Diterpenoids from the Roots of *Suregada glomerulata*

Ren-Yi Yan, Yong-Xia Tan, Xi-Qiang Cui, Ruo-Yun Chen,* and De-Quan Yu

Key Laboratory of Bioactive Substances and Resources Utilization of Chinese Herbal Medicine, Ministry of Education, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, People's Republic of China

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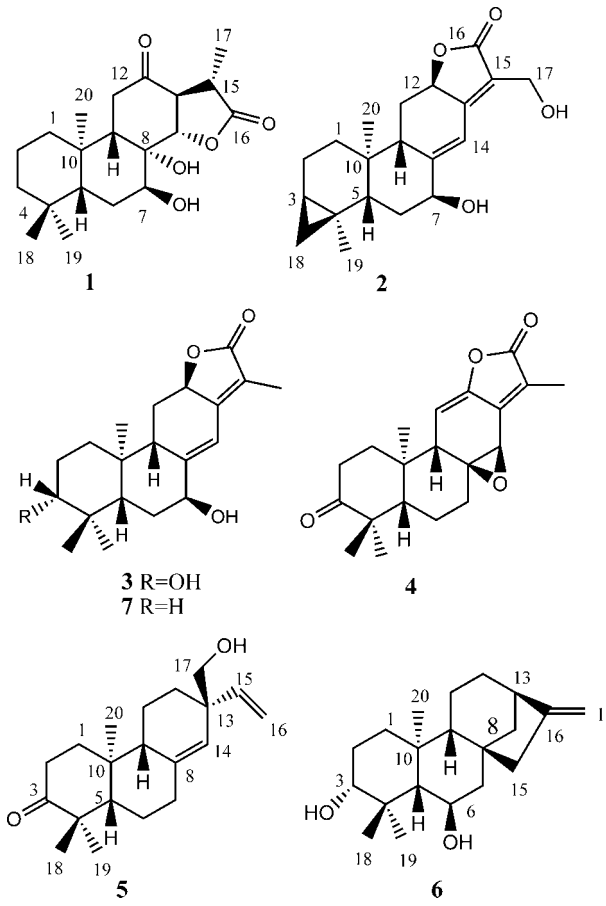
Six new diterpenoids, 7β,8α-dihydroxy-12-oxo-*ent*-abietan-16,14-olide (**1**), 3,4,18β-cyclopropa-7β,17-dihydroxy-*ent*-abieta-8(14),13(15)-dien-16,12-olide (**2**), 3α,7β-dihydroxy-*ent*-abieta-8(14),13(15)-dien-16,12-olide (**3**), 3-oxo-8β,14β-epoxy-*ent*-abieta-11,13(15)-dien-16,12-olide (**4**), 17-hydroxy-*ent*-pimara-8(14),15-dien-3-one (**5**), and 3α,6β-dihydroxy-*ent*-kaur-16-ene (**6**), and two known compounds, 7β-hydroxy-*ent*-abieta-8(14),13(15)-dien-16,12-olide (**7**) and jolkinolide B, were isolated from roots of *Suregada glomerulata*. The structures of the new compounds were elucidated on the basis of 1D and 2D NMR and other spectroscopic studies. The structure of compound **1** was confirmed by X-ray crystallography. Cytotoxic activities were evaluated against five human tumor cell lines.

The genus *Suregada* (*Gelonium*) is comprised of about 40 species distributed in Southeast Asia and Oceania (north of Australia). *S. glomerulata* and *S. aequorea* are the only two species of this genus found in China. Studies on other species of this genus revealed the presence of flavonoids,[1,2] triterpenoids,[3,4] and various diterpenoids.[5–11] In our study, we found that an ethanol extract of *S. glomerulata* (Bl.) Baill. (Euphorbiaceae) showed potent inhibitory activity against rat *a*-glucosidase. Several diterpenoids from the roots of this plant have been reported by our research group.[12,13] In continuation of this investigation, six new diterpenoids (**1**–**6**) and two known diterpenoids (**7**[14] and jolkinolide B[5]) were isolated. The structures of the known compounds were identified by comparison of their spectroscopic data with those values reported previously. In this paper we report the isolation and structure elucidation of new diterpenoids (**1**–**6**) as well as the cytotoxic activities of these compounds.



