Chuktabularins E−T, 16-Norphragmalin Limonoids from *Chukrasia tabularis* var. *velutina*

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Received November 17, 2009

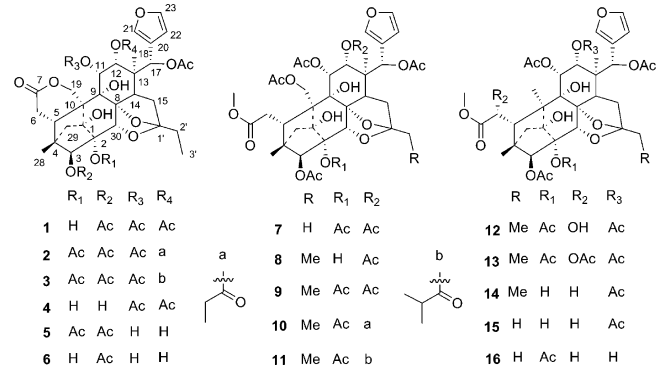
Chuktabularins E−T (**1**−**16**), 16 new 16-norphragmalin limonoids, together with four known compounds, chuktabularins A−D, were isolated from the stem bark of *Chukrasia tabularis* var. *velutina*. These compounds possess a biosynthetically extended propionyl or acetyl group at C-15 and a characteristic ketal moiety between the limonoid skeleton and the acyl substituent at C-15. The structures of these compounds were established on the basis of detailed spectroscopic analysis, and that of **1** was confirmed by a single-crystal X-ray diffraction experiment, representing the first verification of the skeleton of 16-norphragmalin limonoids. Chuktabularins K−O (**7**−**11**) were found to be the first 19-acetoxylated 16-norphragmalin limonoids. Variable-temperature ^{1}H NMR experiments suggested that **7** exists as an equilibrium mixture of conformational isomers in solution. The absolute configuration of **5** was determined by the CD exciton chirality method on its 11,12-di-*p*-chlorobenzoate (**5a**), and those of **1**−**4** and **6**−**16** were proposed by correlating with **5** spectroscopically and biogenetically.

Limonoids, distributed mainly in the plant family Meliaceae, have been a focus in natural products research for their structural diversity and potential biological significance.[1,2] Plants of the genus *Chukrasia* are well-known for their structurally diversified phragmalin-type limonoids,[1,3] which are B,D-seco limonoids with a characteristic A- and B-ring system of tricyclo[3.3.1^{2,10}.1^{1,4}]decane or tricyclo[4.2.1^{10,30}.1^{1,4}]decane,[2b,4] and found also in the other Meliaceae tribes, Swietenieae[5] and Carapeae.[6] Previous chemical studies on this genus have focused mainly on *C. tabularis* A. Juss., leading to the isolation of several phragmalin limonoids with interesting carbon skeletons,[2b,7] some of which exhibit insect antifeedant[7c] and potassium channel-blocking[7f] activities. Limonoids with a 16-norphragmalin skeleton, isolated from *C. tabularis* for the first time in 2007, possess an unprecedented ketal moiety between the phragmalin skeleton and a biosynthetically extended acyl substituent at C-15.[7d] Up to the present time, only eight 16-norphragmalin limonoids have been reported.[7d,g,i]

Chukrasia tabularis var. *velutina*, a timber tree, is a variety of *C. tabularis* and grows mainly in tropical areas of Asia such as India and southern mainland China.[8] Its stem bark has been used traditionally as an astringent, antidiarrheal, and anti-influenza agent in the People's Republic of China.[8b] As a part of our ongoing research program to isolate novel compounds from plants of the Meliaceae, a new class of C-15-acyl phragmalin limonoids featuring a C-16/C-30 δ-lactone ring[7h] and three 16-norphragmalin limonoids with an unprecedented skeleton[7i] were isolated from the stem bark of *C. tabularis* var. *velutina*. Further work on phragmalin-type limonoids present in the air-dried stem bark afforded 16 new 16-norphragmalin limonoids, chuktabularins E−T (**1**−**16**), together with four known compounds, chuktabularins A−D.[7d] These new compounds possess a characteristic ketal moiety between the limonoid skeleton and the biosynthetically extended propionyl or acetyl substituent at C-15.[7d] The structures of compounds **1**−**16** were established on the basis of detailed spectroscopic analysis, and that of **1** was confirmed by single-crystal X-ray diffraction. Herein, we describe the isolation, structural elucidation, and the plausible biosynthetic origin (Supporting Information, S1) of these new compounds.

Results and Discussion

Chuktabularin E (**1**) was isolated as colorless crystals, and its molecular formula was established as $C_{36}H_{44}O_{16}$ by the HRESIMS ion at *m/z* 755.2527 [M + Na]$^+$. The IR absorption bands at 3418 and 1755 cm^{-1} suggested the presence of hydroxy and ester groups. The ^{1}H and ^{13}C NMR data (Tables 1 and 2) and information from 2D NMR studies (HMBC, HSQC, and NOESY) suggested **1** as being a phragmalin-type limonoid[7] and revealed the presence of a β-substituted furanyl ring [δ_H 6.43, 7.39, 7.50; δ_C 122.2, 109.5, 143.5, 140.5], an ethyl group [δ_H 2.01 (m, 2H), 1.10 (t, J = 7.6 Hz, 3H); δ_C 26.1, 8.2], two angular methyls [δ_H 0.93 (s, 3H), 0.92 (s, 3H); δ_C 18.7, 15.1], and four acetyls. A pair of germinal doublets at δ_H 1.96 (d, J = 11.6 Hz) and 2.06 (d, J = 11.6 Hz) was assigned to the H-29 protons of the characteristic phragmalin 4,29,1-ring bridge, which was confirmed by the HMBC correlations observed from the H-29 protons to the quaternary carbons at δ_C 86.0 (C-1), 85.4 (C-3), 44.7 (C-4), 41.1 (C-5), and 52.3 (C-10) (Figure 1). Two geminal oxygenated methylene signals at δ_H 4.18 and 5.00 (each d, J = 12.6 Hz) corresponded to a ^{13}C NMR signal at δ_C 69.4 (C-19), which showed correlations with carbons at δ_C 41.1 (C-5), 75.3 (C-9), and 52.3 (C-10) and suggested that the 19-methyl group is oxygenated. The HMBC correlations between C-7 (δ_C 172.9) and H-6 (δ_H 2.31) and one of the oxygenated C-19 methylene signals at δ_H 5.00 (H-19a) indicated the presence of the characteristic C-6−C-7 appendage of a phragmalin-type limonoid and the C-7/C-19 δ-lactone ring.[7d,h,9]



A HMBC correlation between H-15a [δ_H 2.52 (dd, J = 12.0, 8.0 Hz)] and the ketal resonance at δ_C 113.7 (C-1′), instead of the correlation between H-15 and the C-16 carbonyl in common phragmalins, indicated that **1** is a 16-decarboxylated phragmalin limonoid. The HMBC correlations between the ketal carbon and the ethyl group signals [δ_H 2.01 (m, 2H) and δ_H 1.10 (t, J = 7.6 Hz, 3H)] suggested the linkage of the ethyl to the ketal carbon, i.e., a biosynthetically extended propionyl group attached at C-15.[7d]

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10.1021/np900734c
Published on Web 04/20/2010

