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Dibenzocyclooctadiene Lignans from *Kadsura polysperma* and Their Antineurodegenerative Activities

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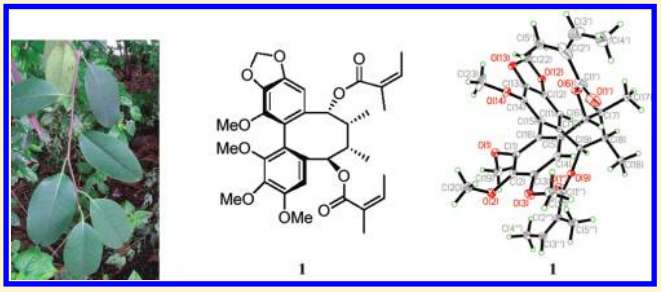
Supporting Information

ABSTRACT: Eleven new dibenzocyclooctadiene lignans, polysperlignans A–K (**1**–**11**), and eight known analogues (**12**–**19**) were isolated from the stems of *Kadsura polysperma*. Their structures and absolute configurations were established using a combination of MS, NMR, CD, and single-crystal X-ray diffraction techniques. Selected compounds were evaluated for activity against β-amyloid- or hydrogen peroxide-induced neurotoxicity on PC12 cells, and **1**, **2**, **4**, **5**, **13**, and **16** showed statistically significant neuroprotective effects in these in vitro assays.



The economically and medicinally important family Schisandraceae, a family of climbing plants, contains the genera *Schisandra* and *Kadsura*.[1] Some plants of this family are commonly used in Traditional Chinese Medicine for their sedative and tonic effects.[2] In pharmacology research, some dibenzocyclooctadiene lignans from *S. chinensis* exhibited therapeutic potential against oxidative neuronal damage induced by excitotoxin and may be useful in the treatment and prevention of neurodegenerative diseases.[3,4] In order to discover whether *Kadsura* species have additional secondary metabolites with antineurodegenerative activity, our research group initiated activity screening of dibenzocyclooctadiene lignans from *Kadsura* species in the relevant models of neurodegenerative disease and found that some of them exihibited considerable neuroprotective effects in an in vitro assay.[5,6]

Kadsura polysperma Yang (Schisandraceae) is an evergreen liana, growing in the jungle at elevations of 250–1800 m in Sichuan Province, P. R. China.[7] Previous chemical investigations of this plant collected in Chongqing City, P. R. China, led to the isolation of four triterpene lactones, polysperlactones A and B, heteroclitalactone D, and schisanlactone E.[8] Motivated by a search for more dibenzocyclooctadiene lignans with novel structures and neuroprotective activity, *K. polysperma* from Emei Mountain was studied for the first time. As a result, 19 dibenzocyclooctadiene lignans were isolated, including 11 new compounds, polysperlignans A–K (**1**–**11**), and eight analogues. The isolation, structure elucidation, and antineurodegenerative activity of selected compounds are reported in this paper.

RESULTS AND DISCUSSION

A 70% aqueous acetone extract of the stems of *K. polysperma* was partitioned between EtOAc and H_2O. The EtOAc solubles were dried and subjected to silica gel, MCI CHP-20 gel, Sephadex LH-20, and Lichroprep RP-18 gel column chromatography (CC) and semipreparative HPLC to afford 11 new compounds, polysperlignans A–K (**1**–**11**), together with eight known lignans, interiotherin C (**12**),[9] kadsurin (**13**),[10] kadsuphilin A (**14**),[11] isogomisin O (**15**),[12] tiegusanin I (**16**),[13] yunnankadsurin B (**17**),[14] methyl schisantherin F (**18**),[15] and ananolignan A (**19**).[5] The structures of the known compounds were determined by comparing spectroscopic data with literature values, and the absolute configurations of **1** and **7** were determined by X-ray analysis (CCDC 853853 and 853854, respectively).

Polysperlignan A (**1**) was isolated as colorless crystals. The HREIMS of **1** gave a $[M + Na]^+$ ion peak at m/z 619.2522 (calcd 619.2519), consistent with the molecular formula $C_{33}H_{40}O_{10}$. The UV spectrum with λ_{max} (CH_3OH) values at 191 and 219 nm, and its IR spectrum with absorption bands at 1619 and 1462 cm^{-1} (aromatic moiety), indicated that **1** was a dibenzocyclooctadiene lignan.[16,17] The ^1H NMR spectrum (Table 1) displayed two aromatic singlets for a biphenyl moiety at δ_H 6.70 (H-4) and 6.52 (H-11), four singlets for methoxy groups at δ_H 3.87 (3H), 3.82 (3H), 3.75 (3H), and 3.41 (3H), and two singlets characteristic of a methylenedioxy group at δ_H

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Chart 1

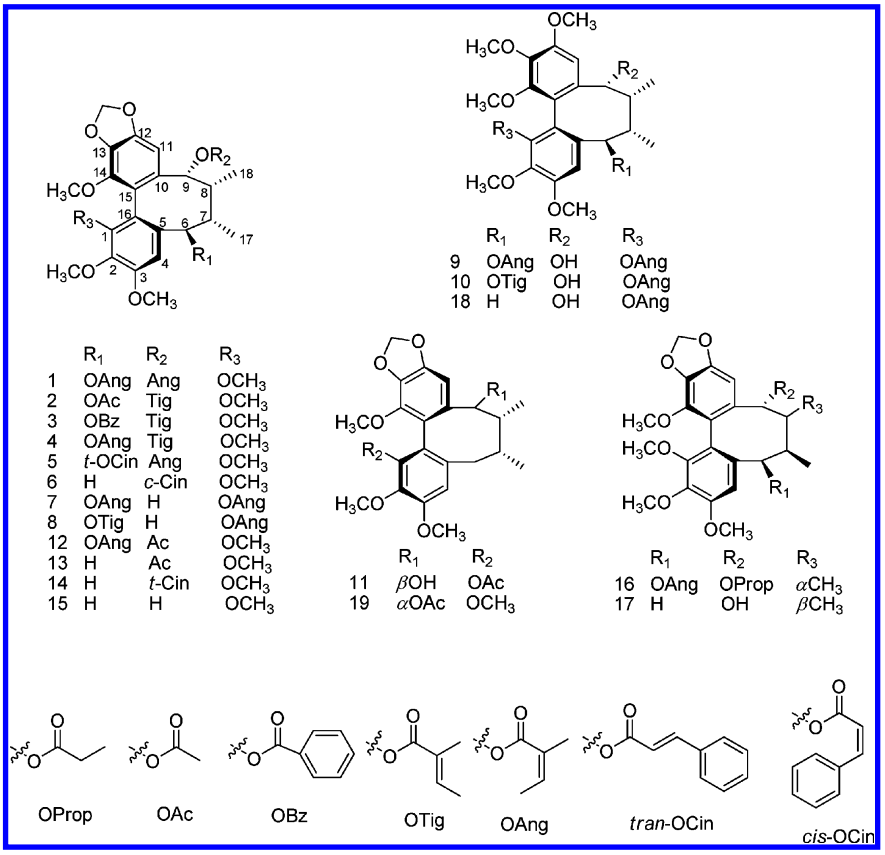

Table 1. ^{1}H NMR Data of Compounds 1–6 in $CDCl_3$ (δ in ppm, J in Hz)

