Sesquiterpenes and Dimeric Sesquiterpenoids from Sarcandra glabra

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Sesquiterpenes and Dimeric Sesquiterpenoids from *Sarcandra glabra*

Xiu-Feng He, Sheng Yin, Yin-Chun Ji, Zu-Shang Su, Mei-Yu Geng, and Jian-Min Yue*

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Two new sesquiterpenes, sarcandralactones A (1) and B (2), and five new dimeric sesquiterpenoids, sarcandrolides A–E (3–7), along with 10 known compounds were isolated from the whole plants of *Sarcandra glabra*. Their structures were elucidated on the basis of spectroscopic analysis. Some of the new isolates exhibit significant cytotoxicities when tested against a small panel of tumor cell lines.

The plants of the Chloranthaceae family are rich sources of sesquiterpenoid oligomers, which have attracted considerable interest due to the diverse structures and significant biological activities, such as antifungal, cytotoxicity, and inhibition of cell adhesion expression. In our recent study, a number of dimeric sesquiterpenoids isolated from *Chloranthus spicatus* were found to exhibit potent and selective inhibition of the delayed rectifier (I<sub>K</sub>) K<sup>+</sup> current. There are three species in the *Sarcandra* genus of the Chloranthaceae family, which are mainly distributed in the southeast of Asia. The plant *Sarcandra glabra* (Thunb.) Nakai, an evergreen shrub growing in southern China, has been applied in the system of Traditional Chinese Medicine (TCM) to treat inflammation, bone fracture, and cancer. Previous chemical investigations of this species have led to the isolation of hepatoprotective sesquiterpenes and sesquiterpenoid glycosides. In this study, two new sesquiterpenes, sarcandralactones A (1) and B (2), and five new dimeric sesquiterpenoids, sarcandrolides A–E (3–7), along with 10 known compounds were isolated from the whole plants of *S. glabra*. We present herein the isolation, structural elucidation, and cytotoxic evaluation of these new isolates.

**Results and Discussion**

The HREIMS of sarcandralactone A (1) displayed a molecular ion at *m/z* 246.1241 [M]<sup>+</sup>, consistent with the molecular formula of C<sub>15</sub>H<sub>20</sub>O<sub>3</sub> requiring seven degrees of unsaturation. The IR spectrum indicated the presence of hydroxy (3439 cm<sup>−1</sup>) and carbonyl (1720 cm<sup>−1</sup>) groups. Its 1<sup>H</sup> NMR spectrum displayed a characteristic upfield shifted resonance at δ<sub>H</sub> 0.69 diagnostic for the cyclopropane ring of lindenane sesquiterpenoids, two methyl singlets, and two resonances at δ<sub>H</sub> 5.08 (s) and 4.97 (s) for a terminal double bond (Table 1). All 15 carbons were resolved in the 13<sup>C</sup> NMR spectrum and were categorized by DEPT experiments as two methyl, four methylene (one olefinic), three methine (one oxygenated), and six quaternary carbons (one oxygenated, three olefinic, and one ester carbonyl) (Table 1). These functionalities accounted for three out of the seven degrees of unsaturation, and the remaining four degrees of unsaturation implied compound 1 to be tetracyclic. The 1<sup>H</sup> and 13<sup>C</sup> NMR data of 1 were similar to those of heterogorgiolide, indicating a lindena-4(15)-en-12,8-olide structural moiety for 1, which was confirmed by the HMBC spectrum. In this experiment, the key correlations from the two protons of the exocyclic double bond [δ<sub>H</sub> 5.08 (s) and 4.97 (s)], the protons of CH<sub>2</sub>-6 [δ<sub>H</sub> 3.18 (d, J = 15.0 Hz) and 2.42 (d, J = 15.0 Hz)], and the angular methyl at δ<sub>H</sub> 1.30 (s, 3H) to the same oxygenated quaternary carbon at δ<sub>C</sub> 80.3 placed the hydroxy group at C-5 (Figure 1a).

