Sesquiterpenoids and Phenylpropanoids from Pericarps of *Illicium oligandrum*

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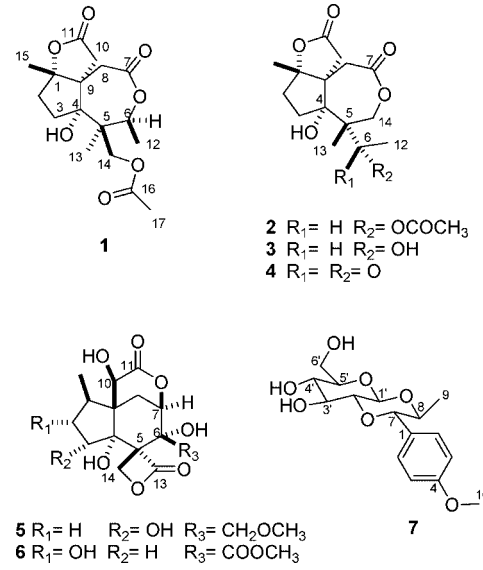
Four new merrillianin-type sesquiterpenes, oligandrumins A−D (**1**−**4**), two new *seco*-prezizaane-type sesquiterpenes, veranisatins D and E (**5** and **6**), and a new phenylpropane glycoside, oligandrumin E (**7**), were isolated from the ethanol extract of pericarps of *Illicium oligandrum*, together with six known sesquiterpenoids and two phenylpropanoids. Their structures were established on the basis of extensive spectroscopic analyses. The structures of **1** and **2** were further confirmed by single-crystal X-ray diffraction experiments. Anislactone B (**13**) and the *erythro* form of anethole glycol (**14**) were shown to attenuate the damage induced by H_2O_2 in SH-SY5Y cells.

Illicium plants (Magnoliaceae) are rich in *seco*-prezizaane-type sesquiterpenes.[1−3] These sesquiterpenes were reported to exhibit diverse biological activities including neurotoxic and neurotrophic effects.[3,4] *seco*-Prezizaane-type sesquiterpenes are classified into six subtypes: anisatin, pseudoanisatin, majucin, pseudomajucin, minwanensin, and cycloparvifloralone subtypes.[5] A new subtype sesquiterpene, merrillianin, with a dilactone moiety was found in 2002.[6]

Structural and biological diversity of *seco*-prezizaane-type sesquiterpenes prompted us to investigate *Illicium oligandrum*, a plant distributed in Hainan and Guangxi Provinces, China. Previous study on the fruits of this plant revealed the occurrence of sesquiterpene lactones and neolignan glycosides.[7] In this paper, we describe the isolation and structural elucidation of four new merrillianin-type sesquiterpenes (**1**−**4**, named oligandrumins A−D), two new *seco*-prezizaane-type sesquiterpenes (**5** and **6**, named veranisatins D and E), and a new phenylpropane glycoside, oligandrumin E (**7**), from the pericarps of *I. oligandrum*. Six known sesquiterpenes, anisatin (**8**),[8] pseudoanisatin (**9**),[9] 2α-hydroxyneoanisatin (**10**),[10] 1α-hydroxy-3-deoxypseudoanisatin (**11**),[11] pseudomajucin (**12**),[12] and anislactone B (**13**),[13] as well as two phenylpropanoid compounds, *erythro* and *threo* forms of anethole glycol (**14**, **15**),[14] were also separated and identified (see Supporting Information for structures of compounds **8**−**15**). The neuroprotective properties of some isolates were assessed against H_2O_2-induced SH-SY5Y cell damage.



Results and Discussion

Compound **1** had the molecular formula $C_{17}H_{24}O_7$ as established by HREIMS (*m/z* 340.1527, calcd 340.1522), requiring six degrees of unsaturation. The ^{13}C NMR and DEPT spectra (Table 1) exhibited 17 resonances including four methyl, five methylene, one methine, and seven quaternary carbons. Resonances at δ_C 174.9, 173.0, and 170.6 suggested the presence of three ester carbonyl groups, which was also supported by the IR absorption bands at 1782, 1738, and 1728 cm^{-1}. The presence of an OH group was deduced from the IR absorption band at 3566 cm^{-1}. Lack of an olefinic functionality required the presence of three rings to satisfy the degrees of unsaturation. The ^1H NMR spectrum (Table 2) showed the signals of four methyl groups at δ_H 1.25 (s), 1.50 (d, $J = 6.5$ Hz), 1.70 (s), and 2.00 (s) and three hydromethine protons at δ_H 4.90 (1H, q, $J = 6.5$ Hz), 4.70 (1H, d, $J = 11.8$ Hz), and 4.20 (1H, d, $J = 11.8$ Hz). Detailed analyses of the 1D and 2D NMR spectra indicated the structure of **1** (Figure 1) and allowed assignment of all proton and carbon signals. HMBC correlations from H_3-15 to C-2 and C-9, from H_2-2 to C-4, and from H_2-3 to C-1 are indicative of a five-membered carbon ring. The HMBC correlations from H_2-8 to C-4, C-7, and C-9, as well as from H-6 to C-4 and C-7, indicated a seven-membered lactone ring, which was deduced to be fused at C-4 and C-9 of the five-membered ring. This conclusion was supported by the key long-range correlation of H-8/C-1. The doublet methyl at δ_H 1.50, coupled with H-6, was attached to the oxygenated carbon C-6 (δ_C 80.4). The singlet methyl at δ_H 1.25, showing HMBC correlation to C-5, and the oxymethylene at δ_H 4.70 and 4.20 correlating to C-6 suggested that they were both located at C-5. An acetoxyl group was placed at C-14 according to the HMBC correlations from H_3-17 and H_2-14 to C-16 (δ_C 170.6). The remaining ester carbonyl group, combined with a methylene, formed a five-membered lactone ring with C-1 and C-9. This assignment was supported by the downfield shift of C-1 (δ_C 97.1) and HMBC correlations from H_2-10 to C-1, C-4, and C-11.

