Tetranortriterpenoids from *Chisocheton paniculatus*

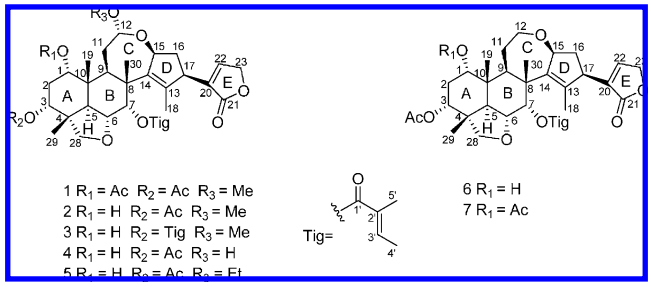
Ming-Hua Yang, Jun-Song Wang, Jian-Guang Luo, Xiao-Bing Wang, and Ling-Yi Kong*

Department of Natural Medicinal Chemistry, China Pharmaceutical University, 24 Tong Jia Xiang, Nanjing 210009, People's Republic of China

Received August 6, 2009

Seven new tetranortriterpenoids (**1**−**7**), named chisonimbolinins A−G, were isolated from twigs of *Chisocheton paniculatus.* Their structures were elucidated on the basis of extensive spectroscopic analyses, and the structure of **1** was confirmed by a single-crystal X-ray diffraction study. Cytotoxic activity of compounds **1**−**7** was evaluated using HeLa and SMMC-7721 tumor cell lines.

Limonoids isolated from species of the family Meliaceae have been of interest due to their diverse structures and reported antifeedant, antimicrobial, antimalarial, and cytotoxic activities.[1] The genus *Chisocheton* contains about 50 species distributed mainly in India and Malaysia. *Chisocheton paniculatus* Hiern (Meliaceae) is the only species growing in southern China. Previous investigations revealed that *C. paniculatus* is a rich source of protolimonoids and ordinary limonoids,[2] some of which have antifungal activity.[3] In the current work, seven new C-*seco*-type tetranortriterpenoids (**1**−**7**), named chisonimbolinins A−G, and six known triterpenoids were isolated from twigs of *C. paniculatus*. Compounds **6** and **7** are the first C-*seco*-type tetranortriterpenoids having a C-12,15-ether linkage rather than a C-12,15-hemiacetal or -lactone linkage.[4,5] To the best of our knowledge, this is the first report of C-*seco*-type tetranortriterpenoids from the genus *Chisocheton*. Since cytotoxic activities of C-*seco*-type tetranortriterpenoids have been reported,[6] and the characteristic unsaturated five-membered lactone ring E is essential to activities of cardenolides,[7] we evaluated cytotoxic activity of these compounds using HeLa and SMMC-7721 tumor cell lines.



Results and Discussion

Chisonimbolinin A (**1**) was isolated as colorless crystals (MeOH/$CHCl_3$). Its molecular formula, $C_{36}H_{48}O_{11}$, was established from the quasi-molecular ion peak at *m*/*z* 679.3086 $[M + Na]^+$ (calcd for $C_{36}H_{48}O_{11}Na$, 679.3089) in the HRESIMS. IR peaks at 1755 and 1740 cm^{-1} revealed the presence of ester carbonyl groups. Its ^1H NMR spectrum (Table 1) indicated one methoxy group (δ_H 3.39, 3H, s), two acetyl groups (δ_H 2.07 and 2.00, each 3H, s), and one tigloyl group [δ_H 6.92 (1H, qd, 7.1, 1.2), 1.79 (3H, d, 7.1), and 1.90 (3H, s)]. In addition to the above substituents, its ^{13}C NMR spectrum (Table 2) exhibited 26 signals, indicating four methyl, five methylene (two oxygenated), 10 methine (one olefinic, one hemiacetal, and five oxygenated), and seven quaternary (four olefinic) carbons, consistent with a ring C-*seco*-nimbolinin skeleton.[4] Comparison of the NMR data of **1** with 12-*O*-methylnimbolinin B[8] indicated that the A, B, C, and D rings were similar, but differed in ring E. The furan ring signals were absent and, instead, signals of an α,*β*-unsaturated-*γ*-lactone ring system were present[9] [δ_H 4.77 (2H, s) and 7.13 (1H, s); δ_C 137.7, 145.5, 174.4, and 70.3] in **1**, which was confirmed by the HMBC correlations (Figure 1). Locations of the substituents were also determined by HMBC experiments. HMBC cross-peaks were observed from H-1 (δ_H 4.72, 1H, s) and H-3 (δ_H 4.93, 1H, s) to the two acetyl carbonyl signals (δ_C 169.7), from H-7 (δ_H 5.77, 1H, d, 2.4) to the tigloyl carbonyl signal (δ_C 166.1), and from the methoxy proton signal (δ_H 3.39, 3H, s) to C-12 (δ_C 98.3).