The relative configuration of 1 was established on the basis of a ROESY spectrum (Figure 1b), in which correlations of H-1/4/H-2β and H-1/4/H-8 revealed that H-1, H-4, and the cyclopropane ring were cofacial and were arbitrarily assigned a β-orientation. Consequently, H-1 and H-3 were assigned as α-oriented. The configuration of the C-5 stereocenter could not be assigned by the ROESY spectrum since no correlation could be detected. To assign the relative configuration of C-5, the pyridine-induced solvent shift method was applied. The 1<sup>H</sup> NMR data of 1 measured in CDCl<sub>3</sub> and pyridine-<i>d</i><sub>5</sub> showed significant pyridine-induced solvent shifts [Δδ is defined as δ(CDCl<sub>3</sub>) − δ(pyridine-<i>d</i><sub>5</sub>)] for H-2β (Δδ = −0.52), H-14 (Δδ = −0.15), H-6α (Δδ = −0.21), and H-6β (Δδ = −0.22), indicating that the 5-OH was β-oriented. Therefore, the structure of 1 was elucidated as depicted.

Sarcandralactone B (2), a colorless solid, showed a molecular formula of C<sub>15</sub>H<sub>20</sub>O<sub>3</sub> ([M]<sup>+</sup> *m/z* 248.1411) with six degrees of
Table 1. $^1$H NMR (400 MHz) and $^{13}$C NMR Data (100 MHz) of 1 and 2

<table>
<thead>
<tr>
<th>no.</th>
<th>$\delta_{H}$ mult (J in Hz)$^a$</th>
<th>$\delta_{H}$ mult (J in Hz)$^b$</th>
<th>$\delta_{C}^c$</th>
<th>$\delta_{H}$ mult (J in Hz)$^a$</th>
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<th>$\delta_{C}^c$</th>
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<td>2</td>
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<td>0.65 dt (4.1, 8.4), 2.05 m</td>
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<tr>
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<td>2.91 dd (13.8, 3.8)</td>
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<td>10</td>
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<td>2.74 dd (12.1, 6.8)</td>
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<tr>
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<td>5.05 s, 5.02 s</td>
<td>106.4</td>
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</table>

$a$ Measured in CDCl$_3$. $^b$ Measured in pyridine-d$_5$.

Figure 1. Selected HMBC correlations (H→C) and key ROESY correlations (H↔H) of 1.

Figure 2. Selected HMBC correlations (H→C) and key ROESY correlations (H↔H) of 2.

Unsaturation by HREIMS. The IR spectrum showed absorption bands for the presence of hydroxy and carbonyl groups. The $^{13}$C NMR spectrum displayed 15 carbon signals comprising three methyl, three methylene, three sp$^3$ methine (two oxygenated), one sp$^3$ quaternary carbon, one ester carbonyl at $\delta_{C}$ 174.8, and four olefinic carbons (Table 1). Its $^1$H NMR spectrum showed three methyl singlets at $\delta_{H}$ 0.95, 1.70, and 1.84, two oxygenmethines at $\delta_{H}$ 3.56 (dd, $J = 9.6, 6.3$ Hz) and 4.90 (dd, $J = 12.1, 6.8$ Hz), and one olefinic proton at $\delta_{H}$ 5.38 (br s) (Table 1). The above spectroscopic analysis indicated that 2 is likely a eudesmadien-12,8-olide. In the HMBC spectrum (Figure 2a), the correlations from the upfield methyl singlet ($\delta_{H}$ 0.95) to C-1 ($\delta_{C}$ 74.9), C-5, C-9, and C-10 placed the hydroxy group at C-1; the correlations from H-15 ($\delta_{H}$ 1.70) to C-3 ($\delta_{C}$ 121.1), C-4($\delta_{C}$ 132.9), and C-5 indicated the $\Delta^\gamma$ double bond; and the correlations from H-8 to C-7, C-9, and C-11 as well as the correlations from H-12 to C-7, C-11, and C-12 confirmed the presence of a $\gamma$-lactone moiety between C-12 and C-8. In the ROESY spectrum of 2 (Figure 2b), the correlations of H-1/H-5, H-5/H-6, and H-1/H-9c indicated that they were cofacial and were arbitrarily assigned as $\alpha$-oriented. Consequently, the ROESY correlations of H-14/H-8, H-14/H-6$, and H-8/H-6$ indicated that they were $\beta$-oriented. Compound 2 was thus assigned as 1/1′-hydroxy-3,7(11)-eudesmadien-12,8-olide.