position	1[a]	2[a]	3[a]	4[a]	5[b]	6[b]
4	6.70 (s)	6.71 (s)	6.77 (s)	6.75 (s)	6.81 (s)	6.59 (s)
6α	5.87 (d, 8.0)	5.79 (d, 8.0)	6.10 (d, 7.0)	5.92 (d, 7.8)	5.94 (d, 7.3)	2.66 (m)
6β						2.67 (m)
7	2.16 (m)	2.06 (m)	2.35 (m)	2.18 (m)	2.20 (m)	2.06 (m)
8	2.28 (m)	2.21 (overlap)	2.44 (m)	2.27 (m)	2.32 (m)	2.06 (m)
9	5.76 (d, 3.6)	5.83 (d, 4.6)	5.86 (s)	5.85 (d, 3.4)	5.99 (d, 3.0)	5.72 (s)
11	6.52 (s)	6.49 (s)	6.59 (s)	6.50 (s)	6.54 (s)	6.48 (s)
17	0.89 (d, 8.0)	0.95 (d, 7.2)	1.06 (d, 8.0)	1.00 (d, 7.1)	1.03 (d, 7.0)	0.93 (d, 7.0)
18	0.98 (d, 7.1)	1.01 (d, 7.2)	1.15 (d, 7.1)	1.08 (d, 6.6)	1.11 (d, 7.1)	1.08 (d, 6.9)
2′					5.92 (d, 16.0)	5.19 (d, 12.0)
3′	5.90 (overlap)	5.89 (m)	5.91 (overlap)	5.95 (overlap)	7.04 (d, 16.0)	6.72 (d, 12.0)
4′	1.84 (d, 7.2)	1.59 (d, 7.1)	1.62 (d, 8.0)	1.61 (d, 6.4)		
5′	1.28 (s)	1.47 (s)	1.51 (s)	1.49 (s)	7.39 (overlap)	7.58 (d, 7.8)
6′					7.39 (overlap)	7.28 (overlap)
7′					7.39 (overlap)	7.27 (overlap)
8′					7.39 (overlap)	7.28 (overlap)
9′					7.39 (overlap)	7.58 (d, 7.8)
2″						
3″	5.93 (overlap)		7.54 (m)	5.97 (overlap)	5.98 (overlap)	
4″	1.85 (d, 7.2)		7.34 (t, 7.7)	1.86 (d, 7.2)	1.90 (d, 7.2)	
5″	1.49 (s)		7.51 (t, 7.5)	1.49 (s)	1.53 (s)	
6″			7.34 (t, 7.7)			
7″			7.54 (m)			
AcO-6		1.77 (s)				
CH_3O-1	3.41 (s)	3.32 (s)	3.36 (s)	3.33 (s)	3.43 (s)	3.51 (s)
CH_3O-2	3.82 (s)	3.83 (s)	3.83 (s)	3.84 (s)	3.80 (s)	3.87 (s)
CH_3O-3	3.87 (s)	3.88 (s)	3.94 (s)	3.91 (s)	3.97 (s)	3.92 (s)
CH_3O-14	3.75 (s)	3.82 (s)	3.50 (s)	3.77 (s)	3.73 (s)	3.81 (s)
OCH_2O	5.95 (overlap)	5.98 (d, 1.1)	5.90 (overlap)	5.92 (s)	5.98 (overlap)	5.98 (s)
	5.94 (overlap)	5.95 (d, 1.1)	5.90 (overlap)	5.92 (s)	5.98 (overlap)	5.97 (s)

[a]Recorded at 400 MHz. [b]Recorded at 500 MHz.

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5.95 and 5.94. A cyclooctadiene ring was recognized from two secondary methyl doublets at δ_H 0.89 (H_3-17) and 0.98 (H_3-18), two methines at δ_H 2.16 (H-7) and 2.28 (H-8), and two oxymethines at δ_H 5.76 (H-9) and 5.87 (H-6). This was confirmed by $^1H-^1H$ COSY correlation systems of H-6/H-7/H-8/H-9, H-7/H_3-17, and H-8/H_3-18. HMBC correlations of the ethylenedioxy protons and H-11 with C-12 and C-13 and of the four methoxy group signals with C-1, C-2, C-3, and C-14 showed that the methylenedioxy group is connected to C-12 and C-13, and the four methoxy groups are located at C-1, C-2, C-3, and C-14, respectively (Figure 1). The ^{13}C NMR signals at

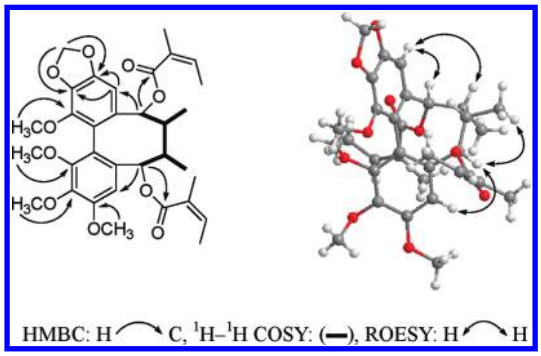

Figure 1. Key HMBC, $^1H-^1H$ COSY, and ROESY correlations of **1**.

δ_C 166.8 s, 127.6 s, 140.2 d, 20.1 q, 15.5 q and 166.7 s, 127.0 s, 138.4 d, 19.7 q, 15.4 q suggested the presence of two tigloyloxy moieties, and HMBC correlations of H-9 (δ_H 5.76) with C-1′ (δ_C 166.8) and of H-6 (δ_H 5.87) with C-1″ (δ_C 166.7) placed the two tigloyloxy groups at C-9 and C-6, respectively.

The CD curve of **1** showed a negative Cotton effect around 250 nm and a positive value near 220 nm, suggesting that **1** possesses an *S*-biphenyl configuration.[14] With the axial chirality defined, a ROESY experiment was used to establish the configuration of the remaining stereocenters. ROESY correlations of H-11 with H-8 and H-9 and of H-6 with H-4 and H_3-17 indicated that H-6, CH_3-17, and CH_3-18 are α-oriented and that H-9 is β-oriented (Figure 1).[17] To confirm the structure and determine its absolute configuration, **1** was crystallized from MeOH to afford a crystal of the orthorhombic space group $P2_12_12_1$, which was analyzed by X-ray crystallography. On the basis of 10 oxygen atoms in the molecule, the final refinement of the Cu Kα data resulted in a Flack parameter of 0.1(2), which in combination with the CD spectrum[17] allowed unambiguous assignment of the absolute configuration (Figure 2). According to the projection of the stereochemical structure, compound **1** was in agreement with a cyclooctadiene lignan with a twisted boat conformation having C-6 (*R*), C-7 (*S*), C-8 (*R*), and C-9 (*R*) absolute configurations. Therefore, the structure of **1** was determined as shown.