Table 1. ^{1}H NMR Data of Compounds **1**−**6** in $CDCl_3$

position	**1**[a]	**2**[b]	**3**[b]	**4**[a]	**5**[a]	**6**[b]
3	5.27, s	5.35, s	5.35, s	3.85, s	5.33, s	5.24, s
5	2.07, m[c]	2.08, m[c]	2.06, m[c]	2.32, m[c]	2.88, brdd (9.0, 8.3)	2.91, brdd (9.0, 8.5)
6a	2.31, m, 2H[c]	2.32, m, 2H[c]	2.30, m, 2H[c]	2.35, m, 2H[c]	2.23, dd (14.7, 10.9)	2.48, dd (15.0, 7.2)
6b					2.47, m[c]	2.23, brd (15.0)
11	5.61, d (3.5)	5.64, d (3.6)	5.64, d (3.6)	5.84, d (3.4)	4.20, brs	4.14, brs
12	5.47, d, (3.5)	5.50, d (3.6)	5.52, d (3.6)	5.24, d (3.4)	4.20, brs	4.24, brs
14	3.23, dd (12.0, 8.0)	3.25, dd (12.0, 7.8)	3.26, dd (12.0, 7.8)	3.15, dd (11.6, 8.6)	2.95, dd (11.6, 7.9)	2.93, dd (12.0, 8.4)
15a	2.52, dd (12.0, 8.0)	2.56, dd (12.0, 7.8)	2.56, dd (12.0, 7.8)	2.38, m[c]	2.46, m[c]	2.40, dd (12.0, 8.4)
15b	1.95, m[c]	1.90, dd (12.0, 12.0)	1.91, dd (12.0, 12.0)	1.92, dd (12.0, 11.7)	1.86, dd (11.7, 11.6)	1.92, dd (12.0, 12.0)
17	6.17, s	6.08, s	6.08, s	6.37, s	6.01, s	6.09, s
18	0.93, s, 3H	0.90, s, 3H	0.90, s, 3H	1.01, s, 3H	1.09, s, 3H	1.11, s, 3H
19a	5.00, d (12.6)	5.03, d (12.6)	5.01, d (12.6)	4.98, d (12.7)	4.90, d (12.7)	4.89, d (12.0)
19b	4.18, d (12.6)	4.18, d (12.6)	4.17, d (12.6)	4.16, d (12.7)	4.15, d (12.7)	4.15, d (12.0)
21	7.50, brs	7.48, brs	7.48, brs	7.61, brs	7.30, brs	7.34, brs
22	6.43, brd (1.0)	6.41, brd (0.6)	6.41, brd (0.6)	6.42, brd (1.0)	6.29, brd (1.0)	6.31, brd (0.6)
23	7.39, t-like (1.7)	7.39, t-like (1.2)	7.39, t-like (1.5)	7.37, t-like (1.7)	7.36, t-like (1.7)	7.37, t-like (1.8)
28	0.92, s, 3H	0.90, s, 3H	0.90, s, 3H	1.02, s, 3H	0.92, s, 3H	0.93, s, 3H
29a	2.06, d (11.6)	2.05, m[c]	2.08, d (11.4)	1.98, d (11.5)	2.09, m[c]	2.04, m[c]
29b	1.96, d (11.6)	2.00, m[c]	2.04, d (11.4)	1.91, d (11.5)	1.97, m[c]	2.00, m[c]
30	4.19, s	4.63, s	4.64, s	4.23, s	4.62, s	4.21, s
2′	2.01, m, 2H[c]	2.00, q (7.5), 2H	2.00, q (7.5), 2H	2.00, m, 2H[c]	1.94, m, 2H[c]	2.02, q (7.8), 2H
3′	1.10, t (7.6), 3H	1.07, t (7.5), 3H	1.07, t (7.5), 3H	1.09, t (7.5), 3H	1.05, t (7.5), 3H	1.07, t (7.8), 3H
OH-1	4.45, brs	4.89, brs	4.89, brs	4.15, brs	4.89, brs	4.45, brs
OH-9		3.27, brs	3.22, brs			4.74, brs
OH-11						5.78, brs
OAc-2		2.11, s, 3H	2.10, s, 3H		2.08, s, 3H	
OAc-3	2.40, s, 3H	2.50, s, 3H	2.49, s, 3H		2.34, s, 3H	2.27, s, 3H
OAc-11	2.12, s, 3H	2.11, s, 3H	2.10, s, 3H	2.06, s, 3H		
OAc-12	2.05, s, 3H			2.03, s, 3H		
$OCOCH_2CH_3$-12		2.35, q (7.5), 2H 1.10, t (7.50), 3H				
$OCOCH(CH_3)_2$-12			2.56, m[c] 1.17, d (7.2), 3H 1.15, d (7.2), 3H			
OAc-17	2.12, s, 3H	2.08, s, 3H	2.09, s, 3H	2.12, s, 3H	2.07, s, 3H	2.11, s, 3H

[a] Recorded at 500 MHz (^{1}H) and 125 MHz (^{13}C). [b] Recorded at 600 MHz (^{1}H) and 150 MHz (^{13}C). [c] Signal pattern unclear due to overlapping.

The HMBC correlation between H-30 (δ_H 4.19, s) and the ketal carbon was consistent with the presence of an ether bridge between C-1′ and C-30. The remaining one degree of unsaturation implied that an additional ring is required. The downfield shifted signal of C-8 (δ_C 89.8) suggested its possible ether linkage to C-1′.[7d] Accordingly, compound **1** was assigned with a 16-norphragmalin limonoid framework.[7d] However, this deduction could not be verified directly by the HMBC spectrum since both C-8 and C-1′ are quaternary carbons. A single-crystal X-ray diffraction experiment (Figure 2) was performed and confirmed the ether linkage between C-8 and C-1′, forming a characteristic 2,7-dioxabicyclo[2.2.1]heptane moiety between the limonoid skeleton and the propionyl group at C-15. Thus, the structure of **1** was determined as shown.

Strong NOESY cross-peaks from H-11 to H-5, H-12, H-17, and H-30, from H-17 to H-12 and H-30, and from H-5 to Me-28 indicated a β-orientation of these six proton signals in **1**. NOESY correlations of H-14 with Me-18, H-29a with H-3, and H-29b with H-19b revealed that these protons adopt an α-orientation. The α-orientation of H-3 was also confirmed by the NOESY correlation between the OAc-3 signal and H-21 of the furan ring. Thus, the relative configuration of **1** in solution was established by a NOESY experiment as depicted (Figure 1), which matched that in the solid state as obtained by the X-ray crystallographic study (Figure 2).

Chuktabularins F (**2**) and G (**3**) exhibited quasimolecular ions at *m*/*z* 811.2794 $[M + Na]^+$ and 825.2938 $[M + Na]^+$ in the HRESIMS, consistent with the molecular formulas of $C_{39}H_{48}O_{17}$ and $C_{40}H_{50}O_{17}$, respectively. The general features of the ^{1}H and ^{13}C NMR spectroscopic data of **2** and **3** closely resembled those of **1**, with the exception of signals corresponding to a propionyl group [δ_H 2.35 (q, J = 7.5, 2H), 1.10 (t, J = 7.5 Hz, 3H); δ_C 173.5, 27.2, 9.0] and an isobutyryl group [δ_H 2.56 (m), 1.17 (d, J = 7.2 Hz, 3H), 1.15 (d, J = 7.2 Hz, 3H); δ_C 175.9, 34.0, 19.0, 18.8], respectively. Differences were observed in the downfield shifted signals of C-2 ($\Delta\delta_C$ 7.8 and 7.9) and H-30 ($\Delta\delta_H$ 0.44 and 0.45) in comparison to **1**, which suggested the substitution of the acyl group at C-2 in **2** and **3**.[7h] Specification of the sites of ester linkages was obtained by HMBC experiments, with three acetyl groups assigned to C-3, C-11, and C-17 and the additional propionyl and isobutyryl group located at C-12 of **2** and **3**, respectively. Thus, the structures of **2** and **3** were established as the 12-*O*-propionyl and 12-*O*-isobutyryl derivatives of 2-*O*-acetylated **1**, respectively. Their relative configurations were established using their NOESY spectra to be the same as that of **1**.

Chuktabularin H (**4**), a white, amorphous powder, gave the molecular formula $C_{34}H_{42}O_{15}$, as determined by HRESIMS, which showed a quasimolecular ion at *m*/*z* 713.2412 $[M + Na]^+$. The similarity of the ^{1}H and ^{13}C NMR spectroscopic data of **4** (Tables 1 and 2) to those of **1** indicated that **4** possesses the same 16-norphragmalin skeleton with a characteristic ketal moiety, which was confirmed by the presence of a ketal resonance at δ_C 113.0 and key HMBC correlations. The major difference found was the absence of an acetyl signal at C-3, and as a result, the H-3 signal of **4** was shifted upfield to δ_H 3.85 when compared with **1** (δ_H 5.27), consistent with the lack of any HMBC correlation between H-3 and an acetyl carbonyl carbon. Thus, the structure of **4** was demonstrated to be the 3-*O*-deacetyl derivative of **1**.

Chuktabularin I (**5**), an isomer of **4**, gave the same molecular formula of $C_{34}H_{42}O_{15}$, as determined by the HRESIMS ion at *m*/*z* 713.2419 $[M + Na]^+$. The ^{1}H and ^{13}C NMR spectroscopic data of **5** (Tables 1 and 2) indicated that this compound possesses the same 16-norphragmalin skeleton as **4** with a ketal moiety between the main skeleton and the biosynthetically extended propionyl group at C-15 and a C-7/C-19 δ-lactone, and the difference was in the location of the acetyl group. The chemical shift of C-2 was shifted from δ_C 73.4 in **1** to δ_C 81.8 in **5**, which suggested that an acetyl

Table 2. ^{13}C NMR Data of Compounds **1**−**6** in $CDCl_3$

position	**1**[a]	**2**[b]	**3**[b]	**4**[a]	**5**[a]	**6**[b]
1	86.0	85.5	85.5	86.1	85.4	85.7
2	73.4	81.2	81.3	73.3	81.8	73.6
3	85.4	82.9	82.9	86.4	83.4	86.0
4	44.7	45.6	45.6	44.6	45.3	44.2
5	41.1	40.5	40.5	39.9	41.3	41.8
6	31.5	31.4	31.4	31.5	31.3	31.9
7	172.9	172.7	172.5	173.3	175.1	175.5
8	89.8	89.6	89.5	89.3	90.4	90.6
9	75.3	75.2	75.2	75.1	76.7	76.7
10	52.3	52.4	52.4	52.4	51.8	51.8
11	71.4	71.3	71.4	71.4	68.6	68.4
12	72.1	71.8	71.6	72.4	75.7	75.7
13	41.6	41.5	41.4	41.5	42.2	42.2
14	43.8	43.9	44.0	43.9	43.0	42.9
15	33.2	34.0	34.0	33.6	34.0	33.4
17	71.1	71.3	71.3	70.9	71.4	71.0
18	18.7	19.1	19.2	18.0	18.9	18.9
19	69.4	69.4	69.3	69.4	69.6	69.7
20	122.2	122.4	122.4	121.2	122.8	122.3
21	140.5	140.2	140.2	141.9	139.8	140.1
22	109.5	109.5	109.5	109.7	109.9	109.8
23	143.5	143.3	143.3	143.2	143.1	143.2
28	15.1	15.0	15.1	15.0	15.0	15.0
29	38.4	38.8	38.8	38.1	39.1	38.6
30	71.8	70.7	70.7	71.8	70.7	71.5
1′	113.7	113.3	113.3	113.0	113.0	113.4
2′	26.1	25.9	25.9	26.0	26.0	26.1
3′	8.2	7.9	7.9	8.0	7.8	8.2
OAc-2		169.5	169.5		169.5	
		20.9	20.8		20.8	
OAc-3	169.6	169.1	169.1		168.9	169.6
	21.1	21.0	21.0		21.4	21.6
OAc-11	171.1	170.9	170.9	170.1		
	20.9	20.9	20.8	20.9		
OAc-12	170.0			169.8		
	20.6			20.6		
$OCOCH_2CH_3$-12		173.5				
		27.2				
		9.0				
$OCOCH(CH_3)_2$-12			175.9			
			34.0			
			19.0			
			18.8			
OAc-17	169.0	168.8	168.8	170.4	168.9	169.1
	20.8	20.5	20.5	21.2	20.5	20.9

[a] Recorded at 500 MHz (^1H) and 125 MHz (^{13}C). [b] Recorded at 600 MHz (^1H) and 150 MHz (^{13}C).