The coupling constants of H-1 (δ_H 4.72, s), H-3 (δ_H 4.93, s), H-5 (δ_H 2.81, d, 12.7), H-6 (δ_H 4.09, dd, 12.7, 2.7), H-7 (δ_H 5.77, d, 2.4), and H-9 (δ_H 3.13, d, 9.9) suggested that H-1, H-3, and H-7 were equatorial and that H-5, H-6, and H-9 were axial. Strong NOESY cross-peaks (Figure 2a) of the H_3-29 signal at δ_H 1.16 with protons at δ_H 0.97 (H_3-19), δ_H 4.93 (H-3), and δ_H 4.09 (H-6), of H-7 at δ_H 5.77 with δ_H 4.09 (H-6) and δ_H 1.47 (H_3-30), and of H_3-19 with δ_H 4.72 (H-1) indicated a *β*-orientation for these protons and confirmed the chair form of the A and B rings. NOESY correlations from H-9 to H-5 and H-15, and from H-16b to H-15 and H-17, revealed the α-orientation of the protons at these positions. The only uncertainty for the relative configuration of **1** was H-12 since it correlated with both H-11α and H-11*β* in the NOESY spectrum. A single-crystal X-ray diffraction study of **1** (Figure 2b) demonstrated *β*-orientation of H-12 and confirmed the structure of **1** as indicated.

Chisonimbolinin B (**2**), a white, amorphous powder, had the molecular formula $C_{34}H_{46}O_{10}$, as established by HRESIMS. Its IR spectrum displayed OH (3464 cm^{-1}) and carbonyl (1755, 1728 cm^{-1}) absorptions. The ^1H and ^{13}C NMR data of **2** (Tables 1 and 2) resembled those of **1** except for the absence of an acetyl group in **2**. In comparison with **1**, the H-1 signal was shifted upfield by $\Delta\delta_H$ 1.13, suggesting that **2** had a free OH group at C-1.[5b] The acetyl group at C-3 and the tigloyl group at C-7 were evidenced by HMBC cross-peaks from H-3 to the acetyl carbonyl at δ_C 170.7 and from H-7 to the tigloyl carbonyl at δ_C 166.4, respectively. NOESY experiments indicated that the relative configuration of **2** was the same as that of **1**.

Chisonimbolinin C (**3**) was obtained as a white, amorphous powder. The pseudomolecular ion peak at *m*/*z* 677.3287 $[M + Na]^+$ indicated a molecular formula of $C_{37}H_{50}O_{10}$. The NMR data of **3** were closely related to those of **2**, except for the presence of an additional tigloyl group. The tigloyl group was present at C-3 instead of the acetyl group in **2**, which was confirmed by the HMBC correlation between H-3 and the tigloyl carbonyl at δ_C 166.3. The relative configuration of **3** was established to be identical to that of **1** on the basis of a ROESY experiment. Therefore, the structure of chisonimbolinin C (**3**) was established as shown.

* Corresponding author. Tel: +86-25-86185292. Fax: +86-25-85301528. E-mail: cpu_lykong@126.com.