A ROESY correlation observed between H_3-15β and H-8b (δ_H 2.95, d, $J = 14.3$ Hz) revealed that H-8b was β-oriented, while H-8a (δ_H 3.60, d, $J = 14.3$ Hz) was α-oriented. The ROESY correlations of H-8a/H-6, H-6/H_3-13, and H_3-13/H-10a (δ_H 3.40, d, $J = 16.8$ Hz) indicated α-orientations of H-6, CH_3-13, and H-10a. Thus, CH_3-12, CH_2-14, and H-10b (δ_H 2.70, d, $J = 16.8$ Hz) were all β-oriented. Therefore, the structure of **1** was established. The structure was confirmed by an X-ray diffraction experiment (Figure 2).

The molecular formula of **2** was determined to be $C_{17}H_{24}O_7$ by HREIMS (*m/z* 340.1525, calcd 340.1522) and supported by ^{13}C NMR and DEPT data. The IR absorption bands at 1755, 1736, and

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Table 1. ^{13}C NMR Data of Compounds **1**−**6** (100 MHz, δ in ppm)

no.	**1**[a]	**2**[b]	**3**[b]	**4**[b]	**5**[c]	**6**[c]
1	97.1 qC	99.3 qC	99.5 qC	98.7 qC	37.5 CH	49.3 CH
2	36.2 CH_2	35.9 CH_2	36.0 CH_2	35.1 CH_2	41.7 CH_2	78.1 CH
3	36.2 CH_2	34.0 CH_2	34.8 CH_2	34.1 CH_2	71.1 CH	42.6 CH_2
4	86.1 qC	88.2 qC	88.5 qC	88.7 qC	85.0 qC	85.0 qC
5	48.0 qC	50.1 qC	50.3 qC	57.8 qC	62.1 qC	62.8 qC
6	80.4 CH	72.6 CH	69.1 CH	215.3 qC	78.1 qC	79.8 qC
7	173.0 qC	175.5 qC	176.5 qC	174.1 qC	78.5 CH	78.1 CH
8	36.2 CH_2	37.8 CH_2	37.9 CH_2	37.1 CH_2	26.7 CH_2	26.8 CH_2
9	57.4 qC	56.3 qC	54.6 qC	56.4 qC	51.1 qC	52.1 qC
10	39.5 CH_2	38.2 CH_2	38.1 CH_2	37.4 CH	70.0 CH	69.5 CH
11	174.9 qC	178.4 qC	179.1 qC	177.6 qC	173.8 qC	173.7 qC
12	16.8 CH_3	18.7 CH_3	21.2 CH_3	28.5 CH_3	75.3 CH_2	169.3 qC
13	18.7 CH_3	16.1 CH_3	15.9 CH_3	19.5 CH_3	167.7 qC	167.7 qC
14	66.3 CH_2	71.1 CH_2	71.5 CH_2	69.9 CH_2	63.8 CH_2	64.9 CH_2
15	21.9 CH_3	21.7 CH_3	25.0 CH_3	24.8 CH_3	13.2 CH_3	11.0 CH_3
16	170.6 qC	172.1 qC			59.9 CH_3	52.8 CH_3
17	24.9 CH_3	25.0 CH				

[a] In C_5D_5N. [b] In CD_3OD. [c] In CD_3COCD_3.