Results and Discussion

Compound **1** was isolated as colorless needles with a molecular formula of $C_{20}H_{30}O_5$ from the HREIMS (*m*/*z* 350.2082, $[M]^+$), implying six degrees of unsaturation. Its IR spectrum showed characteristic absorption bands for OH (3473 cm^{-1}) and carbonyl groups (1780, 1711 cm^{-1}). The ^1H NMR spectrum indicated the presence of three tertiary methyl (δ_H 0.88, 0.89, 1.07), a secondary methyl (δ_H 1.29, d, J = 6.8 Hz), and two oxymethine (δ_H 3.99, br s; 4.25, d, J = 12.1 Hz) groups. The ^{13}C NMR and DEPT spectra indicated 20 carbons including four methyl, five methylene, four methine, two oxymethine, an ester carbonyl, a ketone carbonyl, a hydroxylated quaternary carbon, and two other quaternary carbon signals. The NMR and IR data, together with the molecular formula, suggested that **1** had four rings, including a lactone ring, in the molecule. The COSY experiment disclosed two partial structures, $CHCH_2$ and $OCHCHCHCH_3$, corresponding to the C-9, C-11 and C-14, C-13, C-15, C-17 fragments. Connections between the fragments were then established through analysis of the HMBC spectrum as shown in Table 1. HMBC correlations between H-18, H-19 and both C-3 and C-5, between H-20 and C-1, C-9, and C-10, between H-7 and C-5, C-8, and C-9, and between H-17 and C-16 enabled the specific location of groups that were not readily identifiable as part of spin systems already identified from the $^1H-^1H$ COSY experiment.

However, no HMBC connectivity necessary for constructing the lactone ring of **1** was observed between H-14 and C-16. Finally, the detailed structure and relative configuration of **1** was established unambiguously from single-crystal X-ray analysis (ORTEP drawing in Figure 1). A view of the solid-state conformation (Figure 1) indicates that rings A, B, and C of compound **1** are in chair conformations and that ring D is in an envelope conformation. The OH group at C-8 is α-oriented. Therefore, compound **1** was identified as 7β,8α-dihydroxy-12-oxo-*ent*-abietan-16,14-olide.

The HREIMS of compound **2** exhibited a molecular ion peak at *m*/*z* 330.1846 $[M^+]$ corresponding to $C_{20}H_{26}O_4$. It showed evidence for an $\alpha,\beta,\gamma,\delta$-unsaturated-$\gamma$-lactone chromophore in the UV (λ_{max} 273.6 nm, log ϵ 4.13) and IR (ν_{max} 1739, 1665 cm^{-1}) spectra. In the ^1H NMR spectrum three upfield proton signals (δ_H 0.16, 0.49/H-18; δ_H 0.67/H-3) correlated by HSQC to ^{13}C shifts at δ_C 21.6 and δ_C 19.3 and a ^{13}C signal for a quaternary carbon at δ_C 15.7, indicating a trisubstituted cyclopropane ring in the molecule. One olefinic proton (δ_H 6.62, br s), one hydroxymethyl (δ_H 4.45/δ_C 55.4), two oxygenated methines (δ_H 4.45/δ_C 72.4; δ_H 4.94/δ_C 76.5), and

* To whom correspondence should be addressed. Tel: +8610-83161622. Fax: +8610-63017757. E-mail: ruoyunchen@hotmail.com.

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Table 1. NMR Data (δ, ppm) for Compounds **1** and **2** in $CDCl_3$

