Lignans with Anti-HIV Activity from *Schisandra propinqua* var. *sinensis*

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Fourteen new lignans, tiegusanins A−N (**1**−**14**), together with 13 known compounds were isolated from the aerial parts of *Schisandra propinqua* var. *sinensis*. The structures and absolute configurations of **1**−**13** were established using a combination of spectroscopic techniques. Compound **14** was obtained as a racemate. When evaluated for inhibitory activity against HIV-1, tiegusanin G (**7**) showed anti-HIV-1 activity with an EC_{50} value of 7.9 μM and a therapeutic index (TI) of more than 25.

The plant family Schisandraceae, consisting of the genera *Schisandra* and *Kadsura*, contains several important medicinal plants. Species of this family have yielded numerous lignans demonstrating various biological activities, including antitumor,[1] cytotoxic,[2−5] anti-HIV,[6,7] antioxidative,[8,9] antihepatitis,[10] and hepatoprotective effects.[11] *Schisandra propinqua* (Wall.) Hook. f. et Thoms. var. *sinensis* Oliv., popularly known as "tie-gu-san" in the Shenlongjia district of mainland China, is used in folk medicine for the treatment of arthritis, traumatic injury, gastralgia, angeitis, and related diseases.[12] Three lignans and one triterpenoid were reported from this species in a previous paper.[2] Motivated by a search for bioactive metabolites from this plant, a reinvestigation of the chemical constituents was carried out. As a result, 27 lignans were isolated, including 14 new substances, tiegusanins A−N (**1**−**14**). The structures of compounds **1**−**14** were established from their spectroscopic data. The absolute configurations of **1**−**13** were determined by CD and ROESY experiments. Most of the compounds were evaluated in an anti-HIV assay, and the results are described herein.

Results and Discussion

A 70% aqueous acetone extract of the aerial parts of *S. propinqua* var. *sinensis* was partitioned between EtOAc and H_2O (1:1). The EtOAc layer was subjected repeatedly to column chromatography on silica gel, MCI gel, Sephadex LH-20, and RP-18 and then purified by HPLC to afford 14 new lignans, tiegusanins A−N (**1**−**14**). Also obtained were 13 known substances, methyl schisantherin F (**15**),[13] kadsurin (**16**),[14] interiotherin C (**17**), [15] (7*S*,8*S*,*R*-biar)-6,6,7,8-tetrahydro-12,13-methylenedioxy-1,2,3,14-tetramethoxy-7,8-dimethyldibenzo[*a*,*c*]cycloocten-9-one (**18**),[16] *meso*-dihydroguaiaretic acid (**19**),[17] *meso*-monomethyldihydroguaiaretic acid (**20**),[18] 4,4′-(2*R*,3*S*)-2,3-dimethylbutane-1,4-diyl)bis(1,2-dimethoxybenzene) (**21**),[19] galgravin (**22**),[20] dimethyltetrahydrofuroguaiacin (**23**),[20] austrobailignan-7 (**24**),[21] (−)-machilusin (**25**),[22] (2*R*,3*S*,4*R*,5*R*)-2-(3,4-dimethoxyphenyl)-3,4-dimethyl-5-piperonyltetrahydrofuran (**26**),[23] and (8*R*,7′*R*,8*R*)-5-hydroxy-4,3′,4′-trimethoxy-2,7′-cyclolignan (**27**).[24] The ^{1}H and ^{13}C NMR spectroscopic data of the new lignans **1**−**14** are listed in Tables 1−5.

In a previous paper, as a modified product of schisantherin F, only ^{1}H NMR data of its five methoxy groups were reported.[13] In the present study, we obtained this compound (**15**) as a new natural product and report its ^{1}H and ^{13}C NMR spectra (Tables 2 and 4) for the first time. The structure and absolute configuration of **15** were established from its extensive NMR spectra and CD data and by single-crystal X-ray analysis (Figure 1). The structural clarification of **15** was very important for the determination of the structures of **1** and **2**, because their NMR spectra were very close to those of **15**.