Table 2. ^1H NMR Data of Compounds **1**−**6** (300 MHz, δ in ppm, J in Hz)

no.	**1**[a]	**2**[b]	**3**[b]	**4**[b]	**5**[c]	**6**[c]
1					2.54, m	2.40, q (6.9)
2a	2.20, m	2.50, m	2.30, m	2.40, m	2.00, m	4.15, dd (8.9, 6.9)
2b	1.90, m	2.10, m	1.90, m	1.90, m	1.75, ddd (12.9, 10.7, 4.4)	
3a	2.70, m	2.30, m	2.20, m	2.10, m	4.90, ddd (10.7, 6.5, 4.4)	2.85, dd (13.8, 8.9)
3b	2.50, m	1.90, m	1.85, m	1.95, m	4.65, d (OH, 6.5)	1.70, d (13.8)
4					5.40, s (OH)	
6	4.90, q (6.5)	5.10, q (6.5)	4.00, q (6.5)		5.95, d (OH, 1.5)	
7					4.25, dd (3.8, 1.9)	4.90, dd (3.7, 2.1)
8a	3.60, d (14.3)	3.00, d (13.2)	2.98, d (13.1)	3.05, d (13.2)	2.44, dd (14.6,1.9)	2.60, dd (14.8, 2.1)
8b	2.95, d (14.3)	2.50, d (13.2)	2.53, d (13.1)	2.80, d (13.2)	2.13, dd (14.6, 3.8)	2.20, dd (14.8, 3.7)
10a	3.40, d (16.8)	2.73, d (17.8)	3.05, d (17.6)	3.25, d (18.0)	4.30, d (3.4)	4.28, s
10b	2.70, d (16.8)	2.68, d (17.8)	2.60, d (17.6)	2.75, d (18.0)	5.25. d (OH, 3.4)	
12	1.50, d (6.5)	1.43, d (6.5)	1.40, d (6.5)	2.50, s	4.00, dd (11.0, 1.5)	
					3.58, d (11.0)	
13	1.25, 3H, s	1.00, 3H, s	0.90, 3H, s	1.58, 3H, s		
14a	4.70, d (11.8)	4.35, d (13.4)	4.30, d (13.6)	4.65, d (14.3)	4.36, d (6.6)	4.30, d (6.2)
14b	4.20, d (11.8)	3.95, d (13.4)	4.10, d (13.6)	4.55, d (14.3)	4.05, d (6.6)	4.05, d (6.2)
15	1.70, 3H, s	1.39, 3H, s	1.40, 3H, s	1.60, 3H, s	1.00, d (7.0)	1.15, d (7.4)
16					3.40, 3H, s	3.82, 3H, s
17	2.00, 3H, s	2.05, 3H, s				

[a] In C_5D_5N. [b] In CD_3OD. [c] In CD_3COCD_3.

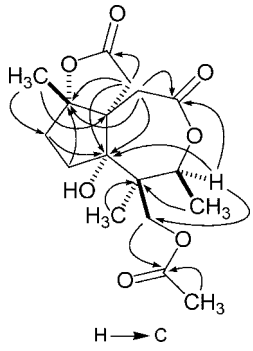

Figure 1. Key HMBC correlations of **1**.

1712 cm^{-1}, combined with three low-field carbon resonances (δ_C 178.4, 175.5, and 172.1), suggested the presence of three ester carbonyl groups. The ^{13}C NMR and DEPT spectra of **2** (Table 1) showed 17 resonances, including four methyl, five methylene, one methine, and seven quaternary carbons. The ^1H NMR spectrum (Table 2) had two methyl singlets (δ_H 1.00 and 1.39), a doublet methyl at δ_H 1.43 (3H, J = 6.5 Hz), an acetoxyl methyl (δ_H 2.05), an oxymethylene at δ_H 4.35 (1H, J = 13.4 Hz) and 3.95 (1H, J = 13.4 Hz), two methylenes at δ_H 3.00 (1H, J = 13.2 Hz), 2.50 (1H, J = 13.2 Hz), 2.73 (1H, J = 17.8 Hz), and 2.68 (1H, J = 17.8 Hz), and an oxymethine at δ_H 5.10 (1H, q, J = 6.5 Hz). The ^1H and ^{13}C NMR data of **2** were similar to those of **1**. However, the carboxyl carbon C-7 (δ_C 175.5) in **2** showed HMBC correlations with one methylene at δ_H 3.00 and 2.50 (H-8) and another oxymethylene at δ_H 4.35 and 3.95, while C-7 (δ_C 173.0) in **1** correlated to one methylene (H-8) and one oxymethine (H-6). Similarly, the carboxyl carbon C-16 (δ_C 172.1) in **2** showed HMBC correlations with one oxymethine (1H, q, J = 6.6 Hz), while C-16 (δ_C 170.6) in **1** correlated to one oxymethylene (H-14). These evidence indicated that a methylene instead of a methine was placed in the seven-membered ring in **2**. The relative configuration of **2** was inferred from the ROESY experiment. ROESY correlations of H_3-15β/H-8a, H_3-15β/H-8b, H-8a/H-3a, H-8a/H-14a, H-3a/H-14a, H-6/H-10b, and H-10b/H_3-12 suggested that CH_3-15, H-8a, H-3a, and H-14a were on the same face and all β-oriented, while H-10b, H-6, and CH_3-12 were on the other face. The ROESY correlation of H_3-13 and H-3b further indicated that CH_3-13 was β-oriented, opposite that in **1**. The structure of **2** including the *S**-configuration of C-6 was finally determined by X-ray diffraction experiment (Figure 3).