	1			**2**		
pos.	δ_H (J = Hz)[a]	δ_C, mult[b]	HMBC	δ_H (J = Hz)[a]	δ_C, mult[b]	HMBC
1a	1.61, m	39.2, CH_2		1.74, m	33.1, CH_2	
1b	0.93, m			0.91, m		
2a	1.62, m	18.2, CH_2		1.98, m	19.5, CH_2	
2b	1.46, m			1.74, m		
3a	1.53, m	41.7, CH_2		0.67, m	19.3, CH	1, 19
3b	1.21, m					
4		32.8, qC			15.7, qC	
5	1.49, m	47.3, CH		1.90, dd (13.6, 3.2)	43.4, CH	6
6a	2.02, ddd (14.0, 13.2, 2.0)	25.9, CH_2	5	2.13, m	34.2, CH_2	
6b	1.73, m			1.74, m		
7	3.99, br s	70.4, CH	5, 8, 9	4.45, br s, overlap	72.4, CH	5, 13
8		72.5, qC			153.5, qC	
9	1.75, m	47.9, CH		2.65, d (8.4)	42.8, CH	1, 12, 14, 20
10		37.9, qC			40.8, qC	
11a	2.56, t (12.8)	37.6, CH_2	9, 10, 12	2.61, dd (13.6, 6.0)	27.5, CH_2	8, 9, 13
11b	2.33, dd (12.8, 4.4)		8, 12, 13	1.55, ddd (13.6, 13.6, 8.4)		9, 10, 12, 13
12		204.6, qC		4.94, dd (13.6, 4.8)	76.5, CH	11, 13, 15
13	3.84, t (12.1)	54.5, CH	8, 12, 14, 15, 17		157.4, qC	
14	4.25, d (12.1)	81.5, CH	12, 15	6.62, br s	115.3, CH	7, 9, 11, 13, 15
15	2.83, m	36.4, CH	12, 13, 16		120.8, qC	
16		177.7, qC			173.9, qC	
17	1.29, d (6.8)	13.5, CH_3	13, 15, 16	4.45, br s, overlap	55.4, CH_2	13, 15, 16
18	0.89, s	33.2, CH_3	3, 4, 5, 19	0.16, t (5.0) *endo*; 0.49, dd (9.2, 4.4) *exo*	21.6, CH_3	4, 5, 19; 3, 4, 19
19	0.88, s	21.6, CH_3	3, 4, 5, 18	0.95, s	23.9, CH_3	3, 4, 5, 18
20	1.07, s	14.5, CH_3	1, 5, 9, 10	0.87, s	13.6, CH_3	1, 5, 9, 10

[a] Recorded at 400 Hz. [b] Recorded at 100 Hz and multiplicity deduced by DEPT and HSQC spectra.

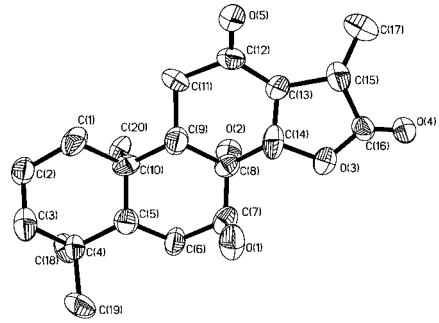

Figure 1. ORTEP structure of compound **1**.

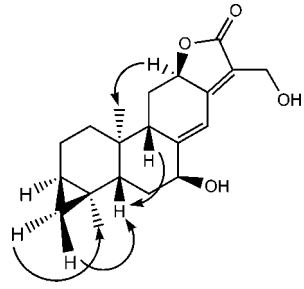

Figure 2. Important NOE interactions for compound **2**.

two tertiary methyl groups (δ_H 0.87/δ_C 13.6; δ_H 0.95/δ_C 23.9) were also inferred from the NMR spectra. The structure of **2** was deduced to have a rearranged abietane skeleton with the help of 2D NMR studies and from comparative studies with reported diterpene lactones.[9,10] The HMBC spectrum of **2** (Table 1) showed correlations of H_2-18 with C-3, C-4, and C-19, H-3 with C-1 and C-19, and H-19 with C-3, C-5, and C-18. According to these correlations the connection of the cyclopropyl moiety (CH-3, CH_2-18, C-4) with the cyclohexane ring was confirmed. Long-range correlations of H-14 with C-7 and of H-17 with C-13, 15, and C-16 confirmed the OH groups at C-7 and C-17, respectively. The relative configuration of **2** was deduced from the NOESY spectrum (Figure 2). The NOEs between H-9/H-5, H-18 *endo*/H-5, and H-12/H-20 suggested the α-orientation of H-20 and β-orientation of the cyclopropane ring. The 7-OH of compound **2** was determined to be β-oriented from the small coupling constant of H-7. The structure of compound **2** was therefore elucidated as 3,4,18β-cyclopropa-7β,17-dihydroxy-*ent*-abieta-8(14),13(15)-dien-16,12-olide.