Tiegusanin A (**1**), obtained as a white powder, showed the molecular ion peak $[M + Na]^+$ at *m*/*z* 525.2445 (calcd 525.2464) in the HRESIMS, corresponding to the molecular formula $C_{28}H_{38}O_8$, requiring 10 degrees of unsaturation. The ^{1}H and ^{13}C NMR spectra of **1** (Tables 1 and 3) indicated the presence of 12 aromatic carbons, two aromatic protons, and five methoxy groups, suggesting the presence of a biphenyl moiety.[25] HMBC correlations of H-11 with C-9, C-10, C-12, C-13, C-15, and C-16, and H-4 with C-2, C-3, C-5, C-6, C-15, and C-16, and ^{1}H−^{1}H COSY correlations of H-6/H-7/H-8, H-7/H_3-17, and H-8/H_3-18 (Figure 2), together with UV absorption bands at 318, 241, 228, and 220 nm and IR absorption bands at 3499 (OH), 1716 (C═O), 1647 (C═C), 1596, 1579 (aromatic ring) cm^{-1} implied that **1** is a dibenzocyclooctadiene lignan possessing a hydroxy group and an ester linkage.[25,26] The signals at δ_C 176.5 s, 41.2 d, 26.6 t, 11.3 q, and 16.5 q suggested the presence of a 2-methylbutyryloxy group (*O*-isovaleryl).[14] Further analysis of the HMBC spectrum showed five methoxy groups to be located at C-2, C-3, C-12, C-13, and C-14, respectively, with two secondary methyl groups (δ_C 15.2 and 20.2) assignable to CH_3-17 and CH_3-18, respectively. Comparison of the NMR data of **1** with those of **15** suggested C-9 of **1** is also substituted by a hydroxy group, and accordingly, the 2-methylbutyryloxy group was located at C-1. Thus, the planar structure of compound **1** was established.

The CD curve of **1** showed a negative Cotton effect around 250 nm and a positive value around 220 nm, suggesting that **1** possesses an *S*-biphenyl configuration,[25] identical to that of **15**.[13] ROESY correlations of H-11 with H-8 and H-9, H-4 with H-6α and H_3-17, H_3-18 with H-9 and H_3-17, and H-8 with H-7 and H-6β (Figure 3) suggested a cyclooctadiene lignan with a twisted boat/chair conformation of **1**, consistent with the absolute configurations of C-7 (*R*), C-8 (*R*), and C-9 (*R*),[9] which were also identical to **15**.[13]

Comparison of the NMR data of **2** and **3** with those of **1** disclosed that the main structural differences between them were the

