Chloramultiols A−F, Lindenane-Type Sesquiterpenoid Dimers from *Chloranthus multistachys*

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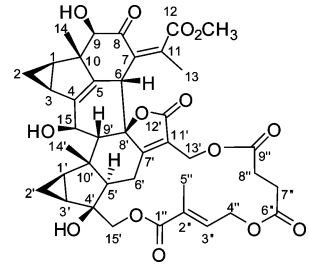
Six new highly complex lindenane-type sesquiterpenoid dimers, chloramultiols A−F (**1**−**6**), along with six known analogues, were isolated from the whole plant of *Chloranthus multistachys*. The structures of **1**−**6** were elucidated on the basis of mass spectrometry (MS) and 1D and 2D NMR spectroscopic analysis. Among them, compounds **1** and **6** contain a unique 18-membered macrocyclic triester ring. All compounds isolated were evaluated for the inhibition of the growth of five tumor cell lines.

Phytochemical investigations on the genus *Chloranthus* (Chloranthaceae) have led to the isolation of a number of sesquiterpenoid oligomers.[1−5] Among these, dimeric lindenane sesquiterpenoids with biological activities including inhibition of cell adhesion molecule expression,[6] potent and selective inhibition on the delayed rectifier (I_K) K^+ current,[7,8] inhibition of tyrosinase,[9] and antifungal activity[10,11] have been of interest to natural product scientists as leads for new therapeutic agents.

Chloranthus multistachys Pei is a perennial herb that is distributed mainly over the eastern region of Asia, and its roots have been applied to treat bone fractures, lumbocrural pain, and pruritus in mainland China, as a folk medicine.[12] Previous studies on this species have resulted in the isolation of one sesquiterpenoid, three bisesquiterpenoids, and nine *ent*-kaurane diterpenoids.[13,14] In the course of a systematic search for sesquiterpenoid dimers from *C. multistachys*, six new lindenane sesquiterpenoids, named chloramultiols A−F (**1**−**6**), and six known analogues, chloramultilides C and D,[10] shizukaols C and D,[15] spicachlorantin B,[16] and cycloshizukaol A[17] were obtained. In this contribution, we present the isolation, structure elucidation, and biological evaluation of compounds **1**−**6**.

Chloramultiol A (**1**) was isolated as a yellow powder. Its molecular formula was established as $C_{40}H_{44}O_{14}$ by high-resolution electrospray ionization mass spectrometry (HRESIMS) at *m*/*z* 771.2633 $[M + Na]^+$ (calcd 771.2628), indicating 19 degrees of unsaturation. The IR absorption bands at 3443, 1738, and 1609 cm^{-1} implied the presence of hydroxy, carbonyl, and double bond functionalities. The ^1H NMR spectrum of **1** (Table 1) showed four methyl group proton signals at δ_H 0.83 (s), 1.03 (s), 1.82 (s), and 1.86 (s), one methoxy group proton signal at δ_H 3.59 (s), and a trisubstituted olefinic proton signal at δ_H 6.55 (m). The ^{13}C and distortionless enhancement by polarization transfer (DEPT) NMR spectra of **1** (Table 2) exhibited 40 signals for carbons consisting of six carbonyls, four double bonds, four methyls, one methoxy, eight methylenes (three oxygenated), nine methines (two oxygenated), and four quaternary carbons (two oxygenated). The $^1H-^1H$ correlation spectroscopy (COSY) spectrum of **1** showed two sets of proton spin systems of a 1,2-disubstituted cyclopropane ring (δ_H 0.42, 1.00, 1.86, and 2.00; δ_H 0.83, 1.27, 1.30, and 1.44). The above information, together with the typical high-field methylene signals at δ_H 0.42 (H-2β, m) for a cyclopropane ring, indicated that compound **1** is a lindenane sesquiterpenoid dimer with an 18-membered triester ring, similar to shizukaol B.[15] Detailed comparison of the ^{13}C NMR data of **1** and shizukaol B[15] indicated a difference in that a methylene at δ_C 25.4 in shizukaol B[15] was replaced by an oxymethine at δ_C 64.6 in **1**. A four proton spin system comprising H-5′/H-6′, H-15/H-9′, H-3″/H-4″, and H-7″/H-8″, as well as the two proton spin systems of a 1,2-disubstituted cyclopropane ring in the $^1H-^1H$ COSY spectrum of **1**, suggested that C-15 is an oxymethine carbon. This was confirmed by the heteronuclear multiple bond correlations (HMBC) of H-15 (δ_H 4.83, d) with C-3 (δ_C 23.3, d), C-4 (δ_C 144.3, s), C-5 (δ_C 136.8, s), C-8′ (δ_C 92.3, s), C-9′ (δ_C 62.1, d), and C-10′ (δ_C 44.0, s). The other $^1H-^1H$ COSY and HMBC correlations shown in Figure 1 supported the planar structure assigned for **1**.