Sarcandrolide A (3) was isolated as a colorless solid. The HREIMS gave a molecular ion at $m/z$ 618.2827 corresponding to the molecular formula C$_{39}$H$_{42}$O$_{9}$. The IR absorptions revealed the presence of carbonyl and hydroxy functionalities. In accord with the molecular formula, 36 carbon resonances were well resolved in the $^{13}$C NMR spectrum (Table 3) and were categorized by DEPT experiments as four carbonyl ($\delta_{C}$ 200.4, 173.4, 170.7, and 168.3), eight olefinic carbons (three persubstituted and one trisubstituted double bond), seven methyl (one O-methyl), five sp$^3$ methylene (one oxygenated), eight sp$^3$ methine (one oxygenated), and four sp$^3$ quaternary carbons (two oxygenated). Its $^1$H NMR spectrum showed two strongly upfield shifted resonances at $\delta_{H}$ 0.28 and 0.70 being interpreted in terms of cyclopropane rings (Table 2). The NMR data of 3 showed close resemblance to those of shizukaol C$_{13}$ except for the significant changes of C-14’ and H-13’, which indicated the presence of a C-13′ methyl group in 3 instead of an oxygenated methylene in shizukaol C$_{13}$. This was confirmed by the HMBC correlations from H$_2$-13′ to C-7′, C-11′, and C-12′. Analysis of the HMBC spectrum finalized the planar structure of 3 (Figure 3a). The relative configuration of 3 was established by a ROESY experiment (Figure 3b). The ROESY correlations of H-1/H-3, H-1/H-2$\alpha$, H-1/H-9, H-5′/H-9, H-3′/H-15′, and H-5′/H-15′ indicated that they were cofacial and were arbitrarily assigned as $\alpha$-oriented. As a consequence, the ROESY correlations of H$_3$-14/H-2$\beta$, H$_3$-14/H-6, H-6/H-9′, and H-9′/H$_3$-14′ revealed that they were $\beta$-oriented. Thus, compound 3 was determined as 13’-deoxyshizukaol C.

The HREIMS of sarcandrolide B (4) displayed a sodiated molecular ion peak at $m/z$ 673.2632 [M + Na]$^{+}$, consistent with the molecular formula C$_{39}$H$_{42}$O$_{11}$. Its $^{13}$C NMR spectrum showed similarities to that of shizukaol C$_{13}$ except for the absence of one olefinic methyl group and the presence of one additional oxygenated methylene in 4 (Table 3). Comparing the $^1$H NMR data of 4 with that of shizukaol C$_{13}$ the olefinic proton H-3″ resonated as a broad triplet at $\delta_{H}$ 6.90 (br t, $J = 6.0$ Hz) in 4 (Table 2), while it was a double quartet at $\delta_{H}$ 6.88 (qq, $J = 7.1, 1.0$ Hz) in shizukaol C$_{13}$ suggesting that C-4″ of 4 was an oxygenated methylene. The HMBC correlations from H$_2$-4″ at $\delta_{H}$ 4.26 (dd, $J = 15.0, 4.9$ Hz) and $\delta_{H}$ 4.44 (dd, $J = 15.0, 7.0$ Hz) to C-2″ and C-3″ confirmed this speculation. The relative configuration of 4 was fixed by the ROESY spectrum, which resulted in the same assignment as shizukaol C in the dimeric core.

Sarcandrolide C (5) was assigned the molecular formula C$_{36}$H$_{42}$O$_{9}$ on the basis of HREIMS ($m/z$ 813.2715 [M + Na]$^{+}$). The $^1$H NMR data exhibited the characteristic upfield shifted resonances ($\delta_{H}$ 0.34 and 0.71) of cyclopropane rings (Table 2), indicating that compound 5 is also likely a lindenane-type sesquit-
erpenoid dimer. The $^{13}$C NMR data of 5 showed similarity to those of shizukaidol G,\textsuperscript{14} except for the presence of two additional signals (δC 169.9 and 20.7) being assignable to the presence of an acetyl group in 5 (Table 3). The O-acetyl group was located at C-2\textsuperscript{00} by the HMBC correlation between H-2\textsuperscript{00} (δH 5.48, dd, J = 4.8, 3.3 Hz) and the carbonyl carbon (δC 198.9) of the acetyl group. Thus sarcandrolide C (5) was determined as 2\textsuperscript{00}-O-acetyltirandacol G.