10.1021/np900485t CCC: $40.75
Published on Web 10/19/2009

Table 1. ^{1}H NMR Data of Compounds **1**−**5** in $CDCl_3$ at 500 MHz

position	**1**	**2**	**3**	**4**	**5**
1	4.72, s	3.59, t (3.0)	3.85, s	3.64 br s	3.59, s
2α	2.15, m	2.16, m	2.00, td (2.9, 16.3)	2.14, m	2.15, m
2*β*	2.23, m	2.18, m	2.31, td (2.9, 16.3)	2.23, m	2.22, m
3	4.93, s	4.88, t (3.0)	5.00, s	4.96, s	4.87, s
5	2.81, d (12.7)	2.81, d (12.8)	2.67, d (12.6)	2.75, d (12.7)	2.83, d (12.7)
6	4.09, dd (12.7, 2.4)	4.10, dd (12.8, 2.8)	4.02, dd (12.6, 2.9)	4.11, dd (12.7, 2.7)	4.09, dd (12.7, 2.4)
7	5.77, d (2.4)	5.73, d (2.8)	5.85, d (2.9)	5.73, d (2.7)	5.70, d (2.4)
9	3.13, d (9.9)	3.03, dd (7.5, 1.5)	3.05, d (10.0)	3.10, t (5.8)	3.05, d (6.0)
11α	1.57, br d (14,4)	1.55, m	1.57, br d (14.6)	1.77, m	1.66, m
11*β*	1.74, m	1.74, m	1.74, m	1.77, m	1.66, m
12	4.55, s	4.71, t (2.3)	4.55, s	5.25, s	4.82, s
15	4.89, d (7.5)	4.91, d (7.5)	4.85, d (7.5)	5.14, d (7.5)	4.93, d (7.5)
16α	2.20, m	2.21, m	1.48, br d (17.4)	1.48, br d (13.7)	2.18, m
16*β*	1.48, br d (13.2)	1.54, br d (14.1)	2.20, m	1.48, br d (13.7)	1.50, br d (12.0)
17	3.25, d (9.3)	3.27, d (9.5)	3.25, d (9.3)	3.24, d (9.2)	3.25, d (9.0)
18	1.86, s	1.89, s	1.86, s	1.87, s	1.87, s
19	0.97, s	0.92, s	0.99, s	0.92, s	0.91, s
21	7.13, s	7.13, d (1.05)	7.13, s	7.14, s	7.12, s
23	4.77, s	4.78, s	4.77, d (1.1)	4.76, s	4.78, s
28α	3.51, d (7.5)	3.57, d (7.5)	3.92, d (7.3)	3.50, d (7.5)	3.66, d (7.5)
28*β*	3.44, d (7.5)	3.50, d (7.5)	3.54, d (7.3)	3.47, d (7.5)	3.48, d (7.5)
29	1.16, s	1.15, s	1.11, s	1.15, s	1.13, s
30	1.47, s	1.49, s	1.46, s	1.49, s	1.48, s
12-OMe	3.39, s	3.39, s	3.39, s		
12-OEt					3.70, m 3.52, m 1.22, t (7.2)
1-OAc	2.07, s				
3-OAc	2.00, s	2.05, s		2.05, s	2.03, s
7-OTig 3′	6.92, qd (7.1, 1.2)	6.91, qd (7.1, 1.0)	6.84, qd (7.1, 1.2)	6.88, qd (7.1, 1.2)	6.93, qd (7.1, 1.2)
4′	1.79, d (7.1)	1.80, dd (7.1, 1.0)	1.79, d (7.1)	1.79, d (7.1)	1.80, d (7.1)
5′	1.90, s	1.89, s	1.86, s	1.87, s	1.87, s
3-OTig 3″			6.96, qd (7.1, 1.2)		
4″			1.84, d (7.1)		
5″			1.94, s		

Chisonimbolinin D (**4**) had the molecular formula $C_{33}H_{44}O_{10}$, as established by HRESIMS. The NMR spectra of **4** were similar to those of **2** except for signals indicating an OH at C-12 rather than an OCH_3.[10] Extensive analysis of its HMBC spectrum was consistent with the structure of **4** as shown. The relative configuration of **4** was supported by the ROESY experiment.

Chisonimbolinin E (**5**) had a molecular formula of $C_{35}H_{48}O_{10}$ (HRESIMS). Comparison of its NMR data with **2** revealed that they shared the same carbon skeleton with the same acetyl and tigloyl groups. The differences were the appearance of ethoxyl signals [δ_H 1.22 (3H, t, 7.2), 3.70 and 3.52 (each 1H, m); δ_C 62.4, 15.0][11] in the spectra of **5**, rather than a methoxy group. The ethoxy group was located at C-12, as demonstrated by the HMBC correlation between its methylene (δ_C 62.4) and H-12 (δ_H 4.82, 1H, s). The HMBC spectrum also placed the acetyl group at C-3, the tigloyl group at C-7, and the OH at C-1. The ROESY experiment indicated that the relative configuration of **5** was the same as that of **1**.

Chisonimbolinin F (**6**) was obtained as a white, amorphous powder. Its HRESIMS displayed a quasi-molecular ion at *m*/*z* 607.2881 $[M + Na]^+$ (calcd for $C_{33}H_{44}O_9Na$, 607.2878). Comparison of the NMR data (Table 3) of **6** with those of **2** indicated that they shared the same A, B, D, and E ring system, the same acetyl and tigloyl groups, and the same positions of these groups. They differed markedly in ring C: the absence of a C-12 hemiacetal methine (δ_H 4.71; δ_C 98.5) and, instead, the appearance of a C-12 methylene (δ_H 3.88 and 3.57; δ_C 70.0) in **6**, which was confirmed by the ^{1}H−^{1}H COSY correlations (H-12−H-11 and H-11−H-9) and HMBC correlations (H-12/C-9 and H-12/C-15) (Figure 3). Compared with **2**, the H-15 doublet of **6** was shifted upfield by $\Delta\delta_H$ 0.38, and the carbon signal of C-15 was shifted downfield by $\Delta\delta_H$ 9.8, which could be explained by the absence of a methoxy group at C-12. The relative configuration of **6** was deduced from a ROESY experiment (Figure 4). Cross-peaks from H-9 to H-5 and H-12b indicated the α-orientation of H-12b.