The molecular formula of **3** was determined to be $C_{20}H_{28}O_4$ on the basis of HREIMS (m/z 332.2009, $[M]^+$) and ^{13}C NMR analyses. The UV and IR spectra of **3** also indicated the presence of an α,β,γ,δ-unsaturated-γ-lactone group (λ_{max} 269.4 nm, log ϵ 4.03; ν_{max} 1733, 1666 cm^{-1}), and this was further supported by NMR data. In the ^1H and ^{13}C NMR spectra of **3**, a number of other characteristic features were identified: three methyl groups (δ_H 0.80/δ_C 16.2; δ_H 0.95/δ_C 16.4; δ_H 0.99/δ_C 29.0) bonded to the two quaternary carbons (δ_C 39.3, 42.2) and one methyl group (δ_H 1.78/δ_C 8.4) bonded to an olefinic carbon; and three oxygenated methines (δ_H 4.88/δ_C 76.5; δ_H 3.25/δ_{OH} 3.50/δ_C 78.5; δ_H 4.42/δ_{OH} 4.08/δ_C 72.0). These indicated that compound **3** was an abietane diterpenoid possessing a structure very similar to that of helioscopinolide A.[15] Comparative study of the chemical shifts of C-5, C-6, C-7, C-8, and C-9 with helioscopinolide A indicated that the additional OH was at C-7 of compound **3**. Long-range correlations of H-14 with C-7, and 7-OH with C-8, in the HMBC spectrum confirmed it. The strong NOE interaction between H-20 and H-12 confirmed that both were oriented on the same side of the molecule. Also, interactions between H-5 and H-9, H-5, and H-3 established the relative configuration of these three carbon centers. Axial orientation of the 7-OH group in compound **3** followed from the small coupling constant of H-7. On the basis of the above evidence, compound **3** was deduced to be 3α,7β-dihydroxy-*ent*-abieta-8(14),13(15)-dien-16,12-olide.

HREIMS of **4** gave a molecular ion at m/z 328.1693 $[M]^+$ ($C_{20}H_{24}O_4$). The UV and IR spectra revealed the presence of α,β,γ,δ-unsaturated-γ-lactone (282.0 nm, 1772, 1655 cm^{-1}) and keto (1701 cm^{-1}) groups. The NMR spectra of **4** exhibited four methyl signals (δ_H 0.95/δ_C 14.7; δ_H 1.16/δ_C 25.7; δ_H 1.09/δ_C 22.2; δ_H 2.09/δ_C 8.7), an oxymethine (δ_H 3.76, br s/δ_C 54.2), one trisubstituted olefinic proton (5.44, d, J = 5.2 Hz), one lactone carbonyl carbon (δ_C 170.3), one keto group (δ_C 214.7), and four olefinic carbons (δ_C 102.6, 125.9, 144.5, 147.9). The ^1H and ^{13}C NMR spectra of **4** were similar to those of 3α-hydroxy-8β,14β-epoxy-*ent*-abieta-11,13 (15)-dien-16,12-olide, isolated from the same plant,[13] except that the C-3 OH was replaced by a keto group. This was confirmed by an HMBC experiment; the two methyl