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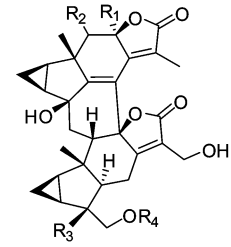
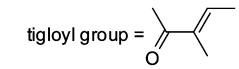
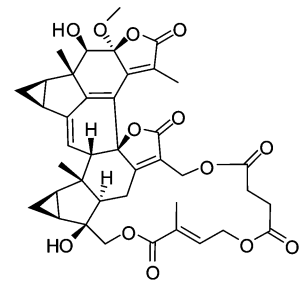


	R_1	R_2	R_3	R_4
2	OH	β–OH	OH	H
3	OCH_3	β–OH	OH	Tig
4	OH	=O	OH	Tig
5	OH	β–OH	H	Ac





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The relative configuration of **1** was established by the rotating frame Overhauser effect spectroscopy (ROESY) correlations shown in Figure 1. The ROESY correlations of H-1/H-3, H-1/H-2α, H-2α/H-3, H-1/H-9, H-3/H-9, H-2β/Me-14, H-6/Me-14, H-1′/H-3′, H-1′/H-2′α, H-2′β/CH_3-14′, and H-2′α/H-3′ indicated the α-orientation of H-9 and H-5′ and the β-orientation of the two cyclopropane rings, H-6, Me-14, and Me-14′. The correlation between H-9 and H-5′ suggested that the configuration of C-8′ is fully consistent with those of other lindenane-type sesquiterpenoids reported. Further, both OH-15 and OH-4′ were established as being β-oriented from the ROESY cross-peaks between H-15/H-1′, H-15/H-5′, and H-3′/H_2-15′. In addition, the geometry of the double bond of the 4-hydroxy-2-methylbut-2-enoyl group on the macrocyclic ester ring was assigned as *E* from the ROESY interaction of H_2-4″ with Me-5″. Hence, the structure of **1** was established as a highly complex lindenane-

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Table 1. ^{1}H NMR Spectroscopic Data for Chloramultiols A−F (**1**−**6**)