Compound **3** had the molecular formula $C_{15}H_{22}O_6$ as confirmed by HREIMS (m/z 298.1426, calcd 298.1416). Its IR absorption bands at 3373 and 1732 cm^{-1} indicated the presence of OH and carbonyl groups. The NMR data of **3** resembled those of **2** except for the absence of the acetyl group. The relative configuration of **3** was determined to be the same as that of **2** by a ROESY experiment.

The molecular formula $C_{15}H_{20}O_6$ of **4** was inferred from the HREIMS, two protons less than that of **3**. The presence of an OH

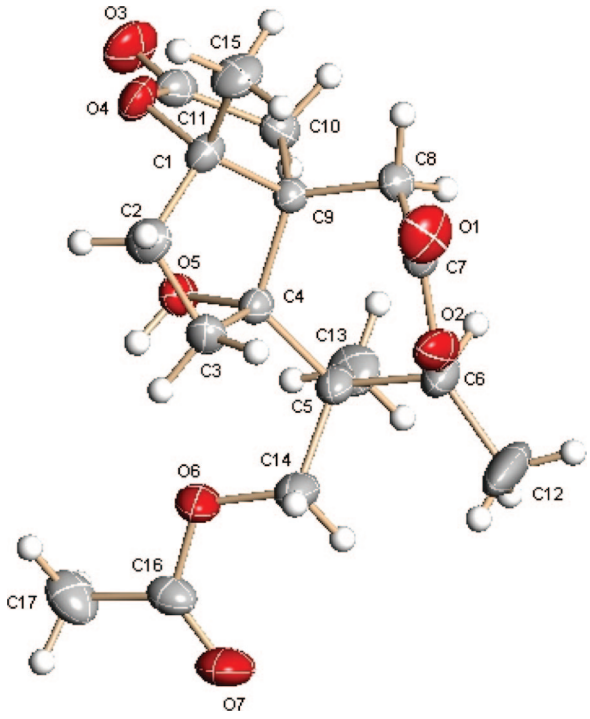

Figure 2. Perspective ORTEP drawing for **1**.

group was supported by the IR absorption band at 3413 cm^{-1}. In comparison with the NMR data of **3**, the absence of the oxymethine at C-6 and the existence of an additional carbonyl resonance at δ_C 215.3 suggested that a carbonyl C-6 was present in **4**. The relative configuration was determined to be the same as that of **3** by a ROESY experiment.

Compound **5** had the molecular formula $C_{16}H_{22}O_9$ on the basis of its HREIMS (*m*/*z* 358.1264, calcd 358.1264). The IR spectrum showed the presence of OH (3570, 3510, 3427, and 3363 cm^{-1}), β-lactone (1834 cm^{-1}), and δ-lactone (1821 cm^{-1}) groups. The NMR data of **5** were similar to those of veranisatin A,[15] except that a methylene in veranisatin A was replaced by an oxygenated methine at δ_H 4.90 (1H, ddd, J = 10.7, 6.5, 4.4 Hz) in **5**. Thus, **5** was suggested to be an OH derivative of veranisatin A. The active proton of this OH group [δ_H 4.65 (1H, d, J = 6.5 Hz)] showed HMBC correlations to C-2 and C-4, suggesting that this OH group was located at C-3. The relative configuration of **5** was determined by the ROESY experiment. A cross-peak of H_3-15β/H-8b suggested that H-8b was β-oriented; thus the configuration of H-8a was α. Correlations of H-8a/H-7 and H-8a/OH-6 revealed that H-7 and OH-6 were both α-oriented and CH_3-12 was β-oriented. Correlations of H-14b/H-12b and H-14b/CH_3-16 indicated H-14b and CH_3-12 were on the same face. The β-orientation of H-3 was assigned by the key ROESY cross-peak of H-3/H-14a. Thus, **5** was established as 3α-hydroxyveranisatin A.

Compound **6** possessed the molecular formula $C_{16}H_{20}O_{10}$ as established by HRESIMS. The IR spectrum showed the presence of OH (3531, 3385, and 3213 cm^{-1}) and carbonyl groups (1807, 1761, and 1743 cm^{-1}). Analysis of the NMR data of **6** indicated that the structure of **6** was similar to that of 2α-hydroxyneoanisatin.[10] The ^1H NMR spectrum of **6** indicated an OCH_3 group (δ_H 3.82) that showed an HMBC correlation to a carbonyl carbon at δ_C 169.3 in the ^{13}C NMR. The downfield shift of H-7 [δ_H 4.90 (1H, dd, J = 3.7, 2.1 Hz)] suggested that the carbonyl ester moiety was substituted at C-6.[15] The relative configuration of **6** was inferred from the ROESY experiment, the same as that of 2α-hydroxyneoanisatin.