The HREIMS of sarcandrolide D (6) exhibited a molecular ion peak at m/z 678.2666 [M]\textsuperscript{+}, corresponding to the molecular formula C\textsubscript{40}H\textsubscript{42}O\textsubscript{12}. The $^1$H NMR spectrum showed characteristic proton resonances for cyclopropane rings and six methyl groups, which were classified according to the chemical shifts as two angular (δH 0.79, 3H) to C-1, C-5, C-9 (δC 78.3), and C-10 revealed that a hydroxy group was located at C-2\textsuperscript{0} of the ketone carbonyl (δC 169.9) and one O-methyl group and the absence of the hemiacetal moiety, suggesting that compound 7 was likely produced by the methanolation of the 8,12-lactone ring of 6. This speculation was confirmed by the HMBC correlations from H-9 to C-10 and C-8 (δC 198.9) and between OCH\textsubscript{3} (δH 3.76) and C-12 (δC 169.6). The relative configuration of 7 was established to be the same as 6 by the ROESY spectrum.

The absolute configurations of 3–7 were determined by applying the CD exciton chirality method.\textsuperscript{15} All five sesquiterpenoid dimers showed a similar CD split pattern in the 210–260 nm region, where positive chirality arose from the exciton coupling of the α,β-unsaturated γ-lactone (C-7\textsuperscript{′}, C-11\textsuperscript{′}, and C-12\textsuperscript{′}) and twisted π-electron system [(C-5–C-8 and C-11–C-12) or (C-7–C-8 and C-11–C-12)] chromophores (Figure 5). The CD spectra of 3–7 also matched very well with those of reported sesquiterpenoid dimers,\textsuperscript{15} supporting these assignments. The absolute configuration of 3–7 was therefore assigned as depicted.

Ten known compounds were identified on the basis of their $^1$H and $^{13}$C NMR and ESIMS data as (+)-spathulenol,\textsuperscript{16} chlorantha-lactone E,\textsuperscript{17} neolitacumone B,\textsuperscript{18} 3-eudesmen-1-ol,\textsuperscript{19} chlo-