Chisonimbolinin G (**7**) had the molecular formula $C_{35}H_{46}O_{10}$. The NMR data of **7** resembled those of **6** including the same C-12 methylene signals (δ_H 3.88, 3.13; δ_C 70.0), with the marked difference being the severely downfield shifted signal of H-1, suggesting acylation of the C-1 OH group. The structure of **7** was confirmed by HMBC and HSQC experiments, and its relative configuration was the same as that of **6** as established by the ROESY spectrum.

The known compounds phellochin,[12] piscidinol A,[13] paniculatin C,[14] hispidol A,[15] agladupol A, and 21-*O*-methyltoosendanpentol[14] were identified by comparison of their spectroscopic data with those reported.

Compounds **1**−**7** were tested for in vitro cytotoxic activity. Compounds **3** and **4** showed moderate cytotoxic activity against the HeLa cell line, with IC_{50} = 13 and 32 *μ*M, respectively. Compounds **2**, **3**, and **4** showed weak cytotoxic activity against the SMMC-7721 cell line in the range IC_{50} 50−65 *μ*M. The other compounds were noncytotoxic (IC_{50} greater than 100 *μ*M).

Experimental Section

General Experimental Procedures. Melting points were obtained on an XT-4 micromelting point apparatus and are uncorrected. Optical rotations were measured with a JASCO P-1020 polarimeter. IR spectra were measured on a Bruker Tensor-27 spectrophotometer. NMR spectra were recorded on a Bruker DRX-500 instrument. ESIMS and HRESIMS experiments were performed on Agilent 1100 Series LC/MSD Trap and Agilent TOF MSD 1946D mass spectrometers, respectively. Absorbents for column chromatography were silica gel (200−300 *μ*m, Qingdao Marine Chemical Co. Ltd.), C_{18} reversed-phase silica gel (150−200 *μ*m, Merck), and MCI gel (CHP20P, 75−150 *μ*m, Mitsubishi Chemical Industries Ltd.). Preparative HPLC was performed using an Agilent 1100 series

Table 2. ^{13}C NMR Data of Compounds **1**−**5** in $CDCl_3$ at 125 MHz

position	1	2	3	4	5
1	71.2	70.9	70.8	71.2	71.0
2	27.8	29.0	30.5	29.3	28.8
3	71.6	72.2	72.5	72.5	72.2
4	42.5	42.4	43.9	42.4	42.4
5	40.1	38.9	39.8	39.3	39.0
6	72.2	72.5	72.1	72.4	72.6
7	74.2	74.4	74.2	74.2	74.4
8	45.4	45.3	45.6	45.3	45.4
9	36.0	36.4	37.2	36.1	36.4
10	40.5	41.2	40.8	40.9	41.2
11	31.5	30.6	31.4	31.1	30.8
12	98.3	98.5	97.9	91.7	96.8
13	139.1	141.0	137.8	141.1	140.8
14	145.0	144.8	145.1	144.6	144.9
15	77.6	77.6	76.5	77.6	77.9
16	36.9	36.9	36.9	37.3	36.9
17	46.3	46.5	46.4	46.4	46.4
18	15.9	16.3	16.3[a]	16.3	16.4
19	16.3	16.4	16.3[a]	16.4	16.5
20	137.7	137.7	137.7	137.6	137.7
21	174.4	174.3	174.4	174.3	174.3
22	145.5	144.8	145.5	145.4	145.3
23	70.3	70.2	70.3	70.2	70.2
28	77.9	77.9	78.0	77.8	77.9
29	19.3	18.9	19.3	18.7	18.9
30	20.8	20.7	21.2	20.8	20.6
12-OMe	55.0	54.7	54.0		
12-OEt					62.4, 15.0
1-OAc	169.7[a], 20.9				
3-OAc	169.7[a], 21.3	170.7, 21.2		170.0, 21.0	170.8, 21.2
7-OTig 1′	166.1	166.4	166.9	166.3	166.3
2′	128.7	128.7	128.7	128.7	128.7
3′	136.8	136.9	137.5	136.9	137.0
4′	12.1	12.1	12.3[b]	12.2	12.0
5′	14.4	14.4	14.4[c]	14.4	14.4
3-OTig 1″			166.3		
2″			128.9		
3″			137.8		
4″			12.3[b]		
5″			14.4[c]		

[a] Overlapped. [b] Overlapped. [c] Overlapped.