Polysperlignan B (**2**) was assigned as $C_{30}H_{36}O_{10}$, as deduced from the HRESIMS (m/z 579.2191 $[M + Na]^+$) and in accordance with its NMR data. The UV, IR, CD, and NMR spectra of **2** suggested the presence of an *S*-biphenyl-configured dibenzocyclooctadiene lignan with almost identical data to ananolignan L.[5] The only difference between them was in the position exchange of two substituents. HMBC correlations of H-6 (δ_H 5.79) with the acetate carbonyl (δ_C 170.1) and of H-9 (δ_H 5.83) with the ester carbonyl (δ_C 167.1 s, C-1′) indicated an acetoxy group at C-6 and a tigloyloxy group at C-9 in **2**.

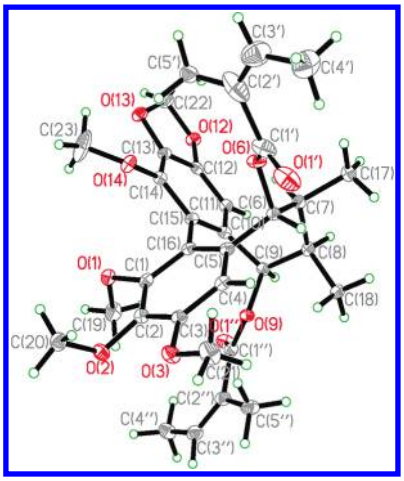

Figure 2. X-ray crystal structure of **1**.

The configuration of **2** was determined through ROESY correlations of H-11/H-8, H-9; H-4/H-6, H_3-17; and H_3-18/H_3-17, which were in agreement with a cyclooctadiene lignan with a twisted boat/chair conformation having C-6 (*R*), C-7 (*S*), C-8 (*R*), and C-9 (*R*) absolute configurations. Thus, the structure of **2** was established as shown, and it was named polysperlignan B.

Comparison of the NMR data of **3** and **4** with those of **2** disclosed that the main structural differences between them concerned the substituent at C-6. Polysperlignan C (**3**) gave the molecular formula $C_{35}H_{38}O_{10}$ from its HRESIMS data at m/z 641.2362 $[M + Na]^+$ (calcd 641.2362). The 1D NMR spectra revealed the presence of a benzoyloxy group (δ_C 165.6 s, 130.8 s, 129.5 d, 127.9 d, 132.7 d, 127.9 d, and 129.5 d). HMBC correlations from H-6 (δ_H 6.10) to the ester carbonyl (δ_C 165.6s) placed the benzoyloxy group at C-6. The molecular formula of **4** was determined as $C_{33}H_{40}O_{10}$ by HRESIMS at m/z 619.2516 $[M + Na]^+$ (calcd 619.2519), and the NMR data of **4** also showed similarities to the data for **2**. However, a signal for an angeloyloxy group (δ_C 166.7 s, 127.6 s, 138.6 d, 15.6q, and 19.8q) was evident at C-6 in **4**, which was confirmed by the HMBC correlations from H-6 (δ_H 5.92) to the ester carbonyl (δ_C 166.7s).

The CD, UV, and IR data suggested that **3** and **4** were *S*-biphenyl-configured dibenzocyclooctadiene lignans. ROESY correlations obtained for **3** and **4** from H-11 to H-8 and H-9, from H-4 to H-6 and H_3-17, and from H_3-17 to H_3-18 indicated that H-6, CH_3-17, and CH_3-18 are α-oriented and that H-9 is β-oriented. Thus, the structures of polysperlignans C and D (**3** and **4**) were established as shown.

Polysperlignans E (**5**) and F (**6**) were determined to have the molecular formulas $C_{37}H_{40}O_{10}$ and $C_{32}H_{34}O_8$ by HRESIMS (m/z 667.2530 $[M + Na]^+$ and 569.2160 $[M + Na]^+$, respectively). Comparison of the spectroscopic data of **5** with those of **1** revealed these substances to be quite similar structurally, except that the angeloyloxy group at C-6 in **1** was changed to a *trans*-cinnamoyl group (δ_C 165.9 s, 117.8 d, 144.8 d, 134.1 s, 128.8 d, 128.0 d, 130.3 d, 128.0 d, and 128.8 d) in **5**, which was confirmed by HMBC correlations from an oxymethine at δ_H 5.94 (H-6) to δ_C 165.9 (C-1′), 38.6 (C-7), 38.4 (C-8), 131.1 (C-5), and 110.5 (C-4). Analysis of the 2D NMR data of compound **6** and comparison of its 1D NMR data with those of **14** revealed that the main structure differences between the two compounds were a *cis*-cinnamoyl group in **6**

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instead of a *trans*-cinnamoyl group at C-9 in **14**. The deduction was determined through ROESY correlations of two olefinic protons, H-2′/H-3′, as well as the coupling constant of $J_{H\text{-}2',3'}$ = 12 Hz. The CD, UV, IR, and NMR spectra suggested that **5** and **6** were *S*-biphenyl-configured dibenzocyclooctadiene lignans. ROESY correlations of H-11 with H-8β and H-9β, of H-4 with H-6α and H_3-17α, and of H_3-18 with H_3-17 suggested the absolute configurations as C-6 (*R*), C-7 (*S*), C-8 (*R*), and C-9 (*R*), which were identical with those of **1**.

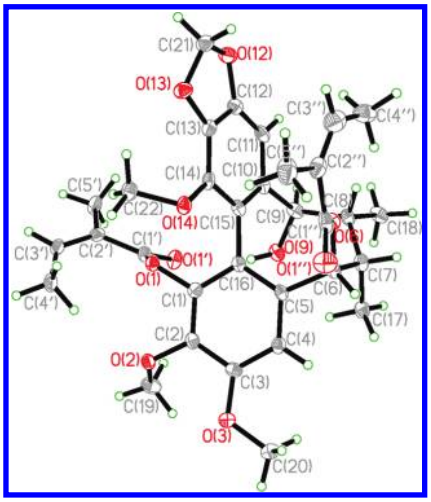

Figure 3. X-ray crystal structure of **7**.