\begin{table}[h]
\centering
\begin{tabular}{cccccc}
\hline
no. & 3 & 4 & 5 & 6 & 7 \\
\hline
1 & 2.06 m & 2.07 m & 2.05 ddd (8.2, 5.7, 4.3) & 1.85 m & 1.96 m \\
2 & 0.28 m, 0.98 m & 0.33 m, 0.99 m & 0.34 m, 1.00 m & 0.88 m, 1.08 m & 0.94 m, 2H \\
3 & 1.83 m & 1.86 m & 1.84 m & 1.78 m & 1.82 m \\
6 & 3.88 d (3.0) & 3.91 br s & 3.93 d (3.8) & 3.85 s & 3.86 s, 3.72 s \\
9 & 3.95 s & 3.91 s & 3.85 s & 3.86 s & 3.86 s \\
13 & 1.82 s, 3H & 1.91 s, 3H & 1.89 s, 3H & 1.53 s, 3H & 1.73 s, 3H \\
14 & 1.00 s, 3H & 1.01 s, 3H & 1.01 s, 3H & 0.81 s, 3H & 1.04 s, 3H \\
15 & 2.57 d (16.8) & 2.56 dd (16.6, 1.8) & 2.56 ddd (16.5, 6.0, 3.8) & 1.74 m & 1.69 dd (13.5, 10.6) \\
1′ & 1.54 m & 1.64 m & 1.61 m & 2.71 m & 2.73 dd (13.6, 6.8) \\
2′ & 0.70 m, 1.23 m & 0.72 m, 1.31 m & 0.71 m, 1.32 m & 1.55 m & 1.54 m \\
3′ & 1.51 m & 1.43 m & 1.39 m & 1.68 m & 1.58 m \\
5′ & 1.74 dd (14.2, 6.2) & 1.90 m & 1.90 m & 2.16 m & 1.54 m \\
6′ & 2.22 dd (18.0, 6.2) & 2.40 dd (18.6, 6.3) & 2.31 dd (19.2, 6.2) & 2.44 dd (17.6, 6.8) & 2.30 dd (18.0, 6.4) \\
9′ & 1.80 m & 1.94 m & 1.88 m & 2.63 m & 2.55 dd (10.4, 7.5) \\
13′ & 1.80 s, 3H & 4.34 d (15.3) & 4.44 d (12.0) & 4.76 d (12.8) & 4.82 s, 2H \\
14′ & 0.83 s, 3H & 0.87 s, 3H & 0.79 s, 3H & 0.96 s, 3H & 0.94 s, 3H \\
15′ & 3.85 d (11.9) & 3.80 d (11.6) & 3.67 d (12.0) & 4.03 d (11.1) & 3.85 d (11.3) \\
3″ & 4.15 d (11.9) & 4.38 d (11.6) & 4.55 d (12.0) & 4.07 d (11.1) & 4.15 d (11.3) \\
3″″ & 6.90 br q (6.6) & 6.77 br (6.0) & 6.56 br t (6.0) & 6.84 br q (7.0) & 6.84 br q (7.0) \\
4′ & 1.85 d (6.6) 3H & 4.26 dd (15.0, 4.9) & 4.61 dd (14.0, 6.4) & 1.78 d (7.0) & 1.83 d (7.0) \\
5″ & 1.83 s, 3H & 1.87 s, 3H & 1.95 d (0.9) & 5.48 dd (4.8, 3.3) & 1.78 s, 3H \\
2″ & 3.77 s, 3H & 3.74 s, 3H & 3.71 s, 3H & 2.03 s, 3H & 3.76 s, 3H \\
OAc & 2.17 s, 3H & 2.03 s, 3H & 2.07 s, 3H & & \\
\hline
\end{tabular}
\caption{$^1$H NMR Data (CDCl\textsubscript{3}, 400 MHz) of 3–7}
\end{table}

The cytotoxic activities of compounds 1–7 were evaluated against the HL-60 (human leukemia) cell line by using the MTT method\textsuperscript{25} and against the A-549 (human lung adenocarcinoma) and BEL-7402 (human hepatocarcinoma) cell lines by using the SRB method,\textsuperscript{22} and with pseudolactic acid B\textsuperscript{23} as the positive control (IC\textsubscript{50} = 4.2 µM against HL-60, 1.6 µM against A-549, and 1.3 µM against BEL-7402). The results revealed that compounds 3–5 showed inhibitory activities against the HL-60 cell line with IC\textsubscript{50} values of 3.1, 8.4, and 8.5 µM, respectively, compounds 3 and 5 showed inhibitory activities against the A-549 cell line with IC\textsubscript{50} values of 7.2 and 4.7 µM, respectively, while none of the tested compounds showed inhibitory activity on the BEL-7402 cell line.
Experimental Section

General Experimental Procedures. Optical rotations were measured on a Perkin-Elmer 341 polarimeter. UV spectra were obtained on a Shimadzu UV-2550 spectrophotometer. IR spectra were recorded on a Perkin-Elmer 341 polarimeter. NMR spectra were obtained on a Bruker DRX 500 spectrometer. HREIMS were measured on a Finnigan MAT-95 mass spectrometer and ESIMS and HRESIMS were obtained on an Esquire 6000 plus mass spectrometer. All solvents used were of analytical grade.