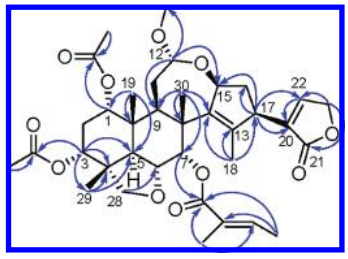


Figure 1. Key HMBC (H → C) correlations of **1**.

instrument with a Shimpak RP-C_{18} column (200 × 20 mm i.d.). Silica gel GF254 plates (Qingdao Marine Chemical Co. Ltd.) were used for thin-layer chromatography.

Plant Material. Twigs of *C. paniculatus* were collected in Xishuangbanna, Yunnan Province, China, in May 2007. The botanical identification was made by Prof. Min-jian Qin, Department of Medicinal Plants, China Pharmaceutical University. A voucher specimen (No. 070705) is deposited in the Department of Natural Medicinal Chemistry, China Pharmaceutical University.

Extraction and Isolation. The air-dried twigs of *C. paniculatus* (30 kg) were crushed and refluxed with 95% EtOH three times. After concentration of the solution, the extract (1.5 kg) was partitioned between H_2O and $CHCl_3$ (6 × 2 L) to give a $CHCl_3$-soluble fraction (300 g), which was chromatographed on a silica gel column eluted with PE/EtOAc (100:1 to 100:50, v/v) to yield 10 fractions (CS1−CS10). Fraction CS8 (26 g) was submitted to a MCI gel column eluted with MeOH/H_2O (3:7 to 10:0, v/v) and then was applied to a silica gel column (eluted with $CHCl_3$/MeOH, 100:1, v/v) to afford fractions

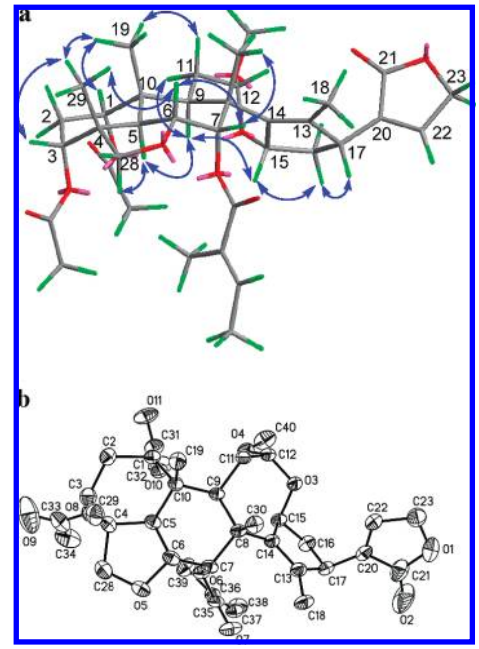


Figure 2. (a) Key NOESY (H ↔ C) correlations of **1**. (b) X-ray structure of **1**.

8A−8D. Fraction 8A (1.3 g) was further purified on a reversed-phase C_{18} column (MeOH/H_2O, 40:60 to 100:0, v/v) to give **1** (18 mg) and **2** (25 mg). Fraction 8B (0.3 g) was purified by preparative HPLC (MeCN/H_2O, 40:60, v/v) to afford **3** (7 mg) and **5** (13 mg). Fraction 8C (2.4 g) was applied to a C_{18} column (eluted with MeOH/H_2O, 40:60 to 100:0, v/v), and the fraction eluted with 50% MeOH was further purified by preparative HPLC (MeCN/H_2O, 40:60, v/v) to afford **4** (15 mg), **6** (10 mg), and **7** (12 mg).

Chisonimbolinin A (1): colorless crystals (MeOH/$CHCl_3$); mp 265−267 °C; $[\alpha]^{27}_D$ −102.9 (*c* 0.110, MeOH); IR (KBr) ν_{max} 3452, 2939, 2900, 1755, 1740, 1717, 1651, 1253, 1054 cm^{-1}; ^1H NMR see Table 1 and ^{13}C NMR see Table 2; negative ESIMS *m/z* 691.7 $[M + Cl]^-$; positive HRESIMS *m/z* found 679.3086 $[M + Na]^+$ (calcd for $C_{36}H_{48}O_{11}Na$, 679.3089).