Polysperlignans G (**7**) and H (**8**) were assigned the same molecular formula, $C_{32}H_{38}O_{10}$, as determined by HRESIMS (*m*/*z* 605.2345 $[M + Na]^+$ and 605.2362 $[M + Na]^+$, respectively). Both compounds were assigned as *S*-biphenyl-configured dibenzocyclooctadiene lignans by analysis of their CD spectra. The 1D NMR spectra of compound **7** exhibited 18 carbon atoms (including 12 aromatic ones, four methines, and two secondary methyls) for the dibenzocyclooctadiene skeleton, in addition to two angeloyloxy groups (δ_C 167.3 s, 127.0 s, 139.0 d, 15.4 q, 20.3 q and δ_C 166.6 s, 127.8 s, 139.0 d, 15.6 q, 19.9 q), a methylenedioxy group, and three methoxy groups. The existence of the angeloyloxy group at C-6 was deduced from the HMBC correlations of H-6 (δ_H 5.88) with the ester carbonyl (δ_C 166.6, C-1″). Furthermore, HMBC correlations of three methoxy groups with C-2, C-3, and C-14, respectively, were used to determine their positions. The occurrence of the methylenedioxy moiety at C-12 and C-13 was demonstrated by the HMBC correlations of the methylenedioxy protons with C-12 and C-13. According to the molecular formula, the methine carbon at C-9 should be substituted by an OH, and another angeloyloxy group was located at C-1, which was deduced from a ROESY correlation of CH_3O-14 with H_3-4′ and the remarkable upfield shift of the signal of H-9. An X-ray crystallographic study and CD experiment were also performed to confirm the structure and determine the absolute configuration of **7** (Figure 3). Thus, **7** was unambiguously elucidated as a cyclooctadiene lignan with a twisted boat/chair conformation having C-6 (*R*), C-7 (*S*), C-8 (*R*), and C-9 (*R*) absolute configurations. Comparison of the NMR data of **8** with those of **7** disclosed that the only structural difference was the angeloyloxy group located at C-6 in **7** being changed to a tigloyloxy moiety (δ_C 166.8 s, 128.4 s, 136.8 d, 14.1 q, and 11.6 q) in **8**. This was confirmed by the HMBC correlations from H-6 (δ_H 5.88) to the ester carbonyl (δ_C 166.8 s, C-1″). The observed ROESY correlations of H-11 with H-8 and H-9, of H-4 with H-6 and H_3-17, and of H_3-17 with H_3-18 indicated that H-6, CH_3-17, and CH_3-18 are α-oriented and that H-9 is β-oriented. Accordingly, the structure of **8** was determined as shown.

Polysperlignans I (**9**) and J (**10**) both had the molecular formula $C_{33}H_{42}O_{10}$, as determined by HRESIMS (*m*/*z* 621.2669 $[M + Na]^+$ and 621.2660 $[M + Na]^+$, respectively). Both compounds were assigned as *S*-biphenyl-configured dibenzocyclooctadiene lignans by comparison of their CD, UV, and ROESY spectra with those of **7**. The only difference found between **7** and **9** concerned the substituent groups at C-12 and C-13. Analysis of the NMR and MS data showed two methoxy groups in **9** instead of a methylenedioxy group in **7**. The ^1H and ^{13}C NMR spectra of **10** were quite similar to those of **9**, except that the angeloyloxy group located at C-6 in **9** was changed to a tigloyloxy group (δ_C 168.4 s, 128.9 s, 139.5 d, 14.3 q, and 11.7 q) in **10**. The observation of a HMBC correlation of H-6 (δ_H 5.88) to the ester carbonyl (δ_C 168.4 s, C-1″) determined the above deduction. ROESY correlations of H-11 with H-8 and H-9 and of H-4 with H-6 and H_3-17 suggested a cyclooctadiene lignan with a twisted boat/chair conformation of **10**, consistent with the absolute configuration C-6 (*R*), C-7 (*S*), C-8 (*R*), and C-9 (*R*). Therefore, the structures of **9** and **10** were determined as shown.

Polysperlignan K (**11**) gave the molecular formula $C_{24}H_{28}O_8$ from its HRESIMS data at *m*/*z* 467.1675 $[M + Na]^+$. The 1D NMR spectra exhibited 18 carbon atoms (including 12 aromatic ones, one methylene, three methines, and two secondary methyls) for the dibenzocyclooctadiene skeleton, in addition to a methylenedioxy group, three methoxy groups, and an acetyl group. By contrast, compounds **11** and **15** had similar planar structures, the only difference was an acetyl group instead of one methoxy group. The HRESIMS also confirmed the above conclusion. The HMBC spectrum showed that the methylenedioxy group was located at C-12 and C-13 and the three methoxy groups were located at C-2, C-3, and C-14, respectively, indicating that an acetyl group was located at C-1. HMBC correlations of H-9 (δ_H 4.47) with C-7 (δ_C 39.1, d), C-8 (δ_C 42.2, d), C-10 (δ_C 136.9, s), C-11 (δ_C 102.2, d), C-15 (δ_C 118.6, s), and C-18 (δ_C 7.9, q) also indicated that C-9 of **11** was substituted by an OH group.

The CD curve of **11** showed a negative Cotton effect around 210 nm and a positive value around 250 nm, suggesting that **11** possessed an *R*-biphenyl configuration. H-9, CH_3-17, and CH_3-18 were deduced to be α-oriented on the basis of the ROESY correlations from H-11 to H-9 and H_3-18 and from H_3-17 to H_3-18. Therefore, the structure of **11** was determined as shown.

Compounds **1**, **2**, **4**−**6**, **9**, and **13**−**19** were assayed for their neuroprotective effects against PC12 neuroblastoma cells, a neuroblastoma cell line used for the study of neurodegenerative disease.[18−20] As seen in Table 5, polysperlignans A and B (**1** and **2**), polysperlignans D and E (**4** and **5**), kadsurin (**13**), and tiegusanin I (**16**) showed the most promising cell survival data against H_2O_2- or Aβ_{25-35}-induced neurotoxicity. Due to limitations in the amounts available, compounds **3**, **7**, **8**, and **10**−**12** were not tested in the bioassay used.

EXPERIMENTAL SECTION

General Experimental Procedures. Optical rotations were measured with a Horiba SEPA-300 polarimeter. UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. A Tensor

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Table 2. ^{1}H NMR Data of Compounds 7−11 (δ in ppm, J in Hz)

position	7[a]	8[a]	9[a]	10[c]	11[b]
4	6.86 (s)	6.82 (s)	6.88 (s)	6.88 (s)	6.65 (s)
6α	5.88 (overlap)	5.88 (d, 8.0)	5.96 (overlap)	5.88 (br s)	2.23 (dd, 13.3, 9.6)
6β					2.05 (overlap)
7	2.10 (m)	2.15 (m)	2.05 (m)	2.06 (m)	1.94 (m)
8	2.02 (m)	2.13 (m)	2.03 (m)	2.05 (m)	1.99 (m)
9	4.75 (s)	4.76 (s)	4.79 (d, 2.4)	4.74 (s)	4.47 (s)
11	6.29 (s)	6.33 (s)	6.36 (s)	6.53 (s)	6.89 (s)
17	1.03 (d, 6.9)	1.02 (d, 7.2)	1.01 (d, 6.1)	0.94 (d, 6.1)	1.02 (d, 7.0)
18	1.17 (d, 7.1)	1.20 (d, 7.2)	1.20 (d, 4.8)	1.15 (d, 5.8)	0.68 (d, 7.0)
3′	6.03 (m)	6.02 (q, 6.4)	5.91 (overlap)	5.99 (overlap)	
4′	1.81 (d, 7.3)	1.81 (d, 6.8)	1.75 (d, 7.2)	1.68 (d, 8.2)	
5′	1.81 (s)	1.81 (s)	1.77 (s)	1.69 (s)	
3″	5.96 (m)	6.12 (m)	5.90 (overlap)	5.99 (overlap)	
4″	1.86 (d, 7.2)	1.66 (d, 7.0)	1.82 (d, 7.2)	1.49 (d, 6.7)	
5″	1.48 (s)	1.59 (s)	1.39 (s)	1.42 (s)	
AcO					1.97 (s)
CH_3O-2	3.80 (s)	3.79 (s)	3.79 (s)	3.69 (s)	3.82 (s)
CH_3O-3	3.90 (s)	3.90 (s)	3.90 (s)	3.84 (s)	3.90 (s)
CH_3O-12			3.83 (s)	3.77 (s)	
CH_3O-13			3.78 (s)	3.66 (s)	
CH_3O-14	3.80 (s)	3.76 (s)	3.60 (s)	3.28 (s)	3.88 (s)
OCH_2O	5.90 (overlap)	5.93 (d, 1.1)			5.97 (s)
	5.90 (overlap)	5.87 (d, 1.1)			5.96 (s)