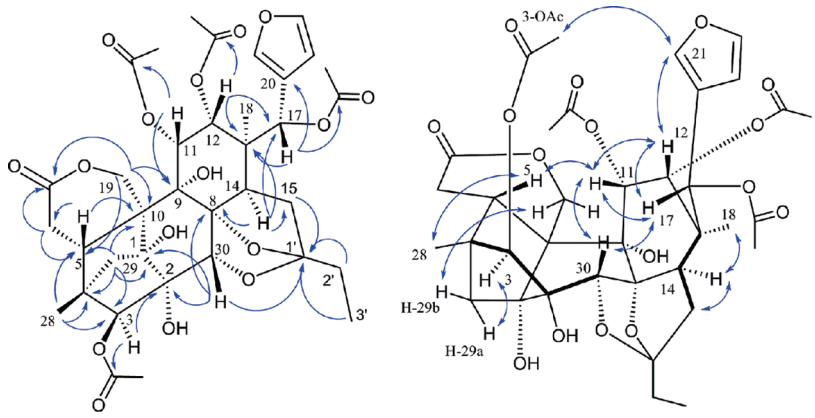

Figure 1. Key HMBC (→) and NOE (↔) correlations of **1**.

group is positioned at C-2.[7h] On the basis of the corresponding HMBC correlations, the other two acetyls were assigned at C-3 and C-17. Thus, the structure of **5** was established as the 2-*O*-acetyl, 11,12-*O*-deacetyl derivative of **1**.

The absolute configuration of **5** was determined by applying the CD exciton chirality method on its 11,12-di-*p*-chlorobenzoate (**5a**), for which the CD spectrum exhibited negative chirality resulting from the exciton coupling between the two chromophores of *p*-chlorobenzoate at 255 ($\Delta\varepsilon$ −4.30, $\pi\rightarrow\pi^*$ transition) and 232 nm ($\Delta\varepsilon$ +1.32, $\pi\rightarrow\pi^*$ transition). The negative chirality indicated that the transition dipole moments of two chromophores are oriented in a counterclockwise manner[10] (Figure 3), corresponding to the absolute configuration of **5a** as 11*R* and 12*R*. Thus, the absolute configuration of **5** was assigned as depicted.

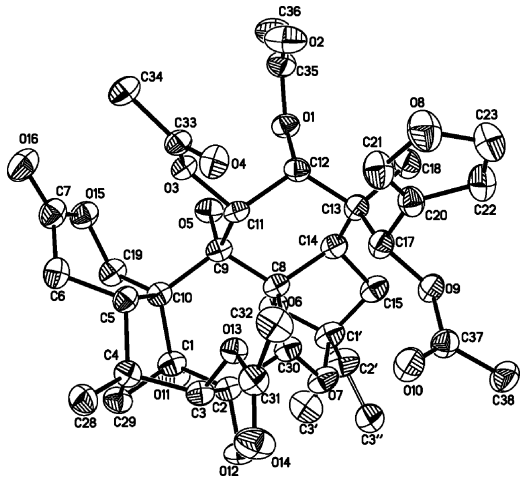

Figure 2. X-ray crystallographic structure of **1**.

Chuktabularin J (**6**) was isolated as a white, amorphous powder, and its molecular formula was established as $C_{32}H_{40}O_{14}$ from the HRESIMS ion at *m*/*z* 671.2331 $[M + Na]^+$. The similarity of the ^1H and ^{13}C NMR spectroscopic data (Tables 1 and 2) of **6** and **5** when compared indicated that these two natural products both possess the same 16-norphragmalin skeleton. However, the C-2 (δ_C 81.8) and H-30 (δ_H 4.62, s) signals of **5** were shifted to δ_C 73.6 and δ_H 4.21 for **6**, which suggested the absence of a 2-*O*-acetyl group in **5**.[7h] Two acetyls were placed at C-3 and C-17 on the basis of the corresponding HMBC correlations. Thus, the structure of **6** was established as the 2-*O*-deacetyl derivative of **5**.

Chuktabularin K (**7**) was obtained as a white, amorphous powder. The HRESIMS showed a quasimolecular ion at *m*/*z* 857.2841 $[M + Na]^+$, consistent with a molecular formula of $C_{40}H_{50}O_{19}$. The IR absorption bands at 3436 and 1751 cm^{-1} suggested the presence of hydroxy and ester groups. The ^1H and ^{13}C NMR data and the information from the subsequent 2D NMR studies (HMBC, HSQC, and NOESY) indicated that **7** is a 16-norphragmalin-type limonoid with a characteristic ketal moiety between the limonoid skeleton and the biosynthetically extended acetyl group at C-15, which was confirmed by the HMBC cross-peaks (Figure 4) from the ketal resonance at δ_C 110.5 (C-1′) to H-15a (δ_H 2.55, dd, J = 11.4, 7.8 Hz), a methyl (δ_H 1.63, s, 3H), and H-30 (δ_H 4.64, s). Two proton signals at δ_H 4.46 and 4.64 (brd, J = 11.7 Hz) were assignable to an oxygenated C-19 methylene with the broadened ^{13}C NMR signal at δ_C 66−67 from the observed HSQC correlations. The HMBC correlations between C-7 (δ_C 173.1) and H-5 (δ_H 2.70, brd, J = 12.0 Hz) and the methoxy protons at δ_H 3.63 (s, 3H) confirmed the characteristic C-6−C-7 appendage of the phragmalin limonoid and also the cleavage of the C-7/C-19 δ-lactone ring. Furthermore, four acetyl groups were assigned at C-3 (δ_C 83.0), C-11 (δ_C 72.0), C-12 (δ_C 72.8), and C-17 (δ_C 71.2) according to their corresponding HMBC correlations. On the basis of the chemical shifts of C-2 (δ_C 82.0) and H-30 (δ_H 4.64, s), the remaining acetyl was attached at C-2.[7i] Two hydroxy proton signals at δ_H 3.55 (s, OH-9) and 4.82 (s, OH-1) were distinguished from the HSQC and HMBC spectra. This evidence permitted the last acetyl to be placed at C-19, the only remaining substitution site. A NOESY experiment of **7** indicated that all the asymmetric carbons have the same relative configuration as those of **1**. Strong cross-peaks from H-11 to H-5, H-17, and H-30 and from H-17 to H-12 and H-30 indicated a β-orientation of these protons. NOESY correlations of H-14 with Me-18 and OH-9, and of H-3 with H-29b, revealed that these protons adopt an α-orientation. Thus, the structure of **7** was determined as depicted.

The C-19 methylene protons of **7** in $CDCl_3$ exhibited two moderately broadened signals at room temperature (303 K) as compared with relatively sharp signals in **1**. Such a phenomenon was attributed to an equilibrium among various conformations in the molecules at room temperature, resulting from restricted rotation about the C-10, C-19 bond. In an attempt to verify this hypothesis, the ^1H NMR spectrum of **7** was recorded at variable temperatures (303, 318, 323, and 333 K) in DMSO-d_6.[11] Expansions of the spectroscopic regions between δ_H 4.30 and δ_H 4.50 are shown in Figure 5. An increase in temperature caused no splitting but rather a sharpening of the C-19 methylene signals, which suggested that signal coalescence of the conformers occurs below room temperature. These results thus confirmed the exchange broadening of the C-19 methylene resonances due to rotational hindrance at the C-10, C-19 bond.

Chuktabularin L (**8**) showed a molecular formula of $C_{39}H_{50}O_{18}$ as determined by the HRESIMS ion at *m*/*z* 829.2891 $[M + Na]^+$. Analysis of its ^1H and ^{13}C NMR data (Table 3) indicated that compound **8** is a congener of **7**, which possesses a 16-norphragmalin skeleton with an acetoxylated C-19 angular methyl. In the HMBC spectrum of **8**, the observed correlations of the ketal resonance at δ_C 113.2 (C-1′) with H-15a (δ_H 2.51, dd, J = 12.0, 8.4 Hz), the ethyl signals [δ_H 2.04 (q, J = 7.8 Hz, 2H) and δ_H 1.09 (t, J = 7.8, 3H)], and H-30 (δ_H 4.21, s) suggested that **8** has a propionyl group at C-15, like **1**. The upfield shifted signal of C-2 (δ_C 73.9) indicated the absence of the acetyl at C-2 of **7**. Two hydroxy proton signals at δ_H 3.53 (s, OH-9) and 4.42 (s, OH-1) were distinguished using the HSQC and HMBC spectra. Corresponding HMBC correlations ascertained that the hydroxy groups, at C-3, -11, -12, -17, and -19, are all acetylated. The relative configuration was determined to be the same as that of **7** from the NOESY spectrum. Thus, the structure of **8** was demonstrated as shown.