position	**1**[a,b]	**2**[a,c]	**3**[a,c]	**4**[a,c]	**5**[a,c]	**6**[b,d]
1	2.00, m	1.83, m	1.83, m	2.20, m	1.85, m	2.12, m
2α	1.00, m	0.79, m	0.81, m	0.93, m	0.81, m	1.10, m
2β	0.42, m	1.00, m	1.04, m	1.13, m	1.01, m	0.64, m
3	1.86, m	1.82, m	1.80, m	1.82, m	1.83, m	2.20, m
6	4.09, s					
9	3.73, s	3.67, s	3.78, s		3.73, s	3.92, s
13	1.82, s	1.55, s	1.57, s	1.68, s	1.54, s	1.77, s
14	1.03, s	0.83, s	0.83, s	1.14, s	0.84, s	0.83, s
15α	4.83, d (1.9)	1.84, m	1.84, m	1.84, m	1.80, m	6.13, d (4.4)
15β		2.62, m	2.68, m	2.71, m	2.69, m	
1′	1.44, m	1.58, m	1.66, m	1.62, m	1.51, m	1.85, m
2′α	0.83, m	0.56, m	0.60, m	0.60, m	0.67, m	1.28, m
2′β	1.27, m	1.14, m	1.18, m	1.20, m	0.70, m	0.69, m
3′	1.30, m	1.68, m	1.68, m	1.78, m	1.28, m	1.43, m
4′					1.56, m	
5′	1.69, m	2.17, m	2.19, m	2.39, m	2.28, m	2.18, m
6′α	2.34, m	2.39, m	2.39, m	2.42, m	2.57, m	2.80, m
6′β	2.71, m	2.89, m	2.91, m	2.91, m	2.62, m	2.56, m
9′	1.94, d (2.3)	2.67, m	2.67, m	2.68, m	2.72, m	2.57, m
13′a	5.04, d (12.0)	4.32, d (13.2)	4.29, d (13.2)	4.28, d (13.2)	4.30, d (13.3)	5.11, d (11.8)
13′b	4.44, d (12.0)	4.25, d (13.2)	4.24, d (13.2)	4.33, d (13.2)	4.25, d (13.3)	4.56, d (11.8)
14′	0.83, s	0.98, s	0.99, s	1.02, s	0.84, s	0.91, s
15′a	4.30, d (11.7)	3.45, brs (2H)	4.05, brs (2H)	4.09, d (11.1)	4.04, m (2H)	4.91, d (11.6)
15′b	3.62, d (11.7)			4.03, d (11.1)		3.66, d (11.6)
2″					2.05, s	
3″	6.55, m		6.97, m	6.90, m		6.62, t (5.3)
4″a	4.95, dd (14.4, 4.6)		1.81, d (7.2)	1.79, d (7.1)		4.82, dd (14.2, 4.9)
4″b	4.57, dd (14.4, 7.6)					4.64, dd (14.2, 7.0)
5″	1.86, s		1.86, s	1.81, s		1.89, s
7″a	2.70, m					2.65, m
7″b	2.74, m					2.45, m
8″a	2.43, m					2.62, m
8″b	2.97, m					2.55, m
−OMe	3.59, s		3.42, s			3.39, s

[a] Recorded on 400 MHz. [b] Measured in $CDCl_3$. [c] Measured in CD_3OD. [d] Recorded on 500 MHz.

type sesquiterpenoid dimer with an 18-membered macrocyclic triester ring, as shown, and this compound has been named chloramultiol A.

Chloramultiol B (**2**) was obtained as a yellow powder, and its molecular formula was determined as $C_{30}H_{34}O_{10}$, with 14 degrees of unsaturation, from the HRESIMS (*m/z* 577.2061 $[M + Na]^+$, calcd 577.2049). Detailed analysis of its IR, UV, and 1D and 2D NMR spectra suggested that compound **2** also possesses a lindenane-type sesquiterpenoid dimeric skeleton. Comparison of the NMR spectroscopic data of **2** (Tables 1 and 2) with those obtained for chloramultilide D[10] indicated these to be closely comparable. The only difference was that the tigloyl group in chloramultilide D[10] was absent in **2**. Accordingly, the structure of **2** was established as shown.