Compound **7** had the molecular formula $C_{16}H_{22}O_7$ (HREIMS). The IR spectrum showed OH (3443 cm^{-1}) and conjugated carbons (1614 cm^{-1}). In the ^1H NMR spectrum (Table 3, **7** in C_5D_5N), aromatic signals at δ_H 7.40 (2H, d, J = 8.8 Hz) and 7.01 (2H, d, J = 8.8 Hz) suggested the presence of a 1,4-disubstituted aromatic ring, which was confirmed by four tertiary resonances at δ_C 129.7 and 114.2 and two quaternary resonances at δ_C 160.2 and 130.8 in the ^{13}C NMR spectrum (Table 3). Signals assignable to protons of a 1,2-dioxygenated propanyl group were observed at δ_H 4.32 (1H, d, J = 9.3 Hz, H-7), 3.95 (1H, m, H-8), and 1.00 (3H, d, J = 6.6 Hz, H-9), as well as a methoxy group at δ_H 3.80 (3H, s, OCH_3-10) that was placed at C-4 by the HMBC correlations from OCH_3-10 to C-4 and a β-glucosyl group with the anomeric proton signal resonating at δ_H 4.90 (1H, d, J = 7.3 Hz, H-1′). Chemical shifts of the glucosidic carbons C-4′ (δ_C 71.8), C-5′ (δ_C 80.3), and C-6′ (δ_C 62.6) were in accordance with a β-glucosyl moiety, which was confirmed by the TOCSY experiment. The linkage of C-7 and C-1 between the propanyl chain and the aromatic ring was established by HMBC correlations of H-7 with C-2, C-6, and C-9. The HMBC correlations of H-1′/C-8, H-2′/C-7, H-7/C-1′ (δ_C 99.4), and H-8/C-2′ (δ_C 81.2) revealed that the glucosyl moiety was connected to the propane chain by etherification at C-1′ and C-2′. Thus **7** was a phenylpropanoid glucoside similar to junipetrioloside A.[16] The relative configuration of **7** was deduced by coupling constants.[17] The large coupling constants (**7** in CD_3OD) between H-7/H-8 (9.2 Hz), H-1′/H-2′ (7.7 Hz), H-2′/H-3′ (9.7 Hz), H-3′/H-4′ (8.5 Hz), and H-4′/H-5′(9.5 Hz) (Table 3) suggested that the relationship of those protons were all *trans*-axial and the two six-membered rings were both in chair conformations.

The neuroprotective effects of some isolated compounds on H_2O_2-induced decrease in cell survival were evaluated in SH-SY5Y cells according to the reported protocol with modification.[18] The results showed that 2 h pretreatment of compounds **7**, **11**, **12**, **13**, and **14** could significantly attenuate SH-SY5Y cell damage induced by H_2O_2. Compounds **13** at 1 μM and **14** at 10 μM were the most effective, which could produce 12.55% and 7.29% increases in cell survival over the H_2O_2 group, respectively. Compounds **7** and **12** at 10 μM and **11** at 1 μM, causing 6.42%, 2.83%, and 2.76% increases in cell viability over the H_2O_2 group, respectively, exerted fewer beneficial effects. The positive control α-tocopherol (vitamin E) caused 7.16% increase in cell viability over the H_2O_2 group at 10 μM concentration.

In conclusion, oligandrumins A−D (**1**−**4**), four new merrillianin-type sesquiterpenes with a five-membered γ-lactone ring fused at C-1 and C-9, were isolated from *Illicium oligandrum*. Oligandrumin E (**7**) is the first phenylpropanoid glucoside from *Illicium oligandrum* whose glucosyl and phenylpropanyl moieties are connected by two ether bridges.

Experimental Section

General Experimental Procedures. Optical rotations were taken on a Perkin-Elmer 341 polarimeter. IR spectra were recorded on a Nicolet Magna FT-IR 750 spectrophotometer using KBr disks. NMR spectra were recorded on Bruker AM-400 and INVOR-600 NMR spectrometers. The chemical shift (δ) values are given in ppm with TMS as internal standard, and coupling constants (J) are in Hz. EIMS and HREIMS spectra were recorded on a Finnigan MAT-95 mass spectrometer. ESIMS and HRESIMS spectra were recorded on a Micromass LC-MS-MS mass spectrometer. Silica gel was used for flash chromatography and was produced by Qingdao Marine Chemical Industrials. TLC was carried out on precoated silica gel GF_{254} plates (Yantai Chemical Industrials), and the TLC spots were viewed at 254 nm and visualized by 5% sulfuric acid in alcohol containing 10 mg/mL vanillin. X-ray crystallographic analysis was carried out on a Bruker Smart Apex CCD diffractometer with graphite-monochromated Mo Kα radiation at λ = 0.71073 Å. Analytical HPLC was performed on a Waters 2690 instrument with a 996 photodiode array detector and coupled with an Alltech ELSD 2000 detector. Chromatographic separation was carried out on a C-18 column (250 × 10 mm, 5 μm, Waters), using a solvent system comprised of H_2O and CH_3CN, with a flow rate of 3 mL/min.