Chuktabularin L (**9**), a white, amorphous powder, gave an ion at *m*/*z* 871.3001 $[M + Na]^+$ in the HRESIMS, 42 mass units more than **8**, corresponding to a molecular formula $C_{41}H_{52}O_{19}$. This evidence, combined with the close similarity of its ^1H and ^{13}C NMR spectra (Table 3) to those of **8**, suggested that **9** is an acetylated derivative of **8**. The C-2 (δ_C 73.9) and H-30 (δ_H 4.21, s) signals of **8** were shifted to δ_C 82.1 and δ_H 4.64 in **9**, which revealed that **9** is a 2-*O*-acetyl derivative of **8**. The relative configuration was determined to be the same as that of **7** from the key NOESY cross-peaks.

Chuktabularins M (**10**) and N (**11**) showed molecular formulas of $C_{42}H_{54}O_{19}$ and $C_{43}H_{56}O_{19}$, as determined by the HRESIMS ions at *m*/*z* 885.3165 $[M + Na]^+$ and 899.3309 $[M + Na]^+$, respectively, which indicated the presence of one more CH_2 and C_2H_4 unit than in **9**. The ^1H and ^{13}C NMR spectra of **10** and **11** were similar to those of **9**, including the characteristic signals of the ketal moiety, the propionyl at C-15, and the acetoxylated C-19 angular methyl group. The main differences were signals for an additional propionyl and isobutyryl group at C-12 in **10** and **11**, instead of the acetyl in **9**, which was deduced on the basis of their corresponding HMBC correlations. Thus, the structures of **10** and **11** were established as the 12-*O*-propionyl and the 12-*O*-isobutyryl derivative of **9**, respectively.

The acetoxylated C-19 methylene exhibited two moderately broadened proton signals in the ^1H NMR spectra of **8**−**11** recorded in $CDCl_3$ at room temperature (303 K). These compounds also exist as equilibrium mixtures of conformational isomers in solution, like compound **7**.

Chuktabularin O (**12**), a white, amorphous powder, was found to possess a molecular formula of $C_{39}H_{50}O_{18}$ from the HRESIMS ion at *m*/*z* 829.2901 $[M + Na]^+$. The similarity of the ^1H and ^{13}C NMR spectra of **12** when compared to those of **1** indicated that **12** possesses a 16-norphragmalin skeleton with a ketal moiety and a propionyl at C-15, which was confirmed by the observed HMBC correlations of the ketal resonance at δ_C 112.6 with the H-15a (δ_H 2.55, dd, J = 11.4, 7.8 Hz), H-30 (δ_H 4.57, s), and ethyl signals [δ_H 1.97 (q, J = 7.8 Hz, 2H); δ_H 1.08 (t, J = 7.8 Hz, 3H)]. Comparison of the 1D and 2D NMR data of **12** with those of **1**

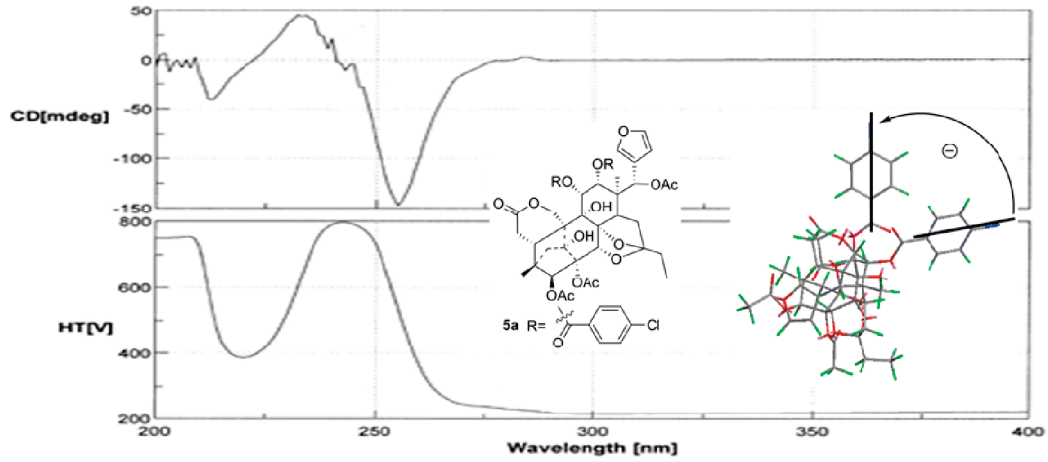

Figure 3. CD spectrum of **5a**. Bold lines denote the electric transition dipole of the chromophores.

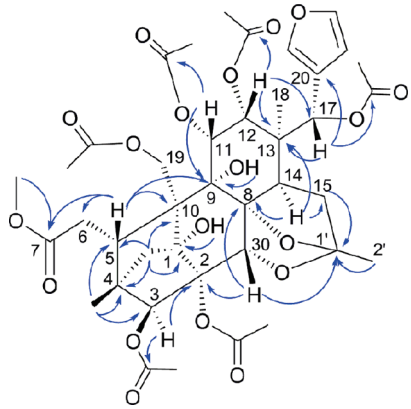

Figure 4. Key HMBC (→) correlations of **7**.

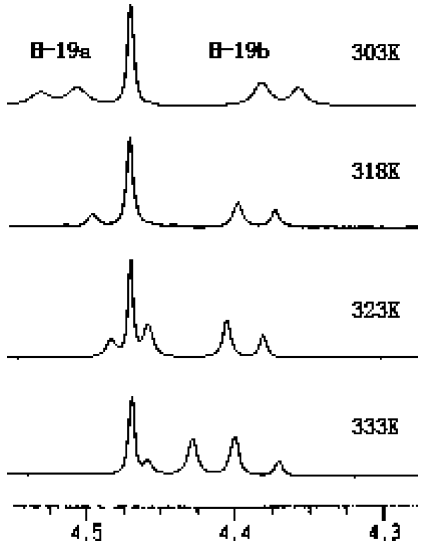

Figure 5. Expanded C-19 methylene signals of **7** in variable-temperature ^{1}H NMR experments.

revealed the absence of any oxygenated C-19 methylene proton signals; instead a normal C-19 methyl at δ_H 1.54 (s, 3H) was present, correlating with C-5 (δ_C 46.5), C-9 (δ_C 76.4), and C-10 (δ_C 54.2) in the HMBC spectrum (Figure 6). A singlet proton signal at δ_H 4.45 was assignable to H-6 from the HMBC correlations observed with the quaternary carbon signals at δ_C 46.5 (C-5) and 175.9 (C-7), which suggested that C-6 is oxygenated. Furthermore, on the basis of the chemical shifts of C-2 at δ_C 82.3 and H-30 at δ_H 4.57, along with the corresponding HMBC correlations, five acetyls were assignable to C-2 (δ_C 82.3), C-3 (δ_C 84.3), C-11 (δ_C 72.7), C-12 (δ_C 72.9), and C-17 (δ_C 71.3), respectively. Strong cross-peaks in the NOESY experiment (Figure 6) indicated a β-orientation of H-5, H-11, H-12, H-17, H-30, and Me-28 and the α-orientation of H-3, H-14, Me-18, and H-29, as in compound **1**. The NOESY correlation of H-5 with H-6 established H-6 as being in a β-orientation. Thus, the structure of **12** was established as shown.

Chuktabularin P (**13**), obtained as a white, amorphous powder, showed a molecular formula of $C_{41}H_{52}O_{19}$ as determined by the HRESIMS ion at *m/z* 871.3008 $[M + Na]^+$. The ^{1}H and ^{13}C NMR data (Table 4) showed close similarities to those of **12**, except for the presence of an additional acetyl group. The differences identified were that the H-6 signal (δ_H 4.45) of **12** was shifted downfield to δ_H 5.56 in **13** and that the C-7 signal (δ_C 175.9) of **12** shifted upfield to δ_C 170.2 for **13** (Table 4). Hence, compound **13** could be assigned as the 6-*O*-acetyl derivative of **12**, and this was supported by the HMBC correlations between H-6 and the acetyl carbonyl carbon (δ_C 169.8). The relative configuration was determined to be the same as that of **12** using the NOESY spectrum. Thus, the structure of **13** was established as the 6-*O*-acetyl derivative of **12**.

Chuktabularin Q (**14**) gave the molecular formula of $C_{37}H_{48}O_{16}$, as deduced from the HRESIMS ion at *m/z* 771.2837 $[M + Na]^+$. The ^{1}H and ^{13}C NMR data (Table 4) and the information obtained from the subsequent 2D NMR studies indicated that **14** possesses the 16-norphragmalin skeleton with a ketal moiety between the carbon skeleton and a propionyl at C-15, in the same manner as chuktabularin C.[5d] Comparison of the ^{1}H and ^{13}C NMR data of **14** and chuktabularin C revealed that the only differences were the chemical shifts of C-2 (δ_C 82.3) and H-30 (δ_H 4.65, s) in chuktabularin C, which were shifted upfield to δ_C 74.0 and δ_H 4.22 in **14**, and indicated that chuktabularin Q is the 2-*O*-deacetyl derivative of chuktabularin C.[7d] Thus, the structure of **14** was demonstrated as depicted, and the relative configuration was determined to be the same as chuktabularin C from the key NOESY correlations observed.