Chloramultiols C and D (**3** and **4**) were obtained as yellow powders. They displayed similar NMR spectroscopic data to those obtained for chloramultilide D,[10] which suggested they have similar structures. The molecular formula, $C_{36}H_{42}O_{11}$, was assigned to compound **3** on the grounds of its HRESIMS at *m/z* 673.2603 $[M + Na]^+$ (calcd 673.2624). Compound **3** was determined to be the 8-*O*-methyl derivative of chloramultilide D.[10] Thus, an additional methoxy group was evident from the NMR data and mass spectrum of **3**, and the signal of C-8 at δ_C 104.7 in chloramultilide D[10] was shifted downfield to δ_C 106.8 in **3**, while the methoxy protons (δ_H 3.42) exhibited a correlation to the C-8 acetal carbon (δ_C 106.8) in the HMBC spectrum (see Figure 2). The molecular formula of **4** was determined to be $C_{35}H_{38}O_{11}$ by HRESIMS at *m/z* 657.2311 $[M + Na]^+$ (calcd 657.2311). The most notable differences between **4** and chloramultilide D[10] were the absence of one oxymethine group and the presence of a ketone carbonyl (δ_C 201.4) in **4**, by comparison of their NMR spectroscopic data (Tables 1 and 2). A ketone carbonyl group could be proposed at C-9 from the correlations from H-1 (δ_H 2.20) and Me-14 (δ_H 1.14) to C-9 (δ_C 201.4) in the HMBC spectrum. In a ROESY experiment of **3**, the correlation of the methoxy group with H-9 indicated that the methoxy group is α-configured. Other ROESY correlations observed in **3** and **4** were identical with those found in chloramultilide D.[10] As a result, the structures of compounds **3** and **4** were established as shown.

Chloramultiol E (**5**) was isolated as a yellow powder. The HRESIMS at *m/z* 603.2191 $[M + Na]^+$ (603.2206) revealed a quasimolecular ion consistent with molecular formula of $C_{32}H_{36}O_{10}$. The NMR data of **5** (Tables 1 and 2) showed the compound to be related to **2**, with major differences being the absence of an oxygenated quaternary carbon and the appearance of a methine and an additional acetyl group. The methine was at C-4′, as evidenced by the $^1H-^1H$ COSY correlations of H-4′/H-3′, H-4′/H-5′, and H-4′/H_2-15′, and HMBC correlations of C-4′ with H-1′, H_2-6′, and H_2-15′. Further, HMBC correlations from H_2-15′ to the acetate carbonyl (C-1″) indicated that the acetoxy group is attached at C-15′. The ROESY correlation of H-3′ with H_2-15′ suggested a β-oriented H-4′. Therefore, the structure of compound **5** was established as shown.

The molecular formula of chloramultiol F (**6**), $C_{40}H_{42}O_{13}$, was established by the HRESIMS at *m/z* 753.2514 $[M + Na]^+$ (753.2523), which was less than that of spicachlorantin B[16] by a H_2O unit. The ^1H and ^{13}C NMR spectra for **6** were similar to those of spicachlorantin B,[16] with differences being in that a double bond between C-4 (δ_C 138.2) and C-15 (δ_C 120.8) occurred in **6** instead of an oxygenated quaternary carbon and a methylene. The $^1H-^1H$ COSY correlation from H-15 (δ_H 6.13) to H-9′ (δ_H 2.57), and the HMBC correlations of H-15 (δ_H 6.13) with C-3 (δ_C 23.9), C-5 (δ_C 156.1), C-6 (δ_C 115.2), C-8′ (δ_C 85.6), C-9′ (δ_C 56.1), and C-10′ (δ_C 48.1) confirmed the above deduction. ROESY correlations suggested the same relative configuration as that of spicachlorantin B.[16] Consequently, the structure of compound **6** was assigned as shown.

The cytotoxic activities of the 12 compounds were evaluated against 5 tumor cell lines (A-549, HL-60, PANC-1, SMMC-7721,