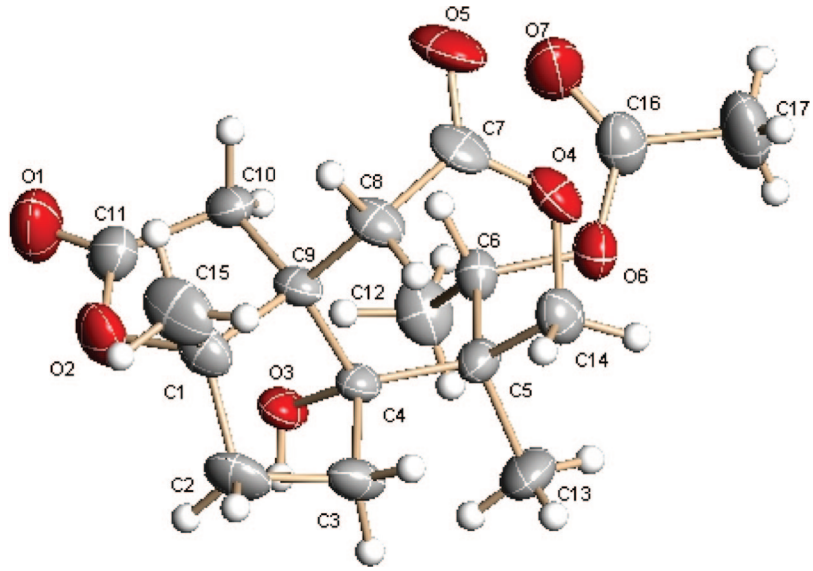

Figure 3. Perspective ORTEP drawing for **2**.

Table 3. ^{1}H and ^{13}C NMR Data of Compound **7** (δ in ppm, J in Hz)

no.	δ_C[a]	δ_H[b]	δ_H[c]
1	130.8 qC		
2	129.7 CH	7.01, d (8.8)	6.90, d (8.8)
3	114.2 CH	7.40, d (8.8)	7.30, d (8.8)
4	160.2 qC		
5	114.2 CH	7.40, d (8.8)	7.30, d (8.8)
6	129.7 CH	7.01, d (8.8)	6.90, d (8.8)
7	84.0 CH	4.32, d (9.3)	4.18, d (9.2)
8	76.8 CH	3.95, m	3.82, m
9	17.1 CH_3	1.00, 3H, d (6.6)	1.00, 3H, d (6.6)
10	55.2 CH_3	3.80, 3H, s	3.80, 3H, s
1′	99.4 CH	4.90, d (7.3)	4.55, d (7.7)
2′	81.2 CH	4.00, m	3.17, dd (9.7, 7.7)
3′	74.9 CH	4.25, m	3.57, dd (9.7, 8.5)
4′	71.8 CH	4.25, m	3.40, dd (9.5, 8.5)
5′	80.3 CH	4.00, m	3.47, ddd (9.5, 5.4, 2.0)
6′	62.6 CH_2	4.60, dd (11.8, 2.3)	3.90, dd (12.0, 5.4)
		4.40, dd (11.8, 5.4)	3.70, dd (12.0, 2.0)

[a] In C_5D_5N, at 100 MHz. [b] In C_5D_5N, at 400 MHz. [c] In CD_3OD, at 400 MHz.

Plant Material. Pericarps of *I. oligandrum* were collected in Guangxi Province, China, and were identified by Professor Jin-gui Shen. A voucher (20061223) was deposited at the herbarium of Shanghai Institute of Materia Medica, Chinese Academy of Sciences.