Chisonimbolinin B (2): white, amorphous powder; $[\alpha]^{27}_D$ −125.5 (*c* 0.095, MeOH); IR (KBr) ν_{max} 3464, 2947, 2887, 1755, 1728, 1707, 1643, 1260, 1050 cm^{-1}; ^1H NMR see Table 1 and ^{13}C NMR see Table 2; negative ESIMS *m/z* 649.4 $[M + Cl]^-$; positive HRESIMS *m/z* found 637.2985 $[M + Na]^+$ (calcd for $C_{34}H_{46}O_{10}Na$, 637.2983).

Chisonimbolinin C (3): white, amorphous powder; $[\alpha]^{27}_D$ −100.8 (*c* 0.105, MeOH); IR (KBr) ν_{max} 3441, 2936, 1754, 1708, 1648, 1263, 1137, 1064 cm^{-1}; ^1H NMR see Table 1 and ^{13}C NMR see Table 2; negative ESIMS *m/z* 689.7 $[M + Cl]^-$; positive HRESIMS *m/z* found 677.3287 $[M + Na]^+$ (calcd for $C_{37}H_{50}O_{10}Na$, 677.3296).

Chisonimbolinin D (4): white, amorphous powder; $[\alpha]^{27}_D$ −98.3 (*c* 0.120, MeOH); IR (KBr) ν_{max} 3440, 2940, 1735, 1647, 1378, 1256, 1134, 1048 cm^{-1}; ^1H NMR see Table 1 and ^{13}C NMR see Table 2; negative ESIMS *m/z* 635.4 $[M + Cl]^-$; positive HRESIMS *m/z* found 623.2833 $[M + Na]^+$ (calcd for $C_{33}H_{44}O_{10}Na$, 623.2827).

Chisonimbolinin E (5): white, amorphous powder; $[\alpha]^{27}_D$ −131.8 (*c* 0.105, MeOH); IR (KBr) ν_{max} 3451, 2972, 2935, 2891, 1756, 1732, 1649, 1377, 1255, 1059 cm^{-1}; ^1H NMR see Table 1 and ^{13}C NMR see Table 2; negative ESIMS *m/z* 663.5 $[M + Cl]^-$; positive HRESIMS *m/z* found 651.3147 $[M + Na]^+$ (calcd for $C_{35}H_{48}O_{10}Na$, 651.3140).

Chisonimbolinin F (6): white, amorphous powder; $[\alpha]^{27}_D$ −88.6 (*c* 0.070, MeOH); IR (KBr) ν_{max} 3441, 2937, 1751, 1645, 1255, 1081, 1137, 1046 cm^{-1}; ^1H and ^{13}C NMR see Table 3; negative ESIMS *m/z* 619.4 $[M + Cl]^-$; positive HRESIMS *m/z* found 607.2881 $[M + Na]^+$ (calcd for $C_{33}H_{44}O_9Na$, 607.2878).

Chisonimbolinin G (7): white, amorphous powder; $[\alpha]^{27}_D$ −90.6 (*c* 0.100, MeOH); IR (KBr) ν_{max} 3442, 2940, 1735, 1648, 1255, 1084, 1139, 1053 cm^{-1}; ^1H and ^{13}C NMR see Table 3; negative ESIMS *m/z* 661.2 $[M + Cl]^-$; positive HRESIMS *m/z* found 649.2988 $[M + Na]^+$ (calcd for $C_{35}H_{46}O_{10}Na$, 649.2983).

Table 3. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR Data of Compounds **6** and **7** in $CDCl_3$

	6		**7**	
position	δ_H (mult, *J*)	δ_C	δ_H (mult, *J*)	δ_C
1	3.60, s	71.7	4.82, t (2.7)	71.9
2α	1.88, m	30.3	2.18, m	27.8
2*β*	2.35, dt (16.3, 2.9)		2.26, m	
3	5.09, t (2.5)	73.4	4.94, t (2.5)	71.5
4		42.6		40.6
5	2.52, d (12.5)	39.4	2.76, d (12.7)	40.3
6	4.11, dd (12.5, 2.5)	72.3	4.10, dd (12.7, 2.7)	72.2
7	5.78, d (2.5)	74.3	5.78, d (2.7)	74.2
8		45.3		45.5
9	2.98, d (9.0)	42.8	2.75, d (9.5)	42.5
10		41.4		42.3
11α	1.57, br d (18.8)	27.5	1.39, br d (14.5)	27.5
11*β*	1.66, m		1.66, m	
12α	3.57, m	70.0	3.13, td (9.5, 2.0)	70.0
12*β*	3.88, dt (8.4, 3.5)		3.88, dt (8.4, 3.5)	
13		139.2		139.5
14		145.4		144.8
15	4.53, d (7.4)	87.4	4.41, d (7.5)	87.8
16α	1.52, br d (17.4)	37.8	1.52, br d (16.4)	37.8
16*β*	2.21, m		2.20, m	
17	3.22, d (9.2)	46.0	3.22, d (8.9)	45.8
18	1.86, s	16.4	1.87, s	16.5
19	0.96, s	16.3	1.03, s	16.3
20		137.7		137.5
21	7.17, s	174.4	7.14, s	174.2
22		145.5		145.5
23	4.76, s	70.3	4.76, s	70.3
28α	3.51, d (7.5)	77.8	3.52, d (7.5)	77.8
28*β*	3.31, d (7.5)		3.48, d (7.5)	
29	1.16, s	18.6	1.18, s	19.0
30	1.50, s	21.3	1.50, s	21.1
1-OAc				169.4
			2.01	20.9
3-OAc		169.1		169.7
	2.06, s	20.9	2.15, s	21.3
7-OTig 1′		166.2		166.0
2′		128.6		128.5
3′	6.84, qd (7.0, 1.2)	136.7	6.84, qd (7.0, 1.2)	136.9
4′	1.79, d (7.0)	12.3	1.81, d (7.0)	12.0
5′	1.86, s	14.5	1.90, s	14.4