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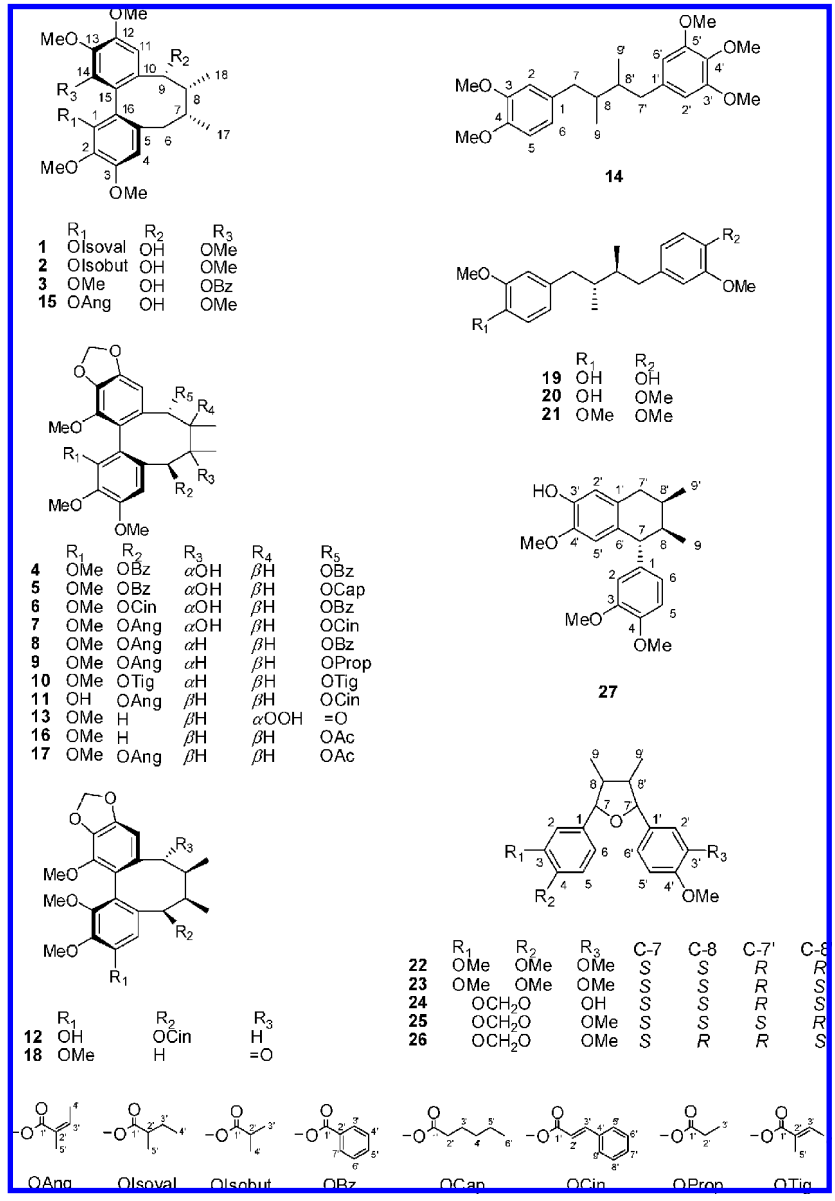
Chart 1



substituent patterns. The ^{1}H and ^{13}C NMR spectra of **2** and **3** (Tables 1 and 3) were quite similar to those of **1**, except that the 2-methylbutyryloxy group in **1** was changed to a 2-methylpropionyloxy group (*O*-isobutyryl, δ_C 176.8 s, 34.0 d, 18.7 q, 18.6 q) in **2**[27] and a benzoyloxy group (δ_C 165.8 s, 129.0 s, 130.2 d, 128.3 d, 133.5 d, 128.3 d, 130.2 d) in **3**.[28] Comparison of the 1D NMR data of **2** with those of **1** and HMBC correlations of the five methoxy groups with C-2, C-3, C-12, C-13, and C-14, respectively, indicated that the 2-methylpropionyloxy group was located at C-1 of **2**. However, the benzoyloxy group in **3** was deduced to be located at C-14 from the observation of HMBC correlations of the five methoxy groups in **3** with C-1, C-2, C-3, C-12, and C-13 (Figure 2) and the close chemical shifts of C-9 with those of **1**. By comparison of CD, UV, and ROESY spectra with those of **1**, compounds **2** and **3** were also assigned as *S*-biphenyl-configured dibenzocyclooctadiene lignans with twisted boat/chair conformations of the cyclooctadiene ring. Therefore, the structures of compounds **2** and **3** were determined as shown.