Table 2. ^{1}H NMR and ^{13}C NMR Data (δ, ppm) of Compounds **3**−**7**

	3 (acetone-d_6)		**4** ($CDCl_3$)		**5** ($CDCl_3$)		**6** ($CDCl_3$)		**7** ($CDCl_3$)
pos.	δ_H (J = Hz)	δ_C	δ_H (J = Hz)	δ_C	δ_H (J = Hz)	δ_C	δ_H (J = Hz)	δ_C	δ_C
1a	1.97, dt (13.2, 3.6)	38.1	2.04, dq (13.2, 5.6, 3.2)	37.9	1.96, dq (13.5, 5.7, 3.0)	37.6	1.84, m	38.6	41.9
1b	1.29, ddd (13.2, 12.8, 5.2)		1.78, m		1.49, m		0.84, m		
2a	1.61, m	28.6	2.64, ddd (15.2, 14.4, 5.6)	33.9	2.64, ddd (15.0, 15.0, 5.7)	34.7	1.69, m	26.9	19.0
2b			2.27, dt, (15.2, 4.0)		2.27, dt (15.0, 3.0)				
3	3.25, m	78.5		214.7		216.7	31.8, dd, (11.7, 5.4)	78.9	39.5
4		39.3		47.9		47.8		39.1	33.1
5	1.80, dd (13.2, 2.8)	47.2	1.71, m	53.9	1.47, m	55.3	0.92, d (10.5)	60.3	47.1
6a	1.92, ddd (3.6, 2.8, 2.4)	31.6	1.74, m	21.5	1.63, m	23.0	4.01, td (10.5, 3.9)	69.1	31.0
6b	1.67, m								
7a	4,42, dd (5.6, 2.8)	72.0	2.18, m	33.7	2.44, dt (15.0, 3.3)	35.4	1.82, m	51.5	72.4
7b			1.66, m		2.10, m		1.61, m		
8		153.2		60.7		140.3		44.3	151.2
9	2.72, br d (8.4)	47.2	2.70, d (5.2)	50.8	1.79, br t (9.6)	50.8	1.05, overlap	55.3	46.7
10		42.2		40.7		38.1		40.8	41.9
11a		28.2	5.44, d (5.2)	102.6	1.51, m	18.6	1.55, m	17.9	27.2
11b	1.37, ddd (13.6, 13.2, 8.4)				1.29, m				
12a	4.88, ddq (13.2, 6.0, 1.2)	76.5		147.9	1.58, m	29.7	1.67, m	33.0	76.1
12b					1.37, m		1.47, m		
13		156.4		144.5		45.2	2.65, br s	43.4	155.1
14a	6.52, br s	115.7	3.76, br s	54.2	5.42, br s	123.8	1.93, br d (11.4)	40.3	115.9
14b							1.23, m		
15		118.4		125.9	5.96, dd (17.1, 10.2)	142.9	2.12, t (2.1)	49.2	118.9
16a		174.7		170.3	5.23, dd (10.2, 1.5)	117.5		155.1	174.9
16b					5.08, dd (17.1, 1.5)				
17	1.78, d (1.2)	8.4	2.09, br s	8.7	3.38, ABq (10.2)	70.4	4.82, br s, 4.76, br s	103.6	8.5
18	0.99, s	29.0	1.16, s	25.7	1.09, s	25.6	1.30, s	33.1	33.6
19	0.80, s	16.2	1.09, s	22.2	1.06, s	22.3	0.99, s	15.7	21.7
20	0.95, s	16.4	0.95, s	14.7	0.90, s	14.4	1.05, s	18.5	16.1

protons (δ 1.09, H-19; δ 1.16, H-18) as well as H-2a (δ 2.64) showed long-range correlations with C-3 (δ 214.7), respectively. Compound **4** showed significant NOE correlations between H-20 and H-19, H-2$_{ax}$ (δ 2.64) and between H-9 and H-5, H-7$_{ax}$ (δ 2.18), which indicated that Me-19 and Me-20 were on one side of the molecule, while H-9 and H-5 were on the opposite side of the molecule. H-14 was α-oriented on the basis of the NOE correlations of H-14 to H-20 and H-7$_{eq}$ (δ 1.66). Thus, compound **4** was assigned as 3-oxo-8β,14β-epoxy-*ent*-abieta-11,13(15)-dien-16,12-olide.

The molecular formula of compound **5** was assigned as $C_{20}H_{30}O_2$ (*m*/*z* 302.2269, $[M]^+$) by HREIMS. It gave IR bands for OH (3461 cm^{-1}), keto (1712 cm^{-1}), and olefinic functionalities (1659 cm^{-1}). The ^{1}H NMR spectrum exhibited signals for an ABX system of a vinyl group at δ 5.23 (dd, J = 1.5, 10.2 Hz, H-16a), 5.08 (dd, J = 1.5, 17.1 Hz, H-16b), and 5.69 (dd, J = 10.2, 17.1 Hz, H-15), an olefinic proton at δ 5.42 (1H, br s, H-14), and an oxygenated methylene at δ 3.38 (ABq, J = 10.2 Hz, H-17). The data were very similar to those of 3α,17-dihydroxy-*ent*-pimara-8(14),15-diene.[16] However, compound **5** exhibited a keto group signal at δ 216.7 instead of the C-3 oxygenated methine. This was supported by long-range correlations of H-18/C-3, H-19/C-3, and H-2a/C-3 in the HMBC spectrum. Furthermore, the relative configuration of **5** was indicated by a NOESY spectrum, which showed NOE correlations between the following proton pairs: H-5/H-9, H-5/H-18, H-20/H-19, H-20/H-16b. Therefore, compound **5** was determined to be 17-hydroxy-*ent*-pimara-8(14),15-dien-3-one.