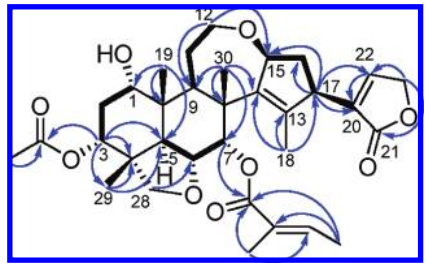


Figure 3. Key HMBC (H → C) and ^{1}H−^{1}H COSY (—) correlations of **6**.

X-ray Crystallographic Data for 1. formula $C_{36}H_{48}O_{11}$; M_r = 656.74; orthorhombic crystalline system; space group $P2_12_12_1$; a = 10.1106(12) Å, b = 20.172(2) Å, c = 33.768(3) Å; V = 6887.1(12) Å^3; Z = 8; d = 1.267 mg/m^3; crystal dimensions 0.49 × 0.40 × 0.33 mm^3; the final indices were R_1 = 0.0456 wR_2 = 0.1052.

Colorless crystals of **1** were obtained in a mixed solvent of MeOH/$CHCl_3$. Crystal data were obtained on a Bruker Smart-1000 CCD with a graphite monochromator with Mo Kα radiation at (λ = 0.71073 Å) 298(2) K. The structure was solved by direct methods using SHELXS-97[17] and expanded using difference Fourier techniques, refined by SHELX-97.[18] Crystallographic data for **1** have been deposited at the Cambridge Crystallographic Data Centre (deposition number CCDC-743108). Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK [fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk].

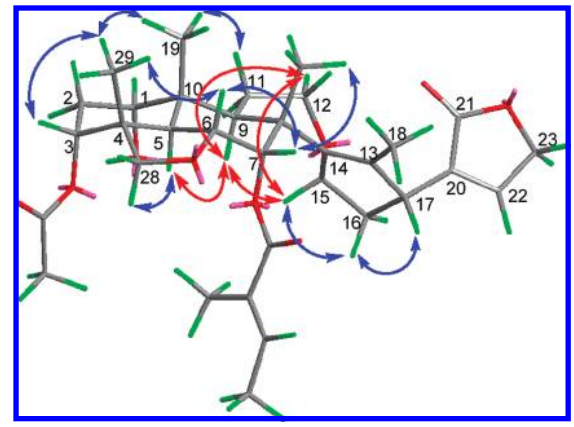


Figure 4. Key ROESY (H ↔ C) correlations of **6**.

Cytotoxicity Bioassays. Compounds **1**−**7** were evaluated for cytotoxic activity against HeLa (human cervical cancer) and SMMC-7721 (human hepatoma cancer) cells by a MTT assay as described in the literature.[19] The cells were obtained from the Cell Bank of the Shanghai Institute of Cell Biology. Fluorouracil was used as a positive control, and the experiments were conducted for three independent replicates.

Acknowledgment. This research work was supported by the Key Project of National Natural Science Foundation of China (Grant No. 30830116).

Supporting Information Available: X-ray crystallographic data for chisonimbolinin A (**1**); ESIMS, 1D, 2D NMR spectra for chisonimbolinins A−G (**1**−**7**). This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) Taylor, D. A. H. *Progress in the Chemistry of Organic Natural Products*; Herz, W., Grisebach, H., Kirby, G. W., Eds.; Springer: New York, 1984; Vol. 45, pp 1−102. (b) Mulholland, D. A.; Parel, B.; Coombes, P. H. *Curr. Org. Chem.* **2000**, *4*, 1011–1054. (c) Roy, A.; Saraf, S. *Biol. Pharm. Bull.* **2006**, *29*, 191–201.