Extraction and Isolation. The air-dried powder of the plant material (4 kg) was percolated with 95% EtOH (3 × 5 L) to give 400 g of crude extract, which was dissolved in water (1 L) and partitioned successively with petroleum ether and EtOAc. The EtOAc-soluble fraction (90 g) was subjected to an MCI gel column (MeOH/H2O, 0% to 100%) to give three fractions, 1a−1g. Fraction 1b was chromatographed over a silica gel column, eluted with petroleum ether/EtOAc, 20:1, to afford four fractions, 1b1−1b4. Fraction 1b1 (150 mg) was purified on a Sephadex LH-20 column, eluted with EtOH, to give (1S,3S,7R,11α)−1,7,11-triol (5 mg), fraction 1b3 (220 mg) gave neolitacumone B (7 mg) by the same purification procedure. Fraction 1d (500 mg) was separated on a reversed-phase C18 silica gel column (MeOH/H2O, 50% to 80%) to afford two fractions, 1d1 and 1d2. Fraction 1d2 was purified by silica gel column chromatography (petroleum ether/aceton, 10:1 to 8:1) to give 1 (7 mg) and 2 (5 mg). Fraction 1e (8 g) was subjected to CC on silica gel (CH2Cl2/MeOH, 200:1 to 20:1) to give five fractions, 1e1−1e5. Fraction 1e2 (870 mg) was subjected to a silica gel column (petroleum ether/EtOAc, 8:1) to afford chloranthalactone E (3 mg). Fraction 1e1 (2.6 g) was chromatographed over a column of reversed-phase C18 silica gel column (MeOH/H2O, 50% to 80%) to afford four fractions, 1e1a−1e3d. Fraction 1e1a (780 mg) was separated over a silica gel column (petroleum ether/aceton, 8:1) to afford chloranthalactone E (3 mg). Fraction 1e3 (2.6 g) was chromatographed over a column of reversed-phase C18 silica gel column (MeOH/H2O, 50% to 80%) to afford four fractions, 1e3a−1e3d. Fraction 1e3a (780 mg) was separated over a silica gel column (petroleum ether/aceton, 8:1 to 3:1), followed by preparative TLC (CH2Cl2/MeOH, 30:1) to afford 3 (5 mg), 4 (30 mg), 5 (5 mg), and chlorahololide F (23 mg). Fraction 1e3b (430 mg) was separated over a silica gel column (petroleum ether/aceton, 8:1 to 6:1), followed by the purification on a Sephadex LH-20 column (EtOH), to give 3−eudesmene-1β,7,11-triol (60 mg). Fraction 1e3d (370 mg) was separated on a silica gel column (petroleum ether/aceton, 8:1) and then purified by preparative TLC (CH2Cl2/MeOH, 30:1) to afford cycloshizukaol A (60 mg). Fractions 1e4 (1.6 g) was chromatographed over a column of reversed-phase C18 silica gel (MeOH/H2O, 50% to 80%) to give three fractions, 1e4a−1e4c. Fraction 1e4a (220 mg) was chromatographed on a silica gel column (petroleum ether/aceton, 8:1 to 6:1), followed by a Sephadex LH-20 column (EtOH), to yield 6 (33 mg), 7 (4 mg), and shizukaol B (16 mg). Fraction 1e4b (670 mg) was

Figure 3. Selected HMBC correlations (H→C) and key ROESY correlations (H→H) of 3.

Table 3. 13C NMR Data (CDCl3, 100 MHz) of 3−7

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δC (δC) of 3−7
UV (MeOH) λ\text{max} (log ε) 217 (4.41) nm; CD (MeOH) λ\text{max} (Δ) 344 (−2.74), 260 (8.64), 219 (−10.00) nm; IR (KBr) ν\text{max} 3446, 2949, 1735, 1649, 1437, 1381, 1267, 1134, 993 cm⁻¹; 1H NMR data, see Table 2; 13C NMR data, see Table 3; EIMS 70 eV m/z (relative intensity) 618 [M⁺] (1), 514 (4), 344 (10), 274 (26), 226 (100), 211 (39), 197 (22), 83 (84), 55 (48); HREIMS m/z 618.2827 (calcd for C₅₈H₆₀O₁₃).  

**Sarcandrolide A (3):** colorless solid; [α]ₐ0° +120 (c 0.1, MeOH); UV (MeOH) λ\text{max} (log ε) 217 (4.41) nm; CD (MeOH) λ\text{max} (Δ) 344 (−2.74), 260 (8.64), 219 (−10.00) nm; IR (KBr) ν\text{max} 3446, 2949, 1735, 1649, 1437, 1381, 1267, 1134, 993 cm⁻¹; 1H NMR data, see Table 2; 13C NMR data, see Table 3; EIMS 70 eV m/z (relative intensity) 618 [M⁺] (1), 514 (4), 344 (10), 274 (26), 226 (100), 211 (39), 197 (22), 83 (84), 55 (48); HREIMS m/z 618.2827 (calcd for C₅₈H₆₀O₁₃).  