[a]Recorded at 400 MHz in $CDCl_3$. [b]Recorded at 500 MHz in $CDCl_3$. [c]Recorded in CD_3OD, 600 MHz.

27 spectrophotometer was used for scanning IR spectroscopy with KBr pellets. 1D and 2D NMR spectra were recorded on Bruker AM-400 and DRX-500 spectrometers with TMS as internal standard. Chemical shifts (δ) are expressed in ppm with reference to the solvent signals. Mass spectra were performed on an API QSTAR time-of-flight spectrometer and a VG Autospec-3000 spectrometer, respectively. Semipreparative HPLC was performed on an Agilent 1100 liquid chromatograph with a Zorbax SB-C18 (9.4 mm × 25 cm) column. Column chromatography was performed with silica gel (200−300 mesh, Qingdao Marine Chemical, Inc., Qingdao, People's Republic of China), Lichroprep RP-18 gel (40−63 μM, Merck, Darmstadt, Germany), and MCI gel (75−150 μM, Mitsubishi Chemical Corporation, Tokyo, Japan). Fractions were monitored by TLC, and spots were visualized by heating silica gel plates sprayed with 5% H_2SO_4 in EtOH.

Plant Material. The stems of *K. polysperma* were collected in Emei County of Sichuan Province, People's Republic of China, in August 2009, and identified by Prof. Xi-Wen Li, Kunming Institute of Botany. A voucher specimen (KIB 2009081003) has been deposited in the Herbarium of the Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation. The air-dried and powdered stems of *K. polysperma* (10.5 kg) were extracted with 70% aqueous Me_2CO (40 L × 3) at room temperature and concentrated in vacuo to yield a residue, which was partitioned between H_2O and EtOAc. The EtOAc extract (330 g) was chromatographed on a silica gel (100−200 mesh, 3.0 kg) column, eluting with a $CHCl_3$−Me_2CO gradient system (40:1, 20:1, 9:1, 8:2, 7:3, 6:4, 1:1), to give fractions 1−8. Fraction 3 (20 g) was subjected to RP-18 column chromatography (40−100% gradient of CH_3OH−H_2O) to afford subfractions 3.1−3.6. Fraction 3.4 (2.2 g) was chromatographed on silica gel (petroleum ether−Me_2CO, 30:1−2:1) to give six subfractions. Fraction 3.4.2 (1.1 g) was purified by semipreparative HPLC (65% CH_3CN−H_2O) to give three fractions, 3.4.2.1−3.4.2.3. Fraction 3.4.2.1 (160 mg) was chromatographed by semipreparative HPLC (78% CH_3OH−H_2O) to give **6** (7 mg), **13** (12 mg), **14** (7 mg), **15** (23 mg), **17** (10 mg), and **19** (8 mg). Fraction 3.4.2.2 (250 mg) was purified repeatedly by semipreparative HPLC (80% CH_3OH−H_2O) to give **1** (13 mg), **2** (16 mg), **3** (2 mg), **4** (20 mg), **5** (13 mg), **12** (2 mg), and **16** (22 mg). Fraction 3.4.2.3 (120 mg) was separated further by semipreparative HPLC (80% CH_3OH−H_2O) to give **7** (3 mg) and **8** (2 mg). Fraction 3.4.3 (0.2 g) was subjected to semipreparative HPLC (63% CH_3CN−H_2O) to produce **9** (3 mg), **10** (2 mg), and **18** (10 mg). Finally, fraction 3.4.4 (0.1 g) was separated by semipreparative HPLC (60% CH_3CN−H_2O) to yield **11** (2 mg).

Polysperlignan A (**1**): colorless crystals; mp 156−157 °C; $[\alpha]_D^{17}$ +270.1 (*c* 0.07, CH_3OH); CD (CH_3OH) λ_{max} nm ($\Delta\varepsilon$) 226 (+14), 243 (−3); UV (CH_3OH) λ_{max} (log ε) 219 (4.44), 191 (4.08) nm; IR (KBr) ν_{max} 2943, 1706, 1619, 1462, 1231 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 3; positive ESIMS *m/z* 619 (100) $[M + Na]^+$; positive HRESIMS *m/z* 619.2522 $[M + Na]^+$ (calcd for $C_{33}H_{40}O_{10}Na$, 619.2519).

Polysperlignan B (**2**): white solid; mp 86−88 °C; $[\alpha]_D^{27}$ +9.4 (*c* 0.17, $CHCl_3$); CD (CH_3OH) λ_{max} nm ($\Delta\varepsilon$) 228 (+7), 245 (−20); UV ($CHCl_3$) λ_{max} (log ε) 241 (4.07), 223 (3.74), 215 (3.73), 212 (3.71), 205 (3.72), 202 (3.72), 194 (3.73) nm; IR (KBr) ν_{max} 2938, 1707, 1622, 1463, 1249 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 3; positive ESIMS *m/z* 579 (100) $[M + Na]^+$; positive HRESIMS *m/z* 579.2191 $[M + Na]^+$ (calcd for $C_{30}H_{36}O_{10}Na$, 579.2206).

Polysperlignan C (**3**): white solid; mp 69−70 °C; $[\alpha]_D^{17}$ −133.3 (*c* 0.07, CH_3OH); CD (CH_3OH) λ_{max} nm ($\Delta\varepsilon$) 223 (+1), 241 (−1); UV (CH_3OH) λ_{max} (log ε) 218 (4.27) nm; IR (KBr) ν_{max} 2937, 1712, 1622, 1463, 1259 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 3; positive ESIMS *m/z* 641 (100) $[M + Na]^+$; positive HRESIMS *m/z* 641.2362 $[M + Na]^+$ (calcd for $C_{35}H_{38}O_{10}Na$, 641.2362).