Compound **6** was assigned the molecular formula $C_{20}H_{32}O_2$, as established from its HREIMS (*m*/*z* 304.2386, M^+). The ^{1}H NMR spectrum of **6** contained signals indicating three tertiary methyl (δ_H 0.99, 1.05, 1.30), an exocyclic methylene (δ_H 4.76, br s, 4.82, br s), and two oxymethine (δ_H 3.18, dd, J = 5.4, 11.7 Hz; δ_H 4.02, td, J = 3.9, 10.5 Hz) groups. On comparison with 3α-hydroxy-*ent*-kaur-16-ene,[16] the NMR spectrum of **6** lacked the upfield carbon signal attributable to C-7 (δ_C 20.4), and it was replaced by oxymethine signals at δ_H 4.02 and δ_C 69.1. This was associated with relative downfield shifts of C-5 (4.9 ppm), C-7 (12.4 ppm), and C-18 (2.1 ppm). This clearly indicated an additional OH group at C-6, which was substantiated by HMBC correlations between H-5/C-6, H-5/C-7, and H-15/C-7. NOE correlations of H-5/H-3, H-5/H-9, H-6/H-19, H-6/H-20, and H-20/H-14a were helpful in determining the relative configuration of compound **6**. Thus, compound **6** was elucidated as 3α,6β-dihydroxy-*ent*-kaur-16-ene.

Table 3. Cytotoxicity of Compounds **4** and **8** (IC_{50} μg/mL)[a]

compound	A549	Bel 7402	BGC 823	HCT-8	A 2780
4	>10	7.53	>10	>10	8.22
8	6.10	5.95	5.81	6.88	5.09
5-FU	0.18	0.54	0.70	0.54	0.65

[a] A549: human lung cancer cell; Bel 7402: human liver cancer cell; BGC 823: human stomach cancer cell; HCT-8: human colon cancer cell; A 2780: human ovarian cancer cell; 5-FU: 5-fluorouracil.

All of the isolated compounds were evaluated for cytotoxicity against five human tumor cell lines. Jolkinolide B showed weak cytotoxicity against all of the cell lines in which it was tested. Compound **4** exhibited cytotoxcity only against the Bel 7402 and A 2780 cell lines (Table 3). The other six compounds were inactive (IC_{50} >10μg/mL).

Experimental Section

General Experimental Procedures. Melting points were determined on an XT4-100x melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 241 digital polarimeter at 20 °C. UV spectra were taken on a Shimadzu UV-300 spectrophotometer. IR spectra were recorded on an IMPACT 400 spectrometer. The ^{1}H, ^{13}C NMR, COSY, HMQC, HMBC, and NOESY spectra were run on a Mercury-400 spectrometer using solvent peaks as references. EIMS were measured on an AutoSpec Ultima-Tof mass spectrometer at 70 eV. ESIMS were obtained using an Agilent 1100 series LC/MSD Trap SL mass spectrometer. HPLC was carried out on a Waters-600 instrument using a SPD-6AV detector. A reversed-phase C_{18} column (YMC-Pack ODS-A Φ 20 × 250 mm, 10 μm) was employed. Single-crystal X-ray crystallography was determined using a MAC DIP-2030K. Column chromatography was performed with silica gel (160–200 mesh, Qingdao Marine Chemical Group Co., Qingdao, P. R. China) and Sephadex LH-20 (Pharmacia Biotech AB, Uppsala, Sweden). TLC was carried out on precoated silica gel GF254 glass plates. Spots were visualized under UV light or by spraying with 10% H_2SO_4 in 95% EtOH followed by heating.

Plant Material. The roots of *S. glomerulata* were collected in Hainan Province, People's Republic of China, and identified by

Professor Shi-man Huang, Hainan University. A voucher specimen (No. 8710) has been deposited in the herbarium of the Institute of Material Medica, Chinese Academy of Sciences and Peking Union Medical College.