Table 2. ^{13}C NMR Spectroscopic Data for Chloramultiols A−F (**1**−**6**)

position	**1**[a,b]	**2**[a,c]	**3**[a,c]	**4**[a,c]	**5**[a,c]	**6**[b,d]
1	25.5, CH	29.5, CH	29.8, CH	25.3, CH	29.6, CH	28.1, CH
2	16.1, CH_2	9.5, CH_2	10.0, CH_2	9.7, CH_2	9.5, CH_2	14.2, CH_2
3	23.3, CH	31.4, CH	31.5, CH	32.0, CH	31.4, CH	23.9, CH
4	144.3, qC	79.9, qC	78.3, qC	78.0, qC	78.7, qC	138.2, qC
5	136.8, qC	164.6, qC	164.6, qC	161.1, qC	164.3, qC	156.1, qC
6	40.6, CH	124.7, qC	124.2, qC	124.8, qC	124.7, qC	115.2, qC
7	132.3, qC	155.2, qC	153.4, qC	152.3, qC	155.3, qC	124.9, qC
8	200.9, qC	105.0, qC	106.8, qC	96.8, qC	105.2, qC	106.3, qC
9	79.3, CH	78.7, CH	76.6, CH	201.4, qC	79.1, CH	73.4, CH
10	51.1, qC	51.0, qC	51.1, qC	58.0, qC	51.0, qC	49.5, qC
11	146.3, qC	124.9, qC	126.0, qC	128.9, qC	124.8, qC	152.8, qC
12	170.1, qC	173.3, qC	173.1, qC	172.7, qC	173.5, qC	171.4, qC
13	19.7, CH_3	10.7, CH_3	10.8, CH_3	11.5, CH_3	10.6, CH_3	10.6, CH_3
14	15.0, CH_3	14.1, CH_3	14.4, CH_3	21.7, CH_3	14.1, CH_3	15.0, CH_3
15	64.6, CH	41.8, CH_2	41.5, CH_2	41.5, CH_2	41.3, CH_2	120.8, CH
1′	24.8, CH	27.6, CH	27.9, CH	27.9, CH	26.8, CH	25.2, CH
2′	11.4, CH_2	11.0, CH_2	11.1, CH_2	11.0, CH_2	16.8, CH_2	11.0, CH_2
3′	27.6, CH	30.1, CH	30.1, CH	30.1, CH	30.7, CH	28.7, CH
4′	75.7, qC	78.9, qC	78.1, qC	78.4, qC	46.6, CH	77.4, qC
5′	59.0, CH	52.5, CH	53.8, CH	54.1, CH	52.6, CH	59.7, CH
6′	23.1, CH_2	22.2, CH_2	22.0, CH_2	22.9, CH_2	22.7, CH_2	23.1, CH_2
7′	174.4, qC	171.1, qC	170.9, qC	169.8, qC	170.8, qC	171.7, qC
8′	92.3, qC	87.0, qC	86.8, qC	87.0, qC	86.9, qC	85.6, qC
9′	62.1, CH	52.4, CH	51.9, CH	52.2, CH	51.4, CH	56.1, CH
10′	44.0, qC	45.7, qC	45.8, qC	45.9, qC	45.3, qC	48.1, qC
11′	123.1, qC	128.4, qC	128.7, qC	128.0. qC	128.2, qC	122.8, qC
12′	171.9, qC	174.7, qC	174.8, qC	174.5, qC	174.5, qC	174.6, qC
13′	54.1, CH_2	54.6, CH_2	54.5, CH_2	54.7, CH_2	54.7, CH_2	54.0, CH_2
14′	26.1, CH_3	24.6, CH_3	24.6, CH_3	24.6, CH_3	24.1, CH_3	25.0, CH_3
15′	72.7, CH_2	68.3, CH_2	70.7, CH_2	71.5, CH_2	67.5, CH_2	72.3, CH_2
1″	167.5, qC		169.5, qC	170.6, qC	173.2, qC	167.4, qC
2″	129.3, qC		129.7, qC	129.6, qC	21.0, CH_3	129.8, qC
3″	135.3, CH		139.2, CH	139.1, CH		136.0, CH
4″	61.5, CH_2		14.5, CH_3	14.5, CH_3		61.1, CH_2
5″	12.8, CH_3		12.3, CH_3	12.3, CH_3		12.9, CH_3
6″	171.9, qC					171.7, qC
7″	28.5, CH_2					28.9, CH_2
8″	29.1, CH_2					29.0, CH_2
9″	172.3, qC					172.2, qC
-OMe	52.3, CH_3		52.5, CH_3			51.8, CH_3

[a] Recorded on 100 MHz. [b] Measured in $CDCl_3$. [c] Measured in CD_3OD. [d] Recorded on 125 MHz.