Chuktabularin S (**15**) was isolated as a white, amorphous powder, and its molecular formula was determined as $C_{36}H_{46}O_{16}$ from the HRESIMS ion at *m/z* 757.2686 $[M + Na]^+$. The ^{1}H and ^{13}C NMR data (Table 4) of **15** shared close similarities to those of **14**, except for the presence of a methyl group signal in **15** in place of the ethyl signals observed for **14**. In the HMBC spectrum of **15** (Figure 7), the observed correlations for the ketal resonance at δ_C 110.6 (C-1′) with the H-15a (δ_H 2.53, dd, J = 11.4, 7.8 Hz), a methyl (δ_H 1.71), and H-30 (δ_H 4.20, s) signals suggested that **15** possesses an acetyl at C-15, forming a characteristic ketal moiety with the limonoid skeleton, in the same manner as chuktabularin A.[7d] Furthermore, the four acetyl groups were assignable to C-3 (δ_C

Table 3. ^{1}H NMR and ^{13}C NMR Data of Compounds **7**−**11** in $CDCl_3$

	7[a]		**8**[a]		**9**[a]		**10**[a]		**11**[b]	
position	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C
1		84.8		85.1		84.7		84.8		84.8
2		82.0		73.9		82.1		82.1		82.2
3	5.24, s	83.0	5.14, s	85.5	5.24, s	83.1	5.24, s	83.1	5.23, s	83.1
4		45.3		44.6		45.5		45.4		45.5
5	2.70, brd (12.0)	41.6	2.70, brd (12.6)	42.1	2.70, brd (12.0)	41.6	2.70, brd (12.0)	41.6	2.69, brd (12.2)	41.6
6a	2.40, m[c]	33.2	2.41, m[c]	33.2	2.42, m[c]	33.2	2.40, m[c]	33.3	2.36, m[c]	33.4
6b	2.22, m[c]		2.20, dd (16.5, 12.0)		2.20, m[c]		2.20, m[c]		2.20, m[c]	
7		173.1		173.2		173.1		173.1		173.0
8		89.9		90.0		89.8		89.8		89.8
9		77.2		77.1		77.0		77.0		77.0
10		53.8		53.6		53.8		53.8		53.8
11	5.70, d (3.6)	72.0	5.67, d (3.6)	72.0	5.71, d (3.6)	72.0	5.72, brs	72.0	5.72, brs	72.2
12	5.66, d (3.6)	72.8	5.66, d (3.6)	72.6	5.67, d (3.6)	72.8	5.71, brs	72.5	5.72, brs	72.1
13		41.6		41.6		41.5		41.5		41.6
14	3.19, dd (12.0, 7.8)	44.4	3.17, dd (11.4, 8.4)	43.9	3.13, dd (12.0, 7.8)	44.0	3.17, dd (12.0, 7.8)	44.0	3.22, dd (12.0, 8.2)	44.2
15a	2.55, dd (11.4, 7.8)	35.4	2.57, dd (12.0, 8.4)	33.3	2.55, dd (11.4, 7.8)	34.0	2.55, dd (11.4, 7.8)	34.0	2.55, m[c]	34.1
15b	1.92, dd (12.0, 11.4)		1.95, dd (12.0, 11.4)		1.88, dd (12.0, 11.4)		1.88, dd (12.0, 11.4)		1.88, dd (12.0, 11.7)	
17	6.15, s	71.2	6.24, s	71.0	6.16, s	71.3	6.16, s	71.3	6.16, s	71.4
18	0.92, s, 3H	19.0	0.95, s, 3H	18.6	0.92, s, 3H	19.0	0.91, s, 3H	19.0	0.90, s, 3H	19.1
19a	4.64, brd (11.7)	66−67	4.67, brd (12.6)	66.8	4.63, brd (11.7)	66−67	4.66, brd (11.7)	66−67	4.67, brd (11.7)	66−67
19b	4.46, brd (11.7)		4.35, brd (12.6)		4.47, brd (11.7)		4.46, brd (11.7)		4.43, brd (11.7)	
20		122.3		122.1		122.3		122.4		122.4
21	7.64, brs	140.4	7.66, brs	140.7	7.64, brs	140.4	7.64, brs	140.4	7.63, brs	140.4
22	6.50, d (0.6)	109.6	6.55, brs	109.6	6.51, d (0.6)	109.6	6.52, d (1.2)	109.6	6.52, d (1.2)	109.6
23	7.38, t-like (1.8)	143.1	7.39, t-like (1.8)	143.3	7.38, t-like (1.2)	143.1	7.38, t-like (1.8)	143.1	7.38, t-like (1.5)	143.1
28	0.80, s, 3H	16.1	0.82, s, 3H	16.1	0.80, s, 3H	16.1	0.80, s, 3H	16.1	0.80, s, 3H	16.2
29a	2.22[c]	40.2	2.05[c]	39.7	2.10[c]	40.2	2.09[c]	40.2	2.12[c]	40.3
29b	1.85, d (11.4)		1.93[c]		1.86[c]		1.87, d (11.4)		1.87[c]	
30	4.64, s	70.8	4.21, s	71.0	4.64, s	70.5	4.64, s	70.4	4.66, s	70.5
1′		110.5		113.2		112.8		112.8		112.8
2′	1.63, s, 3H	18.7	2.04, q, 2H (7.8)	26.1	1.97, q, 2H (7.8)	26.0	1.96, q, 2H (7.8)	26.0	1.96, q, 2H (7.5)	26.0
3′			1.09, t, 3H (7.8)	8.2	1.07, t, 3H (7.8)	7.9	1.07, t, 3H (7.8)	7.9	1.07, t, 3H (7.5)	7.9
OH-1	4.82, s		4.42, s		4.83, s		4.84, s		4.82, s	
OH-9	3.55, s		3.53, s		3.54, s		3.57, s		3.58, s	
OMe-7	3.63, s, 3H	51.9	3.64, s, 3H	51.9	3.63, s, 3H	51.9	3.63, s, 3H	51.8	3.63, s, 3H	51.8
OAc-2		169.7				169.5		169.5		169.4
	2.10, s, 3H	21.5			2.10, s, 3H	21.5	2.09, s, 3H	21.5	2.07, s, 3H	21.4
OAc-3		169.4		169.9		169.4		169.4		169.3
	2.49, s, 3H	21.1	2.43, s, 3H	21.3	2.50, s, 3H	21.1	2.50, s, 3H	21.1	2.49, s, 3H	21.1
OAc-11		169.3		169.3		169.3		169.2		169.0
	1.95, s, 3H	20.9	1.98, s, 3H	20.9	1.95, s, 3H	20.9	1.95, s, 3H	20.9	1.94, s, 3H	20.8
OAc-12		169.5		169.5		169.4				
	2.06, s, 3H	20.5	2.07, s, 3H	20.5	2.07, s, 3H	20.5				
$OCOCH_2CH_3$-12								173.0		
							2.34, q, 2H (7.8)	27.4		
							1.15, t, 3H (7.8)	9.3		
$OCOCH(CH_3)_2$-12										175.6
									2.55, m	34.1
									1.18, d, 3H (6.9)	19.1
									1.15, d, 3H (6.9)	18.9
OAc-17		168.8		169.0		168.8		168.8		168.7
	2.10, s, 3H	20.5	2.13, s, 3H	20.8	2.10, s, 3H	20.5	2.10, s, 3H	20.5	2.08, s, 3H	20.6
OAc-19		169.7		169.7		169.5		169.5		169.3
	2.07, s, 3H	20.9	2.10, s, 3H	21.5	2.08, s, 3H	20.9	2.08, s, 3H	21.0	2.09, s, 3H	21.0

[a] Recorded at 600 MHz (^{1}H) and 150 MHz (^{13}C). [b] Recorded at 500 MHz (^{1}H) and 125 MHz (^{13}C). [c] Signal pattern unclear due to overlapping.

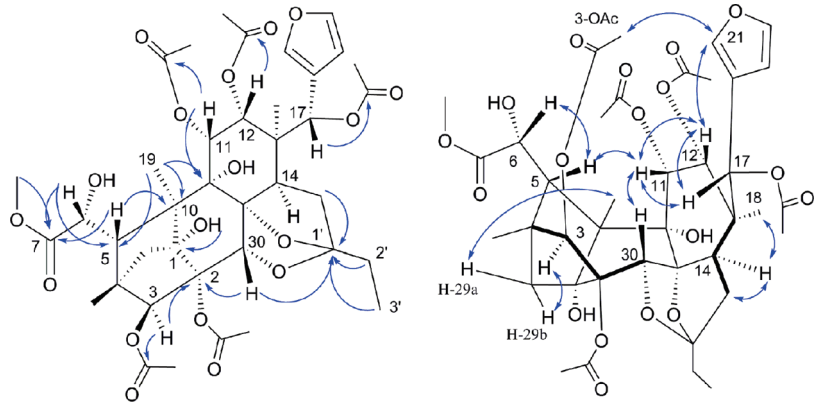

Figure 6. Selected HMBC (→) and NOE (↔) correlations of **12**.