Extraction and Isolation. Air-dried, powdered roots (18 kg) of *S. glomerulata* were extracted three times under reflux with 95% EtOH. After evaporation of EtOH under vacuum, the residue (1770 g) was suspended in distilled H_2O and extracted successively with petroleum ether (60–90 °C), ethyl acetate, and n-BuOH. The ethyl acetate extract was evaporated under reduced pressure to give 550 g of residue. Part of the residue (380 g) was chromatographed over a silica gel column (160–200 mesh, 2.6 kg) eluted using a petroleum ether−EtOAc gradient (9:1–8:2–7:3–6:4) to provide 32 fractions. Fraction 4 (1.4 g) was separated by column chromatography (CC) on silica gel (160–200 mesh, 70 g), eluted with petroleum ether−acetone (99:1–95:5–9:1–8:2–7:3) to give six fractions. Fraction 4-4 (129 mg) was further purified by silica gel CC, eluted with $CHCl_3$, to give jolkinolide B (12 mg). Fraction 5 (1.5 g) was subjected to silica gel CC (160–200 mesh, 75 g), eluted with petroleum ether−acetone (95:5–9:1–8:2), to give eight fractions. Fraction 5-5 (640 mg) was further chromatographed on silica gel, eluted with $CHCl_3$, to give **5** (6 mg). Fraction 8 (5.5 g) was subjected to silica gel CC (160–200 mesh, 250 g), eluted with petroleum ether−acetone (95:5–9:1–8:2), to give 11 fractions. Fraction 8-8 (700 mg) was separated on a Sephadex LH-20 column, using MeOH for elution, to produce six fractions. Fraction 8-8-4 (100 mg), on repeated silica gel CC, afforded compound **1** (4 mg). Compound **4** (37 mg) was isolated from fraction 8-8-5 (120 mg) by preparative TLC on Si gel ($CHCl_3$−Me_2CO, 98:2). Fraction 9 (3.3 g) was separated on a Sephadex LH-20 column using MeOH for elution to produce nine fractions. Fraction 9-3 (400 mg) was passed over a silica gel column with $CHCl_3$−Me_2CO (1:0–100:1–100:2), yielding compound **6** (5 mg) and fraction 9-3-3 (30 mg) finally purified by RP-HPLC, eluted with 75% MeOH in water, to give **7** (4 mg). Fraction 20 (5.1 g) was purified over a silica gel column (250 g) eluted with $CHCl_3$−MeOH (1:0–98:2–95:5–9:1), which yielded eight fractions. Further chromatography of fraction 20-7 (580 mg) over silica gel (25 g), eluted with a gradient of petroleum ether−acetone and acetone, yielded 15 fractions. Fraction 90-7-7 (190 mg), purified by RP-HPLC, eluted with 65% MeOH in water, gave **2** (5 mg). Fraction 20-7-11 (130 mg), purified by RP-HPLC, eluted with 55% MeOH in water, yielded **3** (9 mg).

7*β*,8α-Dihydroxy-12-oxo-*ent*-abietan-16,14-olide (1): colorless needles (EtOAc); mp 240–242 °C; $[\alpha]^{20}_D$ –38.0 (*c* 0.32, $CHCl_3$); IR (KBr) ν_{max} 3473, 2945, 2897, 1780, 1711, 1390, 1061 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) see Table 1, ^{13}C NMR (100 MHz, $CDCl_3$) see Table 1; ESIMS *m/z* 351 $[M + H]^+$, 373 $[M + Na]^+$, 389 $[M + K]^+$, 723 $[2M + Na]^+$; HREIMS *m/z* 350.2082 $[M]^+$ (calcd for $C_{20}H_{30}O_5$, 350.2093).

X-ray Crystal Data of 1. A colorless prism crystal was obtained from EtOAc at 4 °C. $C_{20}H_{30}O_5$, $M = 350.44$, crystal size 0.10 × 0.20 × 0.40 (mm), monoclinic system, space group $P2_1$, $Z = 2$; $a = 7.544(1)$ Å, $b = 6.066(1)$ Å, $c = 20.579(1)$ Å, $\beta = 99.92(4)°$, $V = 927.7(2)$ Å^3; density (calcd) 1.255 g/cm^3. Intensity data were collected on a MAC DIP-2030K image plate diffractometer with graphite monochromator at 295(2) K (Mo Kα radiation, ω scans, $2\nu_{max} = 50.0°$). A total of 1467 unique reflections were collected, of which 1458 were observed ($F^2 \geq 3\sigma F^2$). The structure was solved by direct methods using the SHELXS-97 program and expanded using difference Fourier techniques, refined by the program and method SHELXS-97 and the full-matrix least-squares calculations. The final refinement gave $R_1 = 0.088$ and $wR_2 = 0.207$. Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre, deposit No. CCDC 627092. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB21EZ, UK [fax: +44-(0)-1223-336033 or e-mail: deposit@ ccdc.cam.ac.uk].