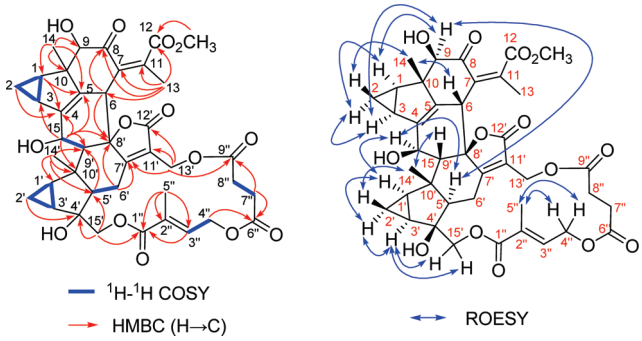

Figure 1. Selected 2D NMR correlations of **1**.

and SK-BR-3), in which cisplatin was used as the positive control. The results showed that none of the tested compounds had any discernible cytotoxic activity against these cell lines ($IC_{50} > 10\ \mu M$).

Experimental Section

General Experimental Procedures. Optical rotations were taken on a Horiba SEAP-300 polarimeter. UV spectra were obtained on a Shimadzu UV-2401PC spectrophotometer. IR spectra were measured with a Bio-Rad FTS-135 spectrometer with KBr pellets. NMR spectra were run on Bruker AM-400 and DRX-500 instruments. Chemical shifts (δ) were expressed in parts per million (ppm) with reference to the solvent signals. FABMS were recorded on a VG Auto Spec-300 spectrometer, and ESIMS and HRESIMS were performed on an API QSTAR time-of-flight spectrometer. Semipreparative high-performance liquid chromatography (HPLC) was performed on an Agilent 1100 liquid chromatograph with a Zorbax SB-C_{18} (9.4 mm × 25 cm) column. Column chromatography was performed either on silica gel (200−300 mesh, Qindao Marine Chemical Inc., Qingdao, People's Republic of China) or RP-18 gel (LiChroprep, 40−63 μm, Merck, Darmstadt, Germany). Sephadex LH-20 for size-exclusion chromatography was purchased from Amersham Biosciences. Fractions were monitored by thin layer chromatography (TLC), and spots were detected with a UV_{254} lamp and by spraying with 10% H_2SO_4 in EtOH followed by heating at 120 °C for 5 min.

Plant Material. The whole plants of *C. multistachys* were collected in August 2007 from Xinning County, Hunan Province, People's Republic of China, and identified by Dr. En-De Liu of Kunming Institute of Botany. A voucher specimen (No. HY0001) has been deposited at the State Key Laboratory of Phytochemistry and Plant Resources in West China.

Extraction and Isolation. Dried and powered whole plants of *C. multistachys* (20 kg) were extracted three times with MeOH under reflux. The filtrate was evaporated under reduced pressure to give a residue, which was suspended in water and partitioned successively with EtOAc and *n*-BuOH. These two extracts were concentrated in vacuo to afford residues of EtOAc (1300 g) and *n*-BuOH (100 g), respectively. The EtOAc extract was subjected to passage over a column containing MCI gel, eluted with MeOH−H_2O mixtures in a gradient (3:7 → 5:5 → 7:3 → 1:0). The 70% MeOH fraction (130 g, a major fraction containing the sesquiterpenoid dimers) was chromatographed over a silica gel column eluted with petroleum ether−acetone (10:1 → 5:1 → 2:1 → 1:1) to yield seven fractions, A−G. Fraction B (13.6 g) was subjected to column chromatography over a RP-18 column eluted with a MeOH−H_2O gradient system (30%, 40%, 50%, and 60%) to obtain six fractions, B1−B5. Fraction B2 was purified further on a