Extraction and Isolation. Air-dried pericarps of *I. oligandrum* (7.2 kg) were ground into powder and extracted with 95% EtOH. After evaporation of the collected percolate, the crude extract (520 g) was partitioned with petroleum ether (PE), CH_2Cl_2, EtOAc, and *n*-BuOH, respectively. The CH_2Cl_2 extract (51 g) was chromatographed on silica gel (100−200 mesh) eluting successively with PE/EtOAc (from 40:1 to 1:1), EtOAc, and MeOH to yield 10 fractions (A−J). Fraction D (8.2 g) was chromatographed on silica gel eluted with PE/EtOAc (from 12:1 to 1:1) to yield three subfractions (D1−D3). Subfraction D2 was further purified by MCI, Sephadex LH-20, and finally by preparative HPLC (H_2O/CH_3CN from 50:1 to 10:3) to yield **14** and **15** (90 and 126 mg, respectively). Fraction G (4.5 g) was purified by MCI with MeOH/H_2O (from 3:10 to 0:10) to yield six subfractions (1−6). Compounds **12** (110 mg), **9** (16 mg), and **11** (16 mg) were obtained from subfraction 1. Subfraction 3 was subjected to column chromatography (CC) over silica gel eluting with $CHCl_3$/MeOH (from 40:1 to 0:1) to give **1** (46 mg). Compound **3** (95 mg) was obtained as colorless cubic crystals from fraction H (350 mg), and the mother liquid was subjected to a silica gel column to afford **2** (50 mg). Fraction I was purified by MCI eluting with MeOH/H_2O (from 3:10 to 0:10) to yield five subfractions (1−5), and compound **7** (21 mg) was obtained from subfraction 3. The EtOAc fraction (43 g) was subjected to CC over silica gel and eluted with PE/EtOAc (5:1, 4:1, 3:1, 2:1, 1:1, 1:2), EtOAc, and MeOH to yield nine fractions (EA−EI). Compound **8** (145 mg) was isolated from fraction EC. Fraction ED was subjected to a silica gel column eluting with $CHCl_3$/MeOH (40:1) to yield eight subfractions (ED1−ED8). Veranisatin D (**5**) (385 mg) was obtained from subfraction ED4, and **13** (40 mg) was isolated from subfraction ED6. Fraction ED7 was purified by CC over MCI repeatedly and then by Sephadex LH-20 eluting with $CHCl_3$/MeOH (6:4) to give a mixture (11 mg) of **6** and **10**. This mixture was further separated by semi-preparative HPLC (H_2O/CH_3CN, 10:1) to afford **6** (3 mg) and **10** (5 mg). Fraction EH was subjected to silica gel eluting with $CHCl_3$/MeOH (200:1) to give seven subfractions (EH1−EH7). Compound **4** (12 mg) was obtained from subfraction EH4 (see Supporting Information for structures of compounds **8**−**15**).

Oligandrumin A (1): white needles (MeOH); mp 242−243 °C; $[\alpha]_D^{23}$ −30 (*c* 0.27, MeOH); IR (KBr) ν_{max} 3566, 1782, 1738, 1728, 1383, 1244, 1194, 1043, 966 cm^{-1}; ^{1}H and ^{13}C NMR data see Tables 1 and 2; ESIMS *m/z* 363.1 $[M + Na]^+$; EIMS *m/z* 340 $[M]^+$ (1), 236 (11), 213 (25), 195 (41), 167 (39), 149 (16), 128 (24), 86 (73), 68 (100); HREIMS *m/z* 340.1527 (calcd for $C_{17}H_{24}O_7$, 340.1522).

Oligandrumin B (2): white cubes; mp 302−304 °C; $[\alpha]_D^{23}$ +41 (*c* 0.17, MeOH); IR (KBr) ν_{max} 3331, 1755, 1736, 1712, 1375, 1256, 1175, 1051, 968 cm^{-1}; ^{1}H and ^{13}C NMR data see Tables 1 and 2; ESIMS *m/z* 681.3 $[2M + H]^+$; EIMS *m/z* 340 $[M]^+$ (3), 322 (4), 280 (7), 236 (26), 212 (29), 195 (39), 167 (47), 86 (74), 68 (100); HREIMS *m/z* 340.1525 (calcd for $C_{17}H_{24}O_7$, 340.1522).

Oligandrumin C (3): white, amorphous powder; $[\alpha]_D^{23}$ +3 (*c* 0.115, MeOH); IR (KBr) ν_{max} 3373, 2970, 1732, 1458, 1385, 1321, 1292, 1173, 1043, 970 cm^{-1}; ^{1}H and ^{13}C NMR data see Tables 1 and 2; ESIMS *m/z* 619.3 $[2M + Na]^+$; EIMS *m/z* 299 $[M + 1]^+$ (3), 280 (16), 236 (45), 195 (88), 167 (100), 149 (41), 121 (48), 86 (29), 71 (48), 69 (70); HREIMS *m/z* 298.1426 (calcd for $C_{15}H_{22}O_6$, 298.1416).

Oligandrumin D (4): white, amorphous powder; $[\alpha]_D^{23}$ +20.6 (*c* 0.345, MeOH); IR (KBr) ν_{max} 3413, 1751, 1732, 1707, 1389, 1354, 1238, 1175, 968, 908, 563 cm^{-1}; ^{1}H and ^{13}C NMR data see Tables 1 and 2; ESIMS *m/z* 615.2 $[2M + Na]^+$; EIMS *m/z* 296 $[M]^+$ (4), 278 (42), 266 (25), 236 (25), 212 (51), 194 (51), 167 (63), 149 (24), 85 (87), 69 (100); HREIMS *m/z* 296.1255 (calcd. for $C_{15}H_{20}O_6$, 296.1260).

Veranisatin D (5): white cubes; mp 212−213.5 °C; $[\alpha]_D^{23}$ −19 (*c* 0.28, MeOH); IR (KBr) ν_{max} 3570, 3510, 3427, 3363, 1834, 1821, 1736, 1460 cm^{-1}; ^{1}H and ^{13}C NMR data see Tables 1 and 2; ESIMS *m/z* 381.0 $[M + Na]^+$; EIMS *m/z* 358 (1), 265 (100), 251 (48), 191 (26), 177 (27), 91 (12); HREIMS *m/z* 358.1264 (calcd for $C_{16}H_{22}O_9$, 358.1264).