3,4,18*β*-Cyclopropa-7*β*,17-dihydroxy-*ent*-abieta-8 (14),13 (15)-dien-16,12-olide (2): white, amorphous powder; $[\alpha]^{20}_D$ +192.4 (*c* 0.26, $CHCl_3$); IR (KBr) ν_{max} 3358, 2956, 2923, 2852, 1739, 1665, 1461, 1377 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 273.6 (4.13) nm; ^1H NMR (400 MHz, $CDCl_3$) see Table 1; ^{13}C NMR (100 MHz, $CDCl_3$) see Table 1; EIMS *m/z* 330 $[M]^+$ (25), 313 (10), 312 (65), 297(10), 294(35), 121(100); HREIMS *m/z* 330.1846 $[M]^+$ (calcd for $C_{20}H_{26}O_4$, 330.1831).

3α,7*β*-Dihydroxy-*ent*-abieta-8 (14),13(15)-dien-16,12-olide (3): white, amorphous powder; $[\alpha]^{20}_D$ +363.0 (*c* 0.43, MeOH); IR (KBr) ν_{max} 3382, 2931, 2871, 1733, 1666, 1030 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 269.4 (4.03) nm; ^1H NMR (400 MHz, acetone-d_6) see Table 2; ^{13}C NMR (100 MHz, acetone-d_6) see Table 2; EIMS *m/z* 332 $[M]^+$ (5), 315 (6), 314 (15), 297 (15), 296 (100), 281 (30); HREIMS *m/z* 332.2009 $[M]^+$ (calcd for $C_{20}H_{28}O_4$, 332.1988).

3-Oxo-8*β*,14*β*-epoxy-*ent*-abieta-11,13(15)-dien-16,12-olide (4): gum; $[\alpha]^{20}_D$ +109.1 (*c* 0.11, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 239.0 (4.34), 282.0 (4.05) nm; IR (KBr) ν_{max} 2931, 2860, 1772, 1701, 1655 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) see Table 2; ^{13}C NMR (100 MHz, $CDCl_3$) see Table 2; ESIMS *m/z* 329 $[M + H]^+$, 351 $[M + Na]^+$, 367 $[M + K]^+$; HREIMS *m/z* 328.1693 $[M]^+$ (calcd for $C_{20}H_{24}O_4$, 328.1675).

17-Hydroxy-*ent*-pimara-8(14),15-dien-3-one (5): gum; $[\alpha]^{20}_D$ –18.9 (*c* 0.35, MeOH); IR (KBr) ν_{max} 3461, 2928, 2856, 1712, 1659, 1043, 870 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) see Table 2; ^{13}C NMR (100 MHz, $CDCl_3$) see Table 2; EIMS *m/z* 302 $[M]^+$ (45), 287 (19), 284 (35), 272 (50), 271 (70), 123 (100); HREIMS *m/z* 302.2269 $[M]^+$ (calcd for $C_{20}H_{30}O_2$, 302.2246).

3α,6*β*-Dihydroxy-*ent*-kaur-16-ene (6): white, amorphous powder; $[\alpha]^{20}_D$ −46.3 (*c* 0.35, $CHCl_3$); IR (KBr) ν_{max} 3354, 2944, 2832, 1653, 1031, 794 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) see Table 2; ^{13}C NMR (100 MHz, $CDCl_3$) see Table 2; EIMS *m/z* 304 $[M]^+$ (10), 287 (11), 286 (45), 271 (30), 123 (100); HREIMS *m/z* 304.2386 $[M]^+$ (calcd for $C_{20}H_{32}O_2$, 304.2402).

Cytotoxicity Testing. Cytotoxicity against human tumor cell lines was measured in a 5-day MTT test using A 549, Bel 7402, BGC 823, HCT-8, and A 2780 cells according to the procedure described previously.[18]

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Supporting Information Available: X-ray data for compound **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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