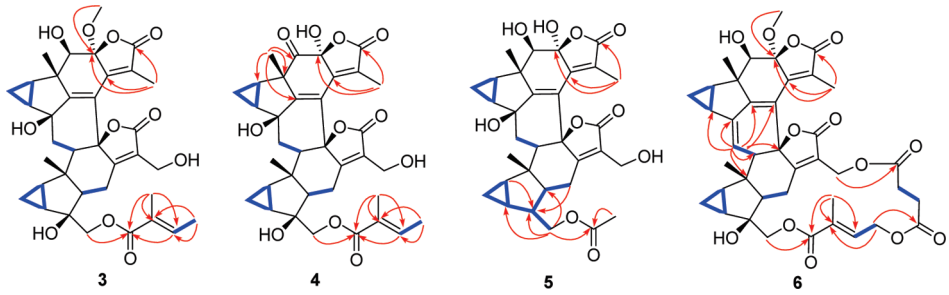

Figure 2. Selected HMBC (red →) and ^{1}H−^{1}H COSY (blue —) correlations of **3**−**6**.

Sephadex LH-20 (MeOH) column to yield cycloshizukaol A (30 mg) and compound **6** (13 mg). Compound **1** (14 mg) and spicachlorantin B (35 mg) were afforded from fraction B3 by column chromatography over silica gel using petroleum ether−acetone (10:1 → 8:1 → 5:1 → 3:1). Fraction B5 was then subjected to column chromatography over silica gel eluted with petroleum ether−acetone (10:1 → 5:1 → 3:1 → 2:1) and purified on a Sephadex LH-20 (MeOH) column to provide shizukaol C (56 mg) and shizukaol D (70 mg). Fraction C (20.8 g) was chromatographed over a silica gel column using petroleum ether−acetone (8:1 → 6:1 → 3:1 → 1:1) as the eluent to provide fractions C1−C4. Fraction C2 was purified by semipreparative HPLC (CH_3CN-H_2O, 35:65; flow rate, 3 mL/min) to afford **3** (15 mg; t_R = 6.34 min) and **4** (11 mg; t_R = 8.08 min). Chloramultilide C (1.2 g) was crystallized from a MeOH solution of fraction C3. Fraction D (15.0 g) was subjected to column chromatography over silica gel using petroleum ether−acetone (8:1 → 5:1 → 2:1 → 1:1) to produce fractions D1−D4. Compound **5** (36 mg) and chloramultilide D (48 mg) were obtained from fraction D3 by column chromatography over a silica gel column eluted with $CHCl_3$−MeOH (80:1). Fraction F was also separated and purified by repeated silica gel column chromatography with $CHCl_3$−MeOH (50:1), to give compound **2** (16 mg).

Chloramultiol A (1): yellow powder; $[\alpha]_D^{20}$ −53.3 (*c* 0.12, MeOH); UV (MeOH) λ_{max} (log ε) 218 (4.37) nm; IR (KBr) ν_{max} 3443, 2930, 2855, 1738, 1609, 1438, 1369, 1270, 1160 cm^{-1}; ^{1}H NMR data ($CDCl_3$, 400 MHz), see Table 1; ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 2; positive ESIMS *m/z* 771 $[M + Na]^+$; positive HRESIMS *m/z* 771.2633 $[M + Na]^+$ (calcd for $C_{40}H_{44}O_{14}Na$, 771.2628).