Veranisatin E (6): white, amorphous powder; $[\alpha]_D^{23}$ +16 (*c* 0.025, MeOH); IR (KBr) ν_{max} 3531, 3385, 3213, 1807, 1761, 1743, 1383, 1103, 916 cm^{-1}; ^{1}H and ^{13}C NMR data see Tables 1 and 2; ESIMS *m/z* 395.1 $[M + Na]^+$; EIMS *m/z* 354 $[M - H_2O]^+$ (3), 310 (11), 295

(36), 251 (53), 233 (89), 159 (38), 125 (100); HRESIMS *m/z* 395.0956 (calcd for $C_{16}H_{22}O_{10}Na$, 395.0954).

Oligandrumin E (7): white, amorphous powder; $[\alpha]_D^{23}$ −22 (*c* 0.05, MeOH); IR (KBr) ν_{max} 3443, 1614, 1514, 1252, 1130, 916, 829 cm^{-1}; ^1H and ^{13}C NMR data see Table 3; EIMS *m/z* 326 $[M]^+$ (9), 233 (22), 137 (100), 97 (47), 73 (85); HREIMS *m/z* 326.1356 (calcd for $C_{16}H_{22}O_7$, 326.1365).

X-ray Crystal Data for 1: colorless, needles, $C_{17}H_{24}O_7$, fw 340.36, orthorhombic, crystal size 0.490 × 0.252 × 0.181 mm, space group $P2_12_12_1$, a = 6.9604(10) Å, b = 10.8145(15) Å, c = 21.741(3) Å, V = 1636.5(4) Å^3, Z = 4, D_{calcd} = 1.381 mg/m^3, $F(000)$ = 728, reflections collected 9762, reflections unique 2158 (R_{int} = 0.1070), final R indices for $I > 2\sigma(I)$, R_1 = 0.0475, wR_2 = 0.1073, R indices for all data R_1 = 0.0548, wR_2 = 0.1100, completeness to 2θ (27.50) 99.5%, maximum transmission 1.0000, minimum transmission 0.7566. The structure was solved by direct methods using the program SHELXS-97. The refinement method was full-matrix least-squares on F^2, and goodness-of-fit on F^2 is 0.973. The X-ray diffraction material has also been deposited in the Cambridge Crystallographic Data Center (CCDC) as deposit no. CCDC 684765.

X-ray Crystal Data for 2: colorless, cubes, $C_{17}H_{24}O_7$, fw 340.36, orthorhombic, crystal size 0.505 × 0.422 × 0.347 mm, space group $P2_12_12_1$, a = 7.8151(13) Å, b = 11.987(2) Å, c = 18.045(3) Å, V = 1690.4(5) Å^3, Z = 4, D_{calcd} = 1.337 mg/m^3, $F(000)$ = 728, reflections collected 9917, reflections unique 2114 (R_{int} = 0.1476), final R indices for $I > 2\sigma(I)$, R_1 = 0.0496, wR_2 = 0.1235, R indices for all data R_1 = 0.0527, wR_2 = 0.1259, completeness to 2θ (26.99) 99.8%, maximum transmission 1.00000, minimum transmission 0.79108. The structure was solved by direct methods using the program SHELXS-97. The refinement method was full-matrix least-squares on F^2, and goodness-of-fit on F^2 is 1.054. The X-ray diffraction material has also been deposited in the Cambridge Crystallographic Data Center (CCDC) as deposit no. CCDC 684764.

Neuroprotective Activity Assay. SH-SY5Y cell survival was evaluated according to the reported protocol with modification.[18] Cells were high passages from the ATCC (American Type Culture Collection) maintained at 37 °C in a humidified atmosphere containing 5% CO_2. Cells were seeded into 96-well plates at a density of 1 × 10^5 cells/mL in MEM/F12 medium supplemented with 10% (v/v) fetal bovine serum. Experiments were carried out 24 h after cells were seeded. Test compounds and positive control α-tocopherol (vitamine E) were made to 10^{-2} M stock solutions with DMSO and then diluted to corresponding concentrations with cell culture medium. Cell survival was evaluated by methylthiazolyltetrazolium bromide (MTT) reduction[19] in order to analyze the cytoprotection of the test compounds. In brief, cells were incubated with test compounds (1 or 10 μM) or α-tocopherol (10 μM) 2 h prior to treatment with 100 μM H_2O_2 for another 24 h without changing the culture medium. Then 10 μL of MTT (5 mg/mL) was added to each well and incubated at 37 °C for 4 h. The cells were finally lysed with 100 μL of DMSO, and the amount of MTT formazan was measured at 490 nm spectral wavelength using a microplate reader.

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Supporting Information Available: ^1H and ^{13}C NMR, HMBC, and ROESY spectra for compounds **1**−**7**, as well as the structures of the known compounds **8**−**15**, are available free of charge via the Internet at http://pubs.acs.org.

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