Table 4. ^{1}H NMR and ^{13}C NMR Data of **12**−**16** (in $CDCl_3$)

	12[a]		**13**[a]		**14**[b]		**15**[a]		**16**[a]	
position	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)	δ_C
1		84.4		84.4		85.1		85.1		84.5
2		82.3		82.2		74.0		73.8		82.1
3	5.14, s	84.3	5.19, s	83.8	5.14, s	85.9	5.14, s	85.8	5.22, s	83.3
4		45.2		45.1		44.7		44.6		45.4
5	2.60, brs	46.5	2.84, brs	45.4	2.60, brd (11.8)	41.7	2.58, brd (11.8)	41.7	2.60, brd (11.8)	41.2
6a	4.45, brs	71.1	5.56, d (0.6)	71.2	2.43, brd (16.5)	34.2	2.44, brd (16.2)	34.1	2.52, brd (16.2)	34.1
6b					2.24, dd (16.5, 12.2)		2.25, brd (16.2, 12.0)		2.24, dd (16.2, 12.0)	
7		175.9		170.2		173.3		173.3		173.3
8		90.0		90.0		90.2		90.3		90.2
9		76.4		76.4		76.2		76.1		78.0
10		54.2		54.2		52.2		52.0		52.3
11	5.63, d (3.6)	72.7	5.63, d (3.0)	72.6	5.65, d (2.3)	72.5	5.66, d (3.3)	72.4	5.51, d (3.0)	73.4
12	5.68, d (3.6)	72.9	5.73, d (3.0)	73.0	5.64, d (2.3)	73.1	5.63, d (3.3)	73.0	4.16, d (3.0)	72.8
13		41.0		41.6		41.7		41.7		42.5
14	3.11, dd (12.0, 7.8)	44.4	3.09, dd (12.0, 7.8)	44.4	3.06, dd (11.8, 8.1)	44.7	3.09, dd (12.0, 7.8)	44.8	3.00, dd (12.0, 7.8)	43.8
15a	2.55, dd (11.4, 7.8)	34.0	2.55, dd (11.4, 7.8)	34.0	2.51, dd (11.8, 8.1)	33.5	2.53, dd (11.4, 7.8)	35.2	2.54, dd (11.4, 7.8)	35.5
15b	1.87, dd (12.0, 11.4)		1.87, dd (12.0, 11.4)		1.91, brd (12.0)		1.97, brd (12.0)		1.91, brd (12.0)	
17	6.11, s	71.3	6.12, s	71.2	6.24, s	71.1	6.24, s	71.0	6.09, s	71.5
18	0.90, s, 3H	19.2	0.91, s, 3H	19.2	0.95, s, 3H	18.7	0.95, s, 3H	19.1	1.05, s, 3H	19.1
19	1.54, s, 3H	17.7	1.26, s, 3H	17.0	1.19, s, 3H	17.7	1.19, s, 3H	17.7	1.21, s, 3H	17.3
20		122.5		122.3		122.1		122.0		122.6
21	7.63, brs	140.3	7.66, brs	140.4	7.67, brs	140.7	7.68, brs	140.7	7.64, brs	140.6
22	6.49, d (1.2)	109.6	6.51, d (1.2)	109.5	6.54, brs	109.6	6.54, brs	109.6	6.47, brs	110.0
23	7.39, t-like (1.8)	143.1	7.39, t-like (1.8)	143.2	7.38, brs	143.2	7.39, brs	143.3	7.36, brs	142.8
28	0.85, s, 3H	16.7	0.91, s, 3H	16.6	0.80, s, 3H	16.1	0.79, s, 3H	16.0	0.77, s, 3H	16.0
29a	2.45, d (11.4)	41.5	2.21, dd (11.4, 1.2)	41.4	1.88, d (11.2)	39.6	1.89, d (11.4)	39.6	1.83, d (11.4)	40.0
29b	1.76, dd (11.4, 1.8)		1.84, d (11.4)		1.72, d (11.2)		1.74, d (11.4)		1.80, d (11.4)	
30	4.57, s	70.7	4.60, s	70.7	4.22, s	71.7	4.20, s	72.0	4.22, s	71.1
1′		112.6		112.8		112.1		110.6		110.7
2′	1.97, q, 2H, (7.8)	26.0	1.98, q, 2H, (7.8)	26.0	2.02, q, 2H, (7.5)	26.2	1.71, s, 3H	18.7	1.71, s, 3H	18.9
3′	1.08, t, 3H, (7.8)	7.9	1.07, t, 3H, (7.8)	7.9	1.09, t, 3H, (7.5)	8.2				
OH-1	4.70, s		4.70, s		4.22, s		4.27, s		4.60, s	
OH-2							3.61, s			
OMe-7	3.77, s, 3H	52.5	3.68, s, 3H	52.6	3.63, s, 3H	51.7	3.64, s, 3H	51.8	3.64, s, 3H	51.8
OAc-2		169.8		169.7						169.7
	2.07, s, 3H	21.0	2.10, s, 3H	21.0					2.08, s, 3H	21.0
OAc-3		169.2		169.2		169.9		170.0		169.5
	2.45, s, 3H	21.0	2.46, s, 3H	21.0	2.41, s, 3H	21.3	2.42, s, 3H	21.3	2.46, s, 3H	21.1
OAc-6				169.8						
			2.20, s, 3H	21.2						
OAc-11		169.6		169.8		169.4		169.5		169.9
	1.94, s, 3H	21.4	2.02, s, 3H	21.5	1.94, s, 3H	21.0	1.95, s, 3H	21.0	2.08, s, 3H	21.4
OAc-12		169.4		169.2		169.2		169.2		
	2.10, s, 3H	20.7	2.10, s, 3H	20.6	2.08, s, 3H	20.6	2.10, s, 3H	20.6		
OAc-17		168.9		168.8		168.8		169.0		169.0
	2.10, s, 3H	20.5	2.10, s, 3H	20.5	2.12, s, 3H	20.8	2.14, s, 3H	20.9	2.09, s, 3H	20.6

[a] Recorded at 600 MHz (^{1}H) and 150 MHz (^{13}C). [b] Recorded at 500 MHz (^{1}H) and 125 MHz (^{13}C).

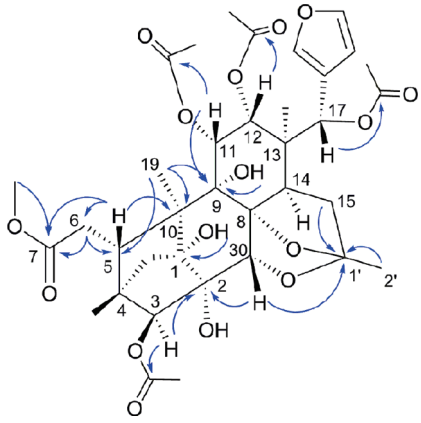

Figure 7. Selected HMBC (→) correlations of **15**.

85.8), C-11 (δ_C 72.4), C-12 (δ_C 73.0), and C-17 (δ_C 71.0), on the basis of their corresponding HMBC correlations. Thus, the structure of **15** was demonstrated as the 2-*O*-deacetyl derivative of chuktabularin A, and the relative configurations of both compound were determined to be the same from the NOESY spectra.

Chuktabularin T (**16**), a white, amorphous powder, gave a molecular formula of $C_{36}H_{46}O_{16}$ as established by the HRESIMS ion at *m*/*z* 757.2681 $[M + Na]^+$. This evidence, when combined with the ^{1}H and ^{13}C NMR spectroscopic data (Table 4) and information obtained from subsequent 2D NMR studies, indicated that **16** is a positional isomer of **15**. The H-12 signal at δ_H 5.64 in **15** appeared at δ_H 4.16 in **16** and the C-2 signal at δ_C 73.8 was shifted downfield to δ_C 82.1, consistent with the transfer of an acetyl from C-12 in **15** to C-2 in **16**. This matched the absence of HMBC correlations between H-12 and the acetyl carbon. Thus, the structure of **16** was determined as the 12-*O*-deacetyl derivative of chuktabularin A.

Four known compounds were identified as chuktabularins A−D by comparison of their physical and spectral data (IR, ESIMS, and NMR) with reported values.[7d] By correlation with chuktabularin I (**5**) on the biosynthetic origin and structure, the absolute configuration of the key chiral carbons in compounds **1**−**4** and **6**−**16** could be proposed as depicted.

Experimental Section

General Experimental Procedures. Optical rotations were measured with a JASCO P-1020 polarimeter. CD spectra were obtained on a JASCO 810 spectropolarimeter. IR (KBr disks) spectra were recorded on a Bruker Tensor 27 spectrometer. NMR spectra were recorded on Bruker ACF-500 and -600 NMR instruments (^{1}H: 500 or 600 MHz, ^{13}C: 125 or 150 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), respectively. 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-park RP-C_{18} column (20 × 200 mm) and a 1100 Series multiple wavelength detector.

Plant Material. The air-dried stem bark of *C. tabularis* var. *velutina* was collected from Xishuangbanna, Yunnan Province, People's Republic of China, in March 2007, and was authenticated by Professor Mian Zhang of the Research Department of Pharmacognosy, China Pharmaceutical University. A voucher specimen (no. 2006-MML) has been deposited in the Department of Natural Medicinal Chemistry, China Pharmaceutical University.