(2) (a) Connolly, J. D.; Labbe, C.; Rycroft, D. S.; Taylor, D. A. H. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2959–2964. (b) Bordoloi, M.; Saikia, B.; Mathur, R. K.; Goswami, B. N. *Phytochemistry* **1993**, *34*, 583–584. (c) Chatterjee, A.; Nayak, L.; Das, B.; Patra, A.; Dhara, K. P.; Mukherjee, K.; Banerji, J. *Indian J. Chem., Sect. B* **1989**, *28*, 231–236.

(3) Sarmah, G. K.; Bhattacharyya, N. K.; Goswami, B. N.; Barua, P.; Kataky, J. C. S. *J. Indian Chem. Soc.* **2003**, *80*, 1163–1168.

(4) (a) Rajab, M. S; Bentley, M. D.; Alford, A. R.; Mendel, M. J. *J. Nat. Prod.* **1988**, *51*, 168–171. (b) Bentley, M. D.; Gaul, F.; Rajab, M. S.; Hassanali, A. *J. Nat. Prod.* **1992**, *55*, 84–87.

(5) (a) Kraus, W.; Bokel, M. *Chem. Ber.* **1981**, *114*, 267–275. (b) Zhou, H. L.; Hamazaki, A.; Fontana, J. D.; Takahashi, H.; Esumi, T.; Wandscheer, C. B.; Tsujimoto, H.; Fukuyama, Y. *J. Nat. Prod.* **2004**, *67*, 1544–1547.

(6) (a) Tada, K.; Takido, M.; Kitanaka, S. *Phytochemistry* **1999**, *51*, 787–791. (b) Zhou, H. L.; Hamazaki, A.; Fontana, J. D.; Takahashi, H. *Chem. Pharm. Bull.* **2005**, *53*, 1362–1365. (c) Itokawa, H.; Qiao, Z. S.; Hirobe, C.; Takeya, K. *Chem. Pharm. Bull.* **1995**, *43*, 1171–1175.

(7) (a) Lv, F. H. *Acta Pharm. Sin.* **1979**, *14*, 632–640. (b) Yao, X. S. *The Medicinal Chemistry of Natural Products*, 3th ed.; People's Medical Publishing House: Beijing, 2001; pp 317−318.

(8) Mulholland, D. K.; Monkhe, T. V.; Coombes, P. H.; Rajab, M. S. *Phytochemistry* **1998**, *49*, 2585–2590.

(9) Mohamad, K.; Hirasawa, Y.; Litaudon, M.; Awang, K.; A. Hadi, A.; Takeya, K.; Ekasari, W.; Widyawaruyanti, A.; Zaini, N. C.; Morita, H. *Bioorg. Med. Chem.* **2009**, *17*, 727–730.

(10) Nakatani, M.; Shimokoro, M.; Zhou, J. B.; Okamura, H.; Iwagawa, T.; Tadera, K.; Nakayama, N.; Naoki, H. *Phytochemistry* **1999**, *52*, 709–714.

(11) Zhang, Q.; Shi, Y.; Liu, X. T.; Liang, J. Y.; Ip, N. Y.; Min, Z. D. *Planta Med.* **2007**, *73*, 1298–1303.

(12) Su, R. H.; Kim, M.; Kawaguchi, H.; Yamamoto, T.; Goto, K.; Taga, T.; Miwa, Y.; Kozuka, M.; Takahashi, S. *Chem. Pharm. Bull.* **1990**, *38*, 1616–1619.
(13) Itokawa, H.; Kishi, E.; Morita, H.; Takeya, K. *Chem. Pharm. Bull.* **1992**, *40*, 1053–1055.
(14) Yadav, R. D.; Kataky, J. C. S.; Mathur, R. K. *J. Indian Chem. Soc.* **1999**, *76*, 575–581.
(15) 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.
(16) Xie, B. J.; Yang, S. P.; Chen, H. D.; Yue, J. M. *J. Nat. Prod.* **2007**, *70*, 1532–1535.
(17) Sheldrick, G. M. *SHELXS-97: Program for X-ray Crystal Structure Solution*; University of Göttingen: Göttingen, Germany, 1997.
(18) Sheldrick, G. M. *SHELX-97: Program for X-ray Crystal Structure Refinement*; University of Göttingen: Göttingen, Germany, 1997.
(19) Lu, Y. Y.; Luo, J. G.; Huang, X. F.; Kong, L. Y. *Steroids* **2009**, *74*, 95–101.

NP900485T