Tiegusanin D (**4**), obtained as a white, amorphous powder, gave the molecular formula $C_{37}H_{36}O_{11}$ from its HRESIMS data at *m*/*z* 679.2136 $[M + Na]^+$ (calcd 679.2155). The UV spectrum of **4** showed absorption maxima at 241, 226, and 223 nm, indicating this compound also to be a dibenzocyclooctadiene lignan.[25] The ^{1}H and ^{13}C NMR spectra of **4** (Tables 1 and 3) showed signals due to a secondary methyl (δ_H 1.36, 3H, d, J = 7.2 Hz), assignable to the CH_3-18 group, a tertiary methyl (δ_H 1.44, 3H, s), assignable to the CH_3-17 group, a methylenedioxy moiety (δ_H 5.79, 5.67, 1H each, AB), four methoxy groups (δ_H 4.02, 3.41, 3.30, 3.16, 3H each, s) on two aromatic rings, two benzoyl groups (δ_H 7.46−7.52, 4H, m; δ 7.30−7.34, 2H, m; δ 7.24−7.28, 4H, m), and a hydroxy group (δ 2.40, 1H, s). Furthermore, HMBC correlations of four methoxy groups with C-1, 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 H_2-9 with C-12 and C-13. HMBC correlations of H-6 with C═O (δ_C 164.7) and H-9 with C═O (δ_C 164.9) showed the occurrence of two benzoyloxy groups at C-6 and C-9. In addition, HMBC correlations of the hydroxy group with C-7 and C-17 showed the location of this hydroxy group at C-7 (δ_C 74.2). The biphenyl group in **4** was determined to have an *S* configuration from its CD spectrum. The observed ROESY correlations of H-11/H-8, H-9; H-4/H-6, OH-7; H_3-17/H-6, H-8; and H_3-18/H-9, OH-7, as well as the *J* value between H-8 and H-9 ($J_{8,9}$ = 0 Hz, $\Phi_{8,9}$ = 90°), were in agreement with a cyclooctadiene lignan with a twisted boat/chair conformation having C-6 (*S*), C-7 (*S*), C-8 (*S*), and C-9 (*R*) absolute configurations, which were the same as those of

Table 1. ^{1}H NMR Data of Compounds **1**−**7** [$CDCl_3$, δ_H (*J* in Hz)]

position	**1**[a]	**2**[a]	**3**[a]	**4**[a]	**5**[a]	**6**[a]	**7**[b]
4	6.72 (1H, s)	6.71 (1H, s)	6.77 (1H, s)	6.97 (1H, s)	6.84 (1H, s)	6.92 (1H, s)	6.82 (1H, s)
6α	2.67 (1H, dd, 13.5, 7.5)	2.67 (1H, dd, 14.0, 7.5)	2.64 (1H, dd, 17.0, 9.0)	5.99 (1H, s)	5.94 (1H, s)	5.99 (1H, s)	5.65 (1H, s)
6*β*	2.60 (1H, dd, 13.5, 1.5)	2.60 (1H, dd, 14.0, 1.5)	2.57 (1H, dd, 17.0, 2.5)				
7	2.02 (1H, m)	2.04 (1H, m)	2.00 (1H, m)				
8	1.81 (1H, m)	1.82 (1H, m)	1.79 (1H, m)	2.45 (1H, q, 7.2)	2.39 (1H, m)	2.45 (1H, q, 7.2)	2.15 (1H, q, 7.2)
9	4.77 (1H, s)	4.79 (1H, s)	4.80 (1H, s)	6.12 (1H, s)	6.00 (1H, s)	6.12 (1H, s)	5.86[c] (1H, s)
11	6.38 (1H, s)	6.39 (1H, s)	6.33 (1H, s)	6.64 (1H, s)	6.59 (1H, s)	6.64 (1H, s)	6.45 (1H, s)
17	0.98 (3H, d, 7.5)	1.00 (3H, d, 7.5)	1.05 (3H, d, 7.0)	1.44 (3H, s)	1.42 (3H, s)	1.44 (3H, s)	1.32 (3H, s)
18	1.19 (3H, d, 7.5)	1.19 (3H, d, 7.5)	1.22 (3H, d, 7.0)	1.36 (3H, d, 7.2)	1.35[c] (3H, d, 7.0)	1.36 (3H, d, 7.2)	1.24 (3H, d, 7.2)
2′	2.37 (1H, m)	2.55 (1H, m)				5.81[c] (1H, d 16.0)	
3′	1.54 (1H, m) 1.37 (1H, m)	1.06 (3H, d, 7.0)	7.95[c] (1H, m)	7.47[c] (1H, m)	7.46[c] (1H, m)	7.06 (1H, d 16.0)	5.96 (1H, q, 7.2)
4′	0.78 (3H, t, 7.2)	0.91 (3H, d, 7.0)	7.30[c] (1H, m)	7.32[c] (1H, m)	7.32[c] (1H, m)		1.79 (3H, d, 7.2)
5′	0.85 (3H, d, 7.0)		7.46 (1H, m)	7.51 (1H, m)	7.51 (1H, m)	7.36[c] (1H, m)	1.35 (3H, s)
6′			7.30[c] (1H, m)	7.32[c] (1H, m)	7.32[c] (1H, m)	7.32[c] (1H, m)	
7′			7.95[c] (1H, m)	7.47[c] (1H, m)	7.46[c] (1H, m)	7.51[c] (1H, m)	
8′						7.32[c] (1H, m)	
9′						7.36[c] (1H, m)	
2″					1.79 (2H, m)		5.74 (1H, d 16.0)
3″				7.26[c] (1H, m)	1.31[c] (2H, m)	7.47[c] (1H, m)	6.99 (1H, d 16.0)
4″				7.25[c] (1H, m)	1.14 (2H, m)	7.46[c] (1H, m)	
5″				7.46[c] (1H, m)	1.21 (2H, m)	7.51[c] (1H, m)	7.31[c] (1H, m)
6″				7.25[c] (1H, m)	0.83 (3H, d, 7.0)	7.46[c] (1H, m)	7.31[c] (1H, m)
7″				7.26[c] (1H, m)		7.47 (1H, m)	7.31[c] (1H, m)
8″							7.31[c] (1H, m)
9″							7.31[c] (1H, m)
OMe-1			3.56 (3H, s)	3.16 (3H, s)	3.60 (3H, s)	3.46 (3H, s)	3.39 (3H, s)
OMe-2	3.86 (3H, s)	3.78 (3H, s)	3.81 (3H, s)	3.41 (3H, s)	3.86 (3H, s)	3.61 (3H, s)	3.57 (3H, s)
OMe-3	3.89 (3H, s)	3.89 (3H, s)	3.92 (3H, s)	4.02 (3H, s)	3.95 (3H, s)	4.00 (3H, s)	3.93 (3H, s)
OMe-12	3.85 (3H, s)	3.86[c](3H, s)	3.77 (3H, s)				
OMe-13	3.79 (3H, s)	3.86[c] (3H, s)	3.64 (3H, s)				
OMe-14	3.60 (3H, s)	3.58 (3H, s)		3.30 (3H, s)	3.31 (3H, s)	3.32 (3H, s)	3.67 (3H, s)
OCH_2O-12,13				5.79 (1H, s) 5.67 (1H, s)	5.77 (1H, s) 5.63 (1H, s)	5.79[c] (1H, s) 5.65 (1H, s)	5.87 (1H, s) 5.86[c] (1H, s)