Extraction and Isolation. The air-dried stem bark (10 kg) was extracted by refluxing with 95% ethanol three times. The EtOH extract was concentrated under reduced pressure (2000 g) and then extracted with $CHCl_3$ to give a chloroform extract (300 g). The oily chloroform extract was dissolved in 2 L of 50% MeOH and H_2O and then extracted with petroleum ether. After removal of the fatty components, 210 g of extract was obtained, which was subjected to passage over a silica gel column eluted with $CHCl_3$−MeOH in a gradient (1:0 to 1:2), to afford eight fractions (Fr. A−H), monitored by TLC. Fr. C (22 g) was chromatographed on a column of silica gel, eluted successively with a gradient of petroleum ether−EtOAc (4:1 to 1:2), to give eight subfractions (Fr. C1−C8). Fr. C5 was chromatographed on a column of reversed-phase C_{18} silica gel, eluted with MeOH−H_2O (5:5 to 7:3), to give three subfractions (Fr. C5a−C5e). Fr. C5c was separated by preparative HPLC using CH_3OH−H_2O (64:35, 10 mL/min) as the mobile phase to give **11** (6 mg). Fr. C7 was chromatographed on a column of reversed-phase C_{18} silica gel, eluted with MeOH−H_2O (5:5 to 7:3), to give three subfractions (Fr. C7a−C7e). Fr. C7b was separated by preparative HPLC using CH_3OH−H_2O (60:40, 10 mL/min) as the mobile phase to give **9** (20 mg), **13** (6 mg), and a mixture that contained **8**, and then the mixture was purified using CH_3CN−H_2O (50:50, 10 mL/min) as the mobile phase to give **8** (12 mg). Fr. C7c was separated by preparative HPLC using CH_3CN−H_2O (55:45, 10 mL/min) as the mobile phase to give **2** (10 mg) and a mixture that contained **10**. This mixture was purified using CH_3OH−H_2O (65:35, 10 mL/min) as the mobile phase to give **10** (7 mg). Fr. C7e was separated by preparative HPLC with CH_3OH−H_2O (65:35, 10 mL/min) as the mobile phase to give **3** (8 mg). Fr. C8 was chromatographed on a column of reversed-phase C_{18} silica gel eluted with MeOH−H_2O (5:5 to 7:3) to give three subfractions (Fr. C8a−C8f). Fr. C8c was separated by preparative HPLC using CH_3OH−H_2O (55:45, 10 mL/min) as the mobile phase to give **7** (26 mg), chuktabularin A (30 mg), and chuktabularin B (26 mg). Fr. C8d was separated by preparative HPLC using CH_3OH−H_2O (60:40, 10 mL/min) as the mobile phase to afford chuktabularin C (15 mg). Fr. C8e was separated by preparative HPLC using CH_3OH−H_2O (60:40, 10 mL/min) as the mobile phase to yield **14** (10 mg), chuktabularin C (18 mg), and a mixture that contained **1**. This mixture was purified by preparative HPLC, with CH_3CN−H_2O (45:55, 10 mL/min) as the mobile phase to give **1** (8 mg). Fr. D (30 g) was chromatographed on a column of silica gel eluted successively with a gradient of petroleum ether−EtOAc (5:2 to 1:2) to give seven subfractions (Fr. D1−D7). Fr. D4 was chromatographed on a column of reversed-phase C_{18} silica gel eluted with MeOH−H_2O (5:5 to 7:3) to give four subfractions (Fr. D4a−D4d). Fr. D4b was separated by preparative HPLC using CH_3CN−H_2O (42:58, 10 mL/min) as the mobile phase to give **4** (20 mg). Fr. D4c was purified by preparative HPLC using CH_3CN−H_2O (45:55, 10 mL/min) as the mobile phase to give **16** (22 mg). Fr. D5 was chromatographed on a column of reversed-phase C_{18} silica gel eluted with MeOH−H_2O (5:5 to 7:3) to give four subfractions (Fr. D5a−D5d). Fr. D5b was separated by preparative HPLC using CH_3OH−H_2O (55:45, 10 mL/min) as the mobile phase to give a mixture containing **15**. This mixture was purified by preparative HPLC using CH_3CN−H_2O (42:58, 10 mL/min) as the mobile phase to give **15** (8 mg). Fr. D5c was separated by preparative HPLC using CH_3OH−H_2O (55:45, 10 mL/min) as the mobile phase to afford **12** (6 mg). Fr. E (20 g) was chromatographed on a column of reversed-phase C_{18} silica gel, eluted with MeOH−H_2O (4:6 to 7:3), to give six subfractions (Fr. E1−E6). Fr. E5 was chromatographed on a column of reversed-phase C_{18} silica gel, eluted with MeOH−H_2O (4:6 to 7:3), to give four subfractions (Fr. E5a−E5d). Fr. E5b was separated by preparative HPLC using CH_3CN−H_2O (40:60, 10 mL/min) as the mobile phase to give **5** (100 mg) and **6** (10 mg).

Chuktabularin E (1): colorless crystals (MeOH−H_2O); $[\alpha]^{25}_D$ +28 (*c* 0.075, CH_3OH); IR (KBr) ν_{max} 3418, 2980, 1755, 1636, 1374, 1211, 1031, 916, 601 cm^{-1}; ^{1}H NMR, see Table 1; ^{13}C NMR, see Table 2; negative ESIMS *m/z* 791.1 $[M + CH_3COO]^-$ (100); positive ESIMS *m/z* 750.2 $[M + NH_4]^+$ (100); HRESIMS *m/z* 755.2527 $[M + Na]^+$ (calcd $C_{36}H_{44}O_{16}Na$, 755.2522).

Chuktabularin F (2): white, amorphous powder; $[\alpha]^{25}_D$ +24 (*c* 0.095, CH_3OH); IR (KBr) ν_{max} 3424, 2984, 1751, 1639, 1375, 1219, 1041, 926, 600 cm^{-1}; ^{1}H NMR, see Table 1; ^{13}C NMR, see Table 2; negative ESIMS *m/z* 823.4 $[M + Cl]^-$ (100); positive ESIMS *m/z* 806.3 $[M + NH_4]^+$ (100); HRESIMS *m/z* 811.2794 $[M + Na]^+$ (calcd $C_{39}H_{48}O_{17}Na$, 811.2784).

Chuktabularin G (3): white, amorphous powder; $[\alpha]^{25}_D$ +23 (*c* 0.080, CH_3OH); IR (KBr) ν_{max} 3432, 2981, 1753, 1638, 1375, 1219, 1040, 924, 602 cm^{-1}; ^{1}H NMR, see Table 1; ^{13}C NMR, see Table 2; negative ESIMS *m/z* 837.5 $[M + Cl]^-$ (100); positive ESIMS *m/z* 820.2 $[M + NH_4]^+$ (100); HRESIMS *m/z* 825.2938 $[M + Na]^+$ (calcd $C_{40}H_{50}O_{17}Na$, 825.2940).

Chuktabularin H (4): white, amorphous powder; $[\alpha]^{25}_D$ +17 (*c* 0.075, CH_3OH); IR (KBr) ν_{max} 3440, 2980, 1750, 1637, 1374, 1234, 1025, 909, 603 cm^{-1}; ^{1}H NMR, see Table 1; ^{13}C NMR, see Table 2; negative ESIMS *m/z* 689.2 $[M - H]^-$ (100); positive ESIMS *m/z* 708.2 $[M + NH_4]^+$ (100); HRESIMS *m/z* 713.2412 $[M + Na]^+$ (calcd $C_{34}H_{42}O_{15}Na$, 713.2416).

Chuktabularin I (5): white, amorphous powder; $[\alpha]^{25}_D$ +25 (*c* 0.090, CH_3OH); IR (KBr) ν_{max} 3442, 2981, 1752, 1642, 1374, 1242, 1037, 902, 601 cm^{-1}; ^{1}H NMR, see Table 1; ^{13}C NMR, see Table 2; negative ESIMS *m/z* 689.3 $[M - H]^-$ (100); positive ESIMS *m/z* 708.4 $[M + NH_4]^+$ (100); HRESIMS *m/z* 713.2419 $[M + Na]^+$ (calcd $C_{34}H_{42}O_{15}Na$, 713.2416).

Chuktabularin J (6): white, amorphous powder; $[\alpha]^{25}_D$ +19 (*c* 0.070, CH_3OH); IR (KBr) ν_{max} 3432, 2979, 1738, 1639, 1374, 1234, 1030, 899, 602 cm^{-1}; ^{1}H NMR, see Table 1; ^{13}C NMR, see Table 2; negative ESIMS *m/z* 683.4 $[M + Cl]^-$ (100); positive ESIMS *m/z* 666.2 $[M + NH_4]^+$ (100); HRESIMS *m/z* 671.2331 $[M + Na]^+$ (calcd $C_{32}H_{40}O_{14}Na$, 671.2310).

Chuktabularin K (7): white, amorphous powder; $[\alpha]^{25}_D$ +23 (*c* 0.090, CH_3OH); IR (KBr) ν_{max} 3436, 2986, 1751, 1641, 1372, 1239, 1039, 876, 602 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 3; negative ESIMS *m/z* 893.3 $[M + CH_3COO]^-$ (100); positive ESIMS *m/z* 852.2 $[M + NH_4]^+$ (100); HRESIMS *m/z* 857.2841 $[M + Na]^+$ (calcd $C_{40}H_{50}O_{19}Na$, 857.2839).

Chuktabularin L (8): white, amorphous powder; $[\alpha]^{25}_D$ +28 (*c* 0.075, CH_3OH); IR (KBr) ν_{max} 3443, 2980, 1749, 1637, 1374, 1224, 1031, 898, 603 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 3; negative ESIMS *m/z* 841.6 $[M + Cl]^-$ (100); positive ESIMS *m/z* 829.2 $[M + Na]^+$ (100); HRESIMS *m/z* 829.2891 $[M + Na]^+$ (calcd $C_{39}H_{50}O_{18}Na$, 829.2889).