**Sarcandrolide B (4):** yellowish powder; UV (MeOH) λ\text{max} (log ε) 216 (4.28) nm; CD (MeOH) λ\text{max} (Δ) 341 (−3.38), 258 (10.82), 217 (−18.6) nm; IR (KBr) ν\text{max} 3439, 2933, 1734, 1651, 1437, 1379, 1277, 1136, 1086, 989 cm⁻¹; 1H NMR data, see Table 2; 13C NMR data, see Table 3; positive mode ESIMS m/z 673 [M + Na⁺]; HREIMS m/z 673.2632 (calcd for C₃₆H₄₂O₁₃Na, 673.2625).  

**Sarcandrolide C (5):** colorless solid; [α]ₐ0° −92 (c 0.1, MeOH); UV (MeOH) λ\text{max} (log ε) 218 (4.43) nm; CD (MeOH) λ\text{max} (Δ) 346 (−1.78), 251 (6.76), 207 (−12.4) nm; IR (KBr) ν\text{max} 3452, 2939, 1751, 1711, 1664, 1616, 1373, 1200, 1161 cm⁻¹; 1H NMR data, see Table 2; 13C NMR data, see Table 3; positive mode ESIMS m/z 813 [M + Na⁺]; negative mode ESIMS m/z 789 [M − H⁺]; HREIMS m/z 813.2715 (calcd for C₅₈H₆₀O₁₃Na, 813.2734).  

**Sarcandrolide D (6):** colorless solid; [α]ₐ0° −26 (c 0.1, MeOH); UV (MeOH) λ\text{max} (log ε) 216 (4.44) nm; CD (MeOH) λ\text{max} (Δ) 273 (18.14), 247 (11.82), 216 (−31.64) nm; IR (KBr) ν\text{max} 3450, 2939, 1751, 1686, 1443, 1383, 1267, 1082, 968 cm⁻¹; 1H NMR data, see Table 2; 13C NMR data, see Table 3; EIMS 70 eV m/z (relative intensity) 678 [M⁺] (62), 660 (80), 642 (100), 556 (58), 512 (61), 482 (60), 410 (76), 379 (77), 223 (55); HREIMS m/z 678.2666 (calcd for C₃₆H₄₂O₁₃).  

**Sarcandrolide E (7):** colorless solid; [α]ₐ0° −91 (c 0.1, MeOH); UV (MeOH) λ\text{max} (log ε) 218 (4.48) nm; CD (MeOH) λ\text{max} (Δ) 341 (−6.68), 262 (22.76), 221 (−14.20) nm; IR (KBr) ν\text{max} 3466, 2937, 1751, 1709, 1648, 1437, 1265, 1132, 972 cm⁻¹; 1H NMR data, see Table 2; 13C NMR data, see Table 3; EIMS 70 eV m/z (relative intensity) 692 [M⁺] (1), 660 (3), 642 (18), 482 (8), 410 (8), 377 (8), 223 (4), 83 (100), 55 (44); HREIMS m/z 692.2805 (calcd for C₃₆H₄₂O₁₃).  

**Cytotoxicity Assay.** Cytotoxic activities were evaluated against the HL-60 cell line by using the MTT method and against the A-549 and BEL-7402 cell lines by using the SRB method, and pseudolaric acid B was used as the positive control (for details see the Supporting Information).

**Acknowledgment.** Financial support from the Key Project of National Natural Science Foundation (Grant No. 30630072; 30721005) and National Science & Technology Major Project “Key New Drug Creation and Manufacturing Program” (Grant No. 2009ZX09301-001) of the People’s Republic of China is gratefully acknowledged. We thank Prof. S.-M. Huang, Department of Biology, Hainan University, for the identification of the plant material.

**Supporting Information Available:** Cytotoxicity assay; IR, EIMS, 1H, 13C, and 2D NMR spectra of compounds 1–7. This material is available free of charge via the Internet at http://pubs.acs.org.

**References and Notes**