2955, 2826, 1767, 1704, 1640, 1379, 1247, 1075, 754, 662 cm^{-1}; ^1H and ^{13}C NMR, see Table 1; negative ESIMS *m/z* 447.1 $[M + Cl]^-$ (100); positive ESIMS *m/z* 413.2 $[M + H]^+$ (100); HRESIMS *m/z* 435.2875 $[M + Na]^+$ (calcd for $C_{27}H_{40}O_3Na$, 435.2870).

Aglaiabbreviatin B (2): white, amorphous powder; $[\alpha]^{25}_D$ −1.0 (*c* 0.085, CH_3OH); IR (KBr) ν_{max} 2941, 2870, 1747, 1641, 1375, 1244, 1018, 953, 822 cm^{-1}; ^1H and ^{13}C NMR, see Table 1; negative ESIMS *m/z* 491.4 $[M + Cl]^-$ (100); positive ESIMS *m/z* 474.3 $[M + NH_4]^+$ (100); HRESIMS *m/z* 479.3145 $[M + Na]^+$ (calcd for $C_{27}H_{40}O_3Na$, 479.3132).

Aglaiabbreviatin C (3): white, amorphous powder; $[\alpha]^{25}_D$ −7.6 (*c* 0.28, CH_3OH); IR (KBr) ν_{max} 3455, 2927, 1753, 1694, 1641, 1463, 1384, 1350, 617 cm^{-1}; ^1H and ^{13}C NMR, see Table 1; negative ESIMS *m/z* 395.5 $[M + Cl]^-$ (100); positive ESIMS *m/z* 378.2 $[M + NH_4]^+$ (100); HRESIMS *m/z* 383.2935 $[M + Na]^+$ (calcd for $C_{24}H_{40}O_2Na$, 383.2921).

Aglaiabbreviatin D (4): white, amorphous powder; $[\alpha]^{25}_D$ +17.0 (*c* 0.18, CH_3OH); IR (KBr) ν_{max} 2950, 2915, 1711, 1644, 1378, 1234, 1004, 668 cm^{-1}; ^1H and ^{13}C NMR, see Table 2; negative ESIMS *m/z* 439.2 $[M - H]^-$ (100); positive ESIMS *m/z* 441.7 $[M + H]^+$ (100); HRESIMS *m/z* 441.3740 $[M + H]^+$ (calcd for $C_{30}H_{49}O_2$, 441.3727).

Aglaiabbreviatin E (5): white, amorphous powder; $[\alpha]^{25}_D$ −3.1 (*c* 0.14, CH_3OH); IR (KBr) ν_{max} 3431, 2943, 2870, 1725, 1642, 1374, 1249, 755, 744 cm^{-1}; ^1H and ^{13}C NMR, see Table 2; negative ESIMS *m/z* 439.5 $[M - H]^-$ (100); positive ESIMS *m/z* 441.4 $[M + H]^+$ (100); HRESIMS *m/z* 441.3734 $[M + H]^+$ (calcd for $C_{30}H_{49}O_2$, 441.3727).

Aglaiabbreviatin F (6): white, amorphous powder; $[\alpha]^{25}_D$ +19.5 (*c* 0.070, CH_3OH); IR (KBr) ν_{max} 3432, 2979, 1738, 1639, 1374, 1234, 1030, 899, 602 cm^{-1}; ^1H and ^{13}C NMR, see Table 2; negative ESIMS *m/z* 553.4 $[M + Cl]^-$ (100); positive ESIMS *m/z* 536.2 $[M + NH_4]^+$ (100); HRESIMS *m/z* 541.3877 $[M + Na]^+$ (calcd for $C_{32}H_{54}O_5Na$, 541.3863).

Determination of Cytotoxic Activities. The following human tumor cell lines were used: K562 (leukemia), SMMC-7721 (hepatocellular carcinoma), MCF-7 (breast cancer), KB (oral epithelial cancer), and multi-drug-resistant cells of MCF-7/ADM and KB/VCR. All cells were cultured in RPMI-1640 or DMEM medium (Hyclone, Logan, UT), supplemented with 10% fetal bovine serum (Hyclone) in 5% CO_2 at 37 °C. The cytotoxicity assay was performed according to the MTT method in 96-well microplates.[19] Briefly, 180 μL of the cell suspension was seeded into each well of 96-well cell culture plates and allowed to adhere for 12 h before test compound addition, while suspended cells were seeded just before test compound addition with an initial density of 1 × 10^5 cells/mL. Each tumor cell line was exposed to each test compound at concentrations of 0.1,1, 10, 100, and 500 μM in triplicate for 48 h, with doxorubicin (Sigma, St. Louis, MO) used as positive control. After treatment, cell viability was detected, and IC_{50} values were calculated by the Reed and Muench method.[20]

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Supporting Information Available: HRESIMS, ^1H and ^{13}C NMR, and 2D NMR spectra of aglaiabbreviatins A−F (**1**−**6**). This material is available free of charge via the Internet at http://pubs.acs.org.

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