Polysperlignan D (**4**): yellow oil; $[\alpha]_D^{27}$ +1.5 (*c* 0.16, $CHCl_3$); CD (CH_3OH) λ_{max} nm ($\Delta\varepsilon$) 236 (+4), 248 (−7); UV ($CHCl_3$) λ_{max} (log ε) 241 (4.00), 231 (3.48), 227 (3.47), 221 (3.45), 218 (3.45), 203 (3.60), 201 (3.61), 194 (3.63) nm; IR (KBr) ν_{max} 2937, 1708, 1623, 1462, 1253 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 3; positive ESIMS *m/z* 619 (100) $[M + Na]^+$; positive HRESIMS *m/z* 619.2516 $[M + Na]^+$ (calcd for $C_{33}H_{40}O_{10}Na$, 619.2519).

Polysperlignan E (**5**): white solid; mp 132−134 °C; $[\alpha]_D^{17}$ −1.7 (*c* 0.08, CH_3OH); CD (CH_3OH) λ_{max} nm ($\Delta\varepsilon$) 231 (+3), 255 (−9); UV (CH_3OH) λ_{max} (log ε) 277 (4.01), 218 (4.47) nm; IR (KBr) ν_{max} 2935, 1710, 1626, 1462, 1232 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 3; positive ESIMS *m/z* 667 (100) $[M + Na]^+$; positive HRESIMS *m/z* 667.2530 $[M + Na]^+$ (calcd for $C_{37}H_{40}O_{10}Na$, 667.2519).

Polysperlignan F (**6**): yellow oil; $[\alpha]_D^{17}$ +380.0 (*c* 0.10, CH_3OH); CD (CH_3OH) λ_{max} nm ($\Delta\varepsilon$) 221 (+1), 241 (−1); UV (CH_3OH) λ_{max} (log ε) 256 (3.81), 218 (4.26) nm; IR (KBr) ν_{max} 2935, 1709, 1624, 1463, 1248 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 3; positive ESIMS *m/z* 569 (100) $[M + Na]^+$; positive HRESIMS *m/z* 569.2160 $[M + Na]^+$ (calcd for $C_{32}H_{34}O_8Na$, 569.2151).

Polysperlignan G (**7**): colorless crystals; mp 129−130 °C; $[\alpha]_D^{23}$ +132.6 (*c* 0.10, $CHCl_3$); CD (CH_3OH) λ_{max} nm ($\Delta\varepsilon$) 224 (+14), 243 (−4); UV ($CHCl_3$) λ_{max} (log ε) 241 (3.69) nm; IR (KBr) ν_{max} 2933, 1706, 1613, 1461, 1233 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 4; positive ESIMS *m/z* 605 (100) $[M + Na]^+$; positive HRESIMS *m/z* 605.2345 $[M + Na]^+$ (calcd for $C_{32}H_{38}O_{10}Na$, 605.2362).

Polysperlignan H (**8**): white solid; mp 129−130 °C; $[\alpha]_D^{24}$ +49.0 (*c* 0.09, CH_3OH); CD (CH_3OH) λ_{max} nm ($\Delta\varepsilon$) 224 (+21), 242 (−18); UV (CH_3OH) λ_{max} (log ε) 290 (2.62), 212 (3.97), 198 (3.41) nm; IR (KBr) ν_{max} 2936, 1706, 1614, 1463, 1265 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 4; positive ESIMS *m/z* 605 (100) $[M + Na]^+$; positive HRESIMS *m/z* 605.2362 $[M + Na]^+$ (calcd for $C_{32}H_{38}O_{10}Na$, 605.2362).

Polysperlignan I (**9**): white solid; mp 65−66 °C; $[\alpha]_D^{17}$ +137.9 (*c* 0.29, CH_3OH); CD (CH_3OH) λ_{max} nm ($\Delta\varepsilon$) 219 (+16), 237 (−6); UV (CH_3OH) λ_{max} (log ε) 216 (4.40), and 193 (4.05) nm; IR (KBr) ν_{max} 2938, 1710, 1644, 1457, 1231 cm^{-1}; ^{1}H and ^{13}C NMR data,

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Table 3. ^{13}C NMR Data of Compounds 1−6 in $CDCl_3$ (δ in ppm)

position	1[a]	2[a]	3[a]	4[a]	5[a]	6[b]
1	151.6 C	151.8 C	151.8 C	151.7 C	151.6 C	150.9 C
2	141.3 C	141.7 C	141.6 C	141.6 C	142.0 C	139.9 C
3	151.8 C	151.5 C	151.7 C	151.8 C	151.8 C	151.4 C
4	110.4 CH	110.3 CH	109.7 CH	110.3 CH	110.5 CH	110.3 CH
5	131.0 C	130.9 C	130.6 C	127.7 C	131.1 C	133.1 C
6	80.5 CH	80.8 CH	81.2 CH	80.6 CH	80.4 CH	38.7 CH_2
7	38.3 CH	37.7 CH	38.8 CH	38.4 CH	38.6 CH	34.8 CH
8	41.5 CH	39.8 CH	38.7 CH	38.4 CH	38.4 CH	41.9 CH
9	81.0 CH	80.0 CH	81.3 CH	80.6 CH	80.7 CH	81.9 CH
10	133.3 C	133.1 C	133.7 C	131.0 C	133.3 C	134.7 C
11	102.5 CH	102.5 CH	102.5 CH	102.6 CH	102.4 CH	102.4 CH
12	148.5 C	148.5 C	148.5 C	148.5 C	148.6 C	148.6 C
13	135.9 C	136.2 C	135.9 C	133.3 C	136.1 C	136.0 C
14	141.6 C	143.7 C	141.4 C	141.8 C	141.5 C	141.4 C
15	121.0 C	121.3 C	121.3 C	121.1 C	121.3 C	120.6 C
16	122.6 C	123.2 C	123.1 C	123.6 C	123.5 C	123.4 C
17	19.9 CH_3	17.6 CH_3	19.4 CH_3	15.6 CH_3	18.4 CH_3	14.6 CH_3
18	9.6 CH_3	18.8 CH_3	14.7 CH_3	15.6 CH_3	16.9 CH_3	19.6 CH_3
1′	166.8 C	167.1 C	167.5 C	166.7 C	165.9 C	164.5 C
2′	127.6 C	127.5 C	127.6 C	127.6 C	117.8 CH	119.1 CH
3′	140.2 CH	137.9 CH	138.2 CH	138.6 CH	144.8 CH	144.4 CH
4′	15.5 CH_3	14.0 CH_3	14.1 CH_3	15.6 CH_3	134.1 C	134.4 C
5′	20.1 CH_3	11.5 CH_3	11.7 CH_3	19.8 CH_3	128.8 CH	130.1 CH
6′					128.0 CH	127.8 CH
7′					130.3 CH	129.1 CH
8′					128.0 CH	127.8 CH
9′					128.8 CH	130.1 CH
1″	166.7 C		165.6 C	167.2 C	166.6 C	
2″	127.0 C		130.8 C	127.6 C	127.7 C	
3″	138.4 CH		129.5 CH	138.1 CH	138.7 CH	
4″	15.4 CH_3		127.9 CH	14.1 CH_3	15.5 CH_3	
5″	19.7 CH_3		132.7 CH	11.6 CH_3	19.8 CH_3	
6″			127.9 CH			
7″			129.5 CH			
AcO-6		170.1 C				
		20.8 CH_3				
CH_3O-1	60.0 CH_3	59.6 CH_3	59.8 CH_3	59.7 CH_3	60.4 CH_3	60.1 CH_3
CH_3O-2	60.3 CH_3	60.4 CH_3	60.5 CH_3	60.5 CH_3	60.8 CH_3	60.6 CH_3
CH_3O-3	55.9 CH_3	55.8 CH_3	55.9 CH_3	55.9 CH_3	55.9 CH_3	55.9 CH_3
CH_3O-14	59.2 CH_3	59.5 CH_3	59.1 CH_3	59.4 CH_3	59.5 CH_3	59.6 CH_3
OCH_2O	100.9 CH_2	101.1 CH_2	101.0 CH_2	101.0 CH_2	101.1 CH_2	101.1 CH_2