Chuktabularin M (9): white, amorphous powder; $[\alpha]^{25}_D$ +29 (*c* 0.085, CH_3OH); IR (KBr) ν_{max} 3437, 2983, 1751, 1640, 1373, 1238, 1038, 903, 602 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 3; negative ESIMS *m/z* 805.3 $[M - COCH_3]^-$ (100); positive ESIMS *m/z* 866.4 $[M + NH_4]^+$ (100); HRESIMS *m/z* 871.3001 $[M + Na]^+$ (calcd $C_{41}H_{52}O_{19}Na$, 871.2995).

Chuktabularin N (10): white, amorphous powder; $[\alpha]^{25}_D$ +22 (*c* 0.075, CH_3OH); IR (KBr) ν_{max} 3435, 2983, 1751, 1639, 1372, 1221, 1038, 903, 602 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 3; negative ESIMS *m/z* 897.5 $[M + Cl]^-$ (100); positive ESIMS *m/z* 880.4 $[M + NH_4]^+$ (100); HRESIMS *m/z* 885.3165 $[M + Na]^+$ (calcd $C_{42}H_{54}O_{19}Na$, 885.3152).

Chuktabularin O (11): white, amorphous powder; $[\alpha]^{25}_D$ +29 (*c* 0.050, CH_3OH); IR (KBr) ν_{max} 3432, 2980, 1751, 1636, 1372, 1221, 1038, 903, 602 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 3; negative ESIMS *m/z* 911.7 $[M + Cl]^-$ (100); positive ESIMS *m/z* 894.3 $[M + NH_4]^+$ (100); HRESIMS *m/z* 899.3309 $[M + Na]^+$ (calcd $C_{43}H_{56}O_{19}Na$, 899.3308).

Chuktabularin P (12): white, amorphous powder; $[\alpha]^{25}_D$ +30 (*c* 0.070, CH_3OH); IR (KBr) ν_{max} 3452, 2982, 1753, 1640, 1373, 1243, 1035, 902, 602 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 4; negative ESIMS

m/z 805.1 $[M - H]^-$ (100); positive ESIMS *m/z* 824.3 $[M + NH_4]^+$ (100); HRESIMS *m/z* 829.2901 $[M + Na]^+$ (calcd $C_{39}H_{50}O_{18}Na$, 829.2889).

Chuktabularin Q (13): white, amorphous powder; $[\alpha]^{25}_D$ +29 (*c* 0.075, CH_3OH); IR (KBr) ν_{max} 3446, 2983, 1758, 1638, 1373, 1219, 1037, 902, 602 cm^{-1}; ^1H and ^{13}C NMR, see Table 4; negative ESIMS *m/z* 805.3 $[M - COCH_3]^-$ (100); positive ESIMS *m/z* 866.3 $[M + NH_4]^+$ (100); HRESIMS *m/z* 871.3008 $[M + Na]^+$ (calcd $C_{41}H_{52}O_{19}Na$, 871.2995).

Chuktabularin R (14): white, amorphous powder; $[\alpha]^{25}_D$ +8 (*c* 0.050, CH_3OH); IR (KBr) ν_{max} 3456, 2979, 1747, 1638, 1374, 1225, 1030, 898, 603 cm^{-1}; ^1H and ^{13}C NMR, see Table 4; negative ESIMS *m/z* 807.1 $[M + CH_3COO]^-$ (100); positive ESIMS *m/z* 766.2 $[M + NH_4]^+$ (100); HRESIMS *m/z* 771.2837 $[M + Na]^+$ (calcd $C_{37}H_{48}O_{16}Na$, 771.2835).

Chuktabularin S (15): white, amorphous powder; $[\alpha]^{25}_D$ +26 (*c* 0.050, CH_3OH); IR (KBr) ν_{max} 3454, 2981, 1752, 1638, 1373, 1226, 1030, 875, 603 cm^{-1}; ^1H and ^{13}C NMR, see Table 4; negative ESIMS *m/z* 779.2 $[M + CH_3COO]^-$ (100); positive ESIMS *m/z* 752.1 $[M + NH_4]^+$ (100); HRESIMS *m/z* 757.2686 $[M + Na]^+$ (calcd $C_{36}H_{46}O_{16}Na$, 757.2678).

Chuktabularin T (16): white, amorphous powder; $[\alpha]^{25}_D$ +4 (*c* 0.080, CH_3OH); IR (KBr) ν_{max} 3448, 2986, 1745, 1640, 1373, 1227, 1034, 876, 603 cm^{-1}; ^1H and ^{13}C NMR, see Table 4; negative ESIMS *m/z* 769.5 $[M + Cl]^-$ (100); positive ESIMS *m/z* 752.3 $[M + NH_4]^+$ (100); HRESIMS *m/z* 757.2681 $[M + Na]^+$ (calcd $C_{36}H_{46}O_{16}Na$, 757.2678).

X-ray crystallographic data for 1: $C_{36}H_{44}O_{16}$, $M = 732.71$, orthorhombic, dimensions 0.23 × 0.20 × 0.18 mm, $d = 1.400$ g/cm^3, space group $P2_12_12_1$, $Z = 4$, $a = 10.4375(14)$ Å, $b = 16.4155(18)$ Å, $c = 20.288(2)$ Å, $\alpha = \beta = \gamma = 90°$, $V = 3476.1(7)$ Å^3, reflections collected/unique 17 981/6140 ($R_{int} = 0.0543$), number of observation $[I > 2\sigma(I)]$ 6140, parameters 482, final *R* indices $[I > 2\sigma(I)]$: $R_1 = 0.0594$, $wR_2 = 0.1242$.

Colorless crystals of **1** was obtained from the mixture MeOH−H_2O. Crystal data were obtained on a Bruker Smart-1000 CCD with a graphite monochromator, with Mo Kα radiation ($\lambda = 0.71073$ Å) at 298(2) K. The crystal structure was solved by direct methods using SHELX-97[12] and expanded using difference Fourier techniques, refined by SHELX-97.[13] Crystallographic data for the structure of **1** have been deposited in the Cambridge Crystallographic Data Centre with a deposition number of CCDC 743107. Copies of these data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK [fax (+44) 1223 336 033; or e-mail: deposit@ccdc.cam.ac.uk].

Preparation of the *p*-Chlorobenzoate of Chuktabularin I (5). Compound **5** (22 mg) was treated with *p*-chlorobenzoic acid (50 mg), DCC (50 mg), and a catalytic amount of DMAP in $CHCl_3$ (4 mL), at room temperature for 48 h. The reaction mixture was purified by silica gel column chromatography (eluted with $CHCl_3$ and CH_3OH) and passage over Sephadex LH-20 using CH_2Cl_2−CH_3OH (1:1) as the mobile phase to give the 11,12-di-*p*-chlorobenzoate (**5a**, 10 mg): white amorphous powder; CD (CH_3OH, $\Delta\varepsilon$) 212 (−1.17), 232 (+1.32), 255 (−4.30) nm; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.55 (1H, s, H-21), 7.39 (1H, s, H-23), 6.45 (1H, brs, H-22), 6.24 (1H, s, H-17), 6.05 (1H, d, $J = 3.3$ Hz, H-11), 5.80 (1H, d, $J = 3.3$ Hz, H-12), 5.40 (1H, s, H-3), 5.02 (1H, d, $J = 12.6$ Hz, H-19a), 4.77 (1H, s, H-3), 4.02 (1H, d, $J = 12.6$, H-19b), 3.50 (1H, dd, $J = 11.7$, 7.9, H-14), 2.62 (3H, s, OAc-3), 2.13 (6H, s, OAc-2, OAc-17), 1.96−2.68 (8H, m, H-6, H-15, H-29, H-2′), 1.12 (3H, t, $J = 7.5$ Hz, H-3′), 0.96 (3H, s, H-18), 0.89 (3H, s, H-28); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.0 (C-7), 143.4 (C-23), 140.3 (C-21), 122.4 (C-20), 113.5 (C-1′), 109.6 (C-22), 89.6 (C-8), 85.6 (C-1), 83.1 (C-3), 81.3 (C-2), 75.9 (C-9), 72.6 (C-11), 72.6 (C-12), 71.3 (C-17), 70.9 (C-30), 69.2 (C-19), 52.4 (C-10), 45.3 (C-4), 44.2 (C-14), 41.8 (C-13), 40.2 (C-5), 38.9 (C-29), 34.1 (C-15), 30.9 (C-6), 26.0 (C-2′), 19.3 (C-18), 15.0 (C-28), 7.8 (C-3′), [169.5, 169.1, 168.7, 21.1, 20.8, 20.5] (OAc-2, OAc-3, OAc-17), [165.1, 164.2, 140.9, 140.6, 132.0, 131.1, 129.3, 128.5, 127.0, 126.1] (*p*-chlorobenzoyl); negative ESIMS *m/z* 1001.8 $[M + Cl]^-$ (100); positive ESIMS *m/z* 984.8 $[M + NH_4]^+$ (100).

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

Supporting Information Available: Biogenetic scheme for compounds **1**−**16**; enlarged X-ray structure of **1**; ^1H NMR, ^{13}C NMR, ESIMS, and HRESIMS spectra of **1**−**16**. This material is available free of charge via the Internet at http://pubs.acs.org.

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NP900734C