Chloramultiol B (2): yellow powder; $[\alpha]_D^{20}$ −4.7 (*c* 0.15, MeOH); UV (MeOH) λ_{max} (log ε) 224 (4.22) nm; IR (KBr) ν_{max} 3418, 2937, 2879, 1750, 1633, 1440, 1383.4, 1251, 1011 cm^{-1}; ^{1}H NMR data (CD_3OD, 400 MHz), see Table 1; ^{13}C NMR (CD_3OD, 100 MHz), see Table 2; positive ESIMS *m/z* 577 $[M + Na]^+$; positive HRESIMS *m/z* 577.2061 $[M + Na]^+$ (calcd for $C_{30}H_{34}O_{10}Na$, 577.2049).

Chloramultiol C (3): yellow powder; $[\alpha]_D^{20}$ −26.9 (*c* 0.22, MeOH); UV (MeOH) λ_{max} (log ε) 218 (4.37) nm; IR (KBr) ν_{max} 3439, 2925, 1757, 1632, 1384, 1268, 1021 cm^{-1}; ^{1}H NMR data (CD_3OD, 400 MHz), see Table 1; ^{13}C NMR (CD_3OD, 100 MHz), see Table 2; positive fast atom bombardment (FAB)MS *m/z* 651 $[M + H]^+$; HRESIMS *m/z* 673.2603 $[M + Na]^+$ (calcd for $C_{36}H_{42}O_{11}Na$, 673.2624).

Chloramultiol D (4): yellow powder; $[\alpha]_D^{20}$ +34.1 (*c* 0.05, MeOH); UV (MeOH) λ_{max} (log ε) 220 (4.44) nm; IR (KBr) ν_{max} 3441, 2925, 1630, 1383, 1269, 1024 cm^{-1}; ^{1}H NMR data (CD_3OD, 400 MHz), see Table 1; ^{13}C NMR (CD_3OD, 100 MHz), see Table 2; positive ESIMS *m/z* 657 $[M + Na]^+$; HRESIMS *m/z* 657.2311 $[M + Na]^+$ (calcd for $C_{35}H_{38}O_{11}Na$, 657.2311).

Chloramultiol E (5): yellow powder; $[\alpha]_D^{20}$ −31.2 (*c* 0.31, MeOH); UV (MeOH) λ_{max} (log ε) 221 (4.14) nm; IR (KBr) ν_{max} 3432, 2938, 1750, 1383, 1263, 1011 cm^{-1}; ^{1}H NMR data (CD_3OD, 400 MHz), see Table 1; ^{13}C NMR (CD_3OD, 100 MHz), see Table 2; positive ESIMS *m/z* 603 $[M + Na]^+$; HRESIMS *m/z* 603.2191 $[M + Na]^+$ (calcd for $C_{32}H_{36}O_{10}Na$, 603.2206).

Chloramultiol F (6): yellow powder; $[\alpha]_D^{20}$ +69.2 (*c* 0.10, MeOH); UV (MeOH) λ_{max} (log ε) 222 (4.58); IR (KBr) ν_{max} 3442, 2939, 1759, 1632, 1383, 1256, 1155, 1014 cm^{-1}; ^{1}H NMR data (CD_3OD, 500 MHz), see Table 1; ^{13}C NMR (CD_3OD, 125 MHz), see Table 2; positive ESIMS *m/z* 753 $[M + Na]^+$; HRESIMS *m/z* 753.2514 $[M + Na]^+$ (calcd for $C_{40}H_{42}O_{13}Na$, 753.2523).

Cytotoxicity Bioassays. Cytotoxicity of compounds against A-549 (human lung adenocarcinoma), HL-60 (human promyelocytic leukemia), PANC-1 (human pancreatic carcinoma, epithelial-like), SMMC-7721 (human hepatocellular carcinoma), and SK-BR-3 (human breast carcinomas) cells was determined by the MTT assay.[18] Cisplatin was used as the positive control antitumor drug and exhibited IC_{50} values for the cell lines of 11.8, 1.6, 14.4, 13.6, and 19.9 μM, respectively.

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Supporting Information Available: NMR spectra of chloramultiols A−F (**1**−**6**). This material is available free of charge via the Internet at http://pubs.acs.org.

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