[a]Recorded at 100 MHz. [b]Recorded at 125 MHz.

see Tables 2 and 4; positive ESIMS m/z 621 (100) $[M + Na]^+$; positive HRESIMS m/z 621.2669 $[M + Na]^+$ (calcd for $C_{33}H_{42}O_{10}Na$, 621.2675).

*Polysperlignan J (**10**):* yellow gum; $[\alpha]_D^{23}$ +39.6 (c 0.10, $CHCl_3$); CD (CH_3OH) λ_{max} nm ($\Delta\varepsilon$) 200 (+18), 237 (−15); UV ($CHCl_3$) λ_{max} (log ε) 241 (3.59) nm; IR (KBr) ν_{max} 2934, 1705, 1649, 1457, 1262 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 2 and 4; positive ESIMS m/z 621 (100) $[M + Na]^+$; positive HRESIMS m/z 621.2660 $[M + Na]^+$ (calcd for $C_{33}H_{42}O_{10}Na$, 621.2675).

*Polysperlignan K (**11**):* yellow oil; $[\alpha]_D^{17}$ −2.2 (c 0.10, $CHCl_3$); CD (CH_3OH) λ_{max} nm ($\Delta\varepsilon$) 218 (−22), 239 (+16); UV ($CHCl_3$) λ_{max} (log ε) 241 (3.47), 193 (2.89) nm; IR (KBr) ν_{max} 2934, 1764, 1615, 1462, 1204 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 2 and 4; positive ESIMS m/z 467 (100) $[M + Na]^+$; positive HRESIMS m/z 467.1675 $[M + Na]^+$ (calcd for $C_{24}H_{28}O_8Na$, 467.1681).

X-ray Crystal Structure Analysis. Colorless crystals of **1** and **7** were obtained from CH_3OH. Intensity data were collected at 100 K on an Bruker APEX DUO diffractometer equipped with an APEX II CCD, using Cu Kα radiation. Cell refinement and data reduction were performed with Bruker SAINT. The structures were solved by direct methods using SHELXS-97.[21] Refinements were performed with SHELXL-97[21] using full-matrix least-squares, with anisotropic displacement parameters for all the non-hydrogen atoms. The H atoms were placed in calculated positions and refined using a riding model. Molecular graphics were computed with PLATON. Crystallographic data (excluding structure factor tables) for the structures reported have been deposited with the Cambridge Crystallographic Data Center as supplementary publications no. CCDC 853853 for **1** and CCDC 853854 for **7**. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB 1EZ, UK [fax: Int. +44(0) (1223) 336 033; e-mail: deposit@ccdc.cam.ac.uk].

*Polysperlignan A (**1**):* $C_{33}H_{40}O_{10}$, M_w = 596.7, orthorhombic, space group, $P2_12_12_1$, Z = 4, a = 10.6604(3) Å, b = 14.6290(3) Å, c = 19.5474(4) Å; $\alpha = \beta = \gamma = 90°$, V = 3048.44(12) $Å^3$, μ(Cu Kα) = 0.79 mm^{-1}, ρ_{calc} = 1.30 $g\cdot cm^{-3}$; S = 1.06, final R indices: R_1 = 0.0531 and wR_2 = 0.1420 for 4976 observed from 5133 independent and 13 947 measured reflections (θ_{max} = 69.2, $I > 2\sigma(I)$ criterion and

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Table 4. ^{13}C NMR Data of Compounds 7−11 (δ in ppm)

position	7[a]	8[b]	9[a]	10[c]	11[a]
1	142.4 C	142.5 C	142.3 C	143.7 C	142.1 C
2	140.2 C	140.3 C	139.0 C	141.1 C	139.0 C
3	151.5 C	151.4 C	151.5 C	152.8 C	153.0 C
4	112.9 CH	112.8 CH	113.0 CH	114.1 CH	109.7 CH
5	132.8 C	132.8 C	132.6 C	134.0 C	139.3 C
6	80.9 CH	81.0 CH	80.7 CH	82.0 CH	34.6 CH_2
7	39.2 CH	39.3 CH	40.1 CH	41.1 CH	39.0 CH
8	39.1 CH	39.2 CH	39.0 CH	39.5 CH	42.2 CH
9	81.6 CH	81.9 CH	83.2 CH	84.2 CH	72.9 CH
10	138.4 C	138.7 C	139.3 C	140.8 C	136.8 C
11	102.0 CH	102.1 CH	106.6 CH	108.3 CH	102.2 CH
12	148.7 C	148.6 C	152.9 C	154.6 C	148.4 C
13	134.8 C	134.7 C	140.4 C	142.1 C	134.5 C
14	141.0 C	141.1 C	151.3 C	152.6 C	140.0 C
15	118.7 C	119.1 C	119.7 C	121.3 C	118.6 C
16	122.3 C	122.3 C	122.6 C	123.5 C	120.8 C
17	14.9 CH_3	14.9 CH_3	14.3 CH_3	14.5 CH_3	21.9 CH_3
18	20.0 CH_3	20.1 CH_3	21.0 CH_3	21.1 CH_3	7.9 CH_3
1′	167.3 C	167.4 C	167.3 C	168.8 C	
2′	127.0 C	127.1 C	127.0 C	128.2 C	
3′	139.0 CH	138.9 CH	138.9 CH	141.2 CH	
4′	15.4 CH_3	15.4 CH_3	15.4 CH_3	15.9 CH_3	
5′	20.3 CH_3	20.3 CH_3	20.2 CH_3	20.6 CH_3	
1″	166.6 C	166.8 C	166.7 C	168.4 C	
2″	127.8 C	128.4 C	127.6 C	128.9 C	
3″	139.0 CH	136.8 CH	138.9 CH	139.5 CH	
4″	15.6 CH_3	14.1 CH_3	15.5 CH_3	14.3 CH_3	
5″	19.9 CH_3	11.6 CH_3	19.9 CH_3	11.7 CH_3	
AcO					168.8 C
					20.5 CH_3
CH_3O-2	60.9 CH_3	61.0 CH_3	61.0 CH_3	61.5 CH_3	60.9 CH_3
CH_3O-3	55.9 CH_3	56.0 CH_3	55.9 CH_3	56.6 CH_3	55.8 CH_3
CH_3O-12			56.0 CH_3	56.5 CH_3	
CH_3O-13			60.5 CH_3	61.0 CH_3	
CH_3O-14	59.1 CH_3	59.1 CH_3	60.4 CH_3	60.4 CH_3	59.6 CH_3
OCH_2O	100.8 CH_2	100.8 CH_2			100.9 CH_2

[a]Recorded at 100 MHz in $CDCl_3$. [b]Recorded at 125 MHz in $CDCl_3$. [c]Recorded in CD_3OD, 150 MHz.

Table 5. Neuroprotective Effects of Compounds 1, 2, 4−6, 9, and 13−19 on Aβ_{25-35}- or H_2O_2-Induced Cytotoxicity on PC12 Cells[a]

	Aβ_{25-35} (1 μM)				H_2O_2 (300 μM)		
	test concentration (μM)				test concentration (μM)		
compound	1 μM	10 μM	vehicle	compound	1 μM	10 μM	vehicle
1	39.9 ± 1.1	46.4 ± 3.7[c]	38.8 ± 1.0	**1**	55.8 ± 1.9	58.2 ± 0.4	53.7 ± 1.7
2	36.4 ± 0.8	34.1 ± 2.0	34.8 ± 0.8	**2**	55.9 ± 2.4	58.9 ± 0.9[e]	53.1 ± 1.1
4	34.4 ± 0.8	50.0 ± 6.4[c]	34.8 ± 0.8	**4**	50.3 ± 0.5	55.8 ± 0.5	53.1 ± 1.1
5	39.0 ± 1.1	39.7 ± 2.0	38.8 ± 1.0	**5**	57.1 ± 2.6	58.9 ± 3.1[d]	53.7 ± 1.7
6	38.4 ± 0.5	36.4 ± 1.8	38.8 ± 1.0	**6**	55.2 ± 0.4	58.5 ± 2.6	53.7 ± 1.7
9	39.0 ± 0.8	41.2 ± 1.6	38.8 ± 1.0	**9**	53.3 ± 0.8	53.7 ± 1.5	53.7 ± 1.7
13	35.1 ± 0.6	32.9 ± 1.9	34.8 ± 0.8	**13**	57.2 ± 0.4[d]	44.0 ± 2.3[e]	53.1 ± 1.1
14	35.3 ± 0.9	32.3 ± 1.3	34.8 ± 0.8	**14**	53.0 ± 1.3	52.5 ± 0.9	53.1 ± 1.1
15	38.0 ± 0.8	33.3 ± 1.3[b]	38.8 ± 1.0	**15**	48.8 ± 1.3	55.8 ± 0.1	53.7 ± 1.7
16	43.1 ± 1.1	39.3 ± 2.8	38.8 ± 1.0	**16**	54.6 ± 1.6	60.7 ± 1.8[e]	53.7 ± 1.7
17	35.2 ± 0.1	33.2 ± 1.8	34.8 ± 0.8	**17**	51.0 ± 0.9	53.3 ± 1.2	53.1 ± 1.1
18	41.4 ± 0.8	41.0 ± 2.1	38.8 ± 1.0	**18**	50.4 ± 2.8	53.4 ± 0.2	53.7 ± 1.7
19	40.3 ± 1.1	40.8 ± 2.2	38.8 ± 1.0	**19**	54.9 ± 0.6	51.8 ± 1.5	53.7 ± 1.7

[a]The data (cell viability, measured by MTT reduction) were normalized and expressed as a percentage of the control group, which is set to 100%. Data expressed as means ± SEM. Three independent experiments were carried out. [b]$p < 0.05$. [c]$p < 0.01$ vs Aβ_{25-35} group. [d]$p < 0.05$. [e]$p < 0.01$ vs H_2O_2 group. Values higher than corresponding Aβ_{25-35} or H_2O_2 control indicate neuroprotection; values lower than corresponding Aβ_{25-35} or H_2O_2 control mean neurotoxicity.

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399 parameters); maximum and minimum residuals are 1.13 and −0.40 e·Å^{-3}, respectively. The Flack[22] parameter value was x = 0.1(2).

Polysperlignan G (7): $C_{64}H_{76}O_{20}$ ($C_{32}H_{38}O_{10} \times 2$), M_w = 1165.3, orthorhombic, space group, $P2_12_12_1$, Z = 4, a = 10.1503(2) Å, b = 19.3759(3) Å, c = 30.2635(5) Å; $\alpha = \beta = \gamma = 90°$, V = 5951.96(18) Å^3, μ(Cu Kα) = 0.80 mm^{-1}, ρ_{calc} = 1.30 g·cm^{-3}; S = 1.29, final R indices: R_1 = 0.115 and wR_2 = 0.287 for 8293 observed from 10 045 independent and 24 240 measured reflections (θ_{max} = 69.6, $I > 2\sigma(I)$ criterion and 777 parameters); maximum and minimum residuals are 0.79 and −0.82 e·Å^{-3}, respectively. The Flack[22] parameter value was x = −0.1(3).

Neuroprotective Activity Assay. PC12 neuroblastoma cells were digested by trypsin and suspended in DMEM medium (low sugar) containing 10% new bovine serum (Gibco). Cells were seeded into 96-well plates (Greiner) at a density of 8 × 10^4 cells per mL, 100 μL per well, maintained at 37 °C in a constant temperature incubator containing 5% CO_2. Serum-free DMEM medium was used to substitute the original medium 24 h after cells were seeded.

Appropriate concentrations of hydrogen peroxide (H_2O_2) and β-amyloid$_{25-35}$ (Aβ_{25-35}) were prepared on the day of application to cultures. The PC12 cells were preincubated with 1 or 10 μM of the different compounds 2 h before H_2O_2 (300 μM) and Aβ_{25-35} (1 μM) were added, and the assays for cell viability were performed 24 h after H_2O_2 and Aβ_{25-35} were added. Cell survival was evaluated by reduction of MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, Sigma).[23] The values of cell survival were normalized against the values for the control group, which was set to 100%. Data were evaluated for statistical significance with one-way ANOVA followed by a LSD test using a computerized statistical package. Differences were considered significant at $p < 0.05$.

■ ASSOCIATED CONTENT

Supporting Information

This material (^{1}H/^{13}C NMR, DEPT, HSQC, HMBC, COSY, ROESY, HRESIMS, IR, CD, and UV spectra of compounds **1**, **6**, and **8** and ^{1}H/^{13}C NMR, DEPT, and HRESIMS spectra of compounds **2**−**5**, **7**, and **9**−**11**, X-ray data of compounds **1** and **7**) is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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