[a] 500 MHz. [b] 400 MHz. [c] Overlapped.

kadangusin C.[29] Therefore, the structure of tiegusanin D (**4**) was established as shown.

Analysis of the 2D NMR data of tiegusanins E−G (**5**−**7**) and comparison of their 1D NMR data with those of **4** revealed that the main structure differences between these compounds were the substituent patterns at C-6 and C-9. The ^{1}H and ^{13}C NMR spectra of **5** (Tables 1 and 3) were quite similar to those of **4** except for the characteristic signals due to a benzoyloxy group and a caproyloxy group (δ_C 171.7 s, 33.7 t, 24.1 t, 22.2 t, 31.0 t, 13.8 t). These two substituents were determined to be located at C-6 and C-9, respectively, by HMBC correlations of H-6 with C-1′ (δ_C 164.7) and H-9 with C-1″ (δ_C 171.7).[10] Similarly, the ^{1}H and ^{13}C NMR spectra of **6** (Tables 1 and 3) were very close to those of **4** except for the characteristic signals due to a benzoyloxy group and a *trans*-cinnamate moiety (δ_C 164.7 s, 116.8 d, 145.5 d, 133.7 s, 128.1 d, 127.9 d, 130.6 d, 127.9 d, 128.1 d) at C-6 and C-9, instead of two benzoyl groups.[31] HMBC correlations of H-6 with C-1′ (δ_C 164.7) and H-9 with C-1″ (δ_C 164.9) in **6** established the locations of the *trans*-cinnamate moiety at C-6 and the benzoyloxy group at C-9. Comparison of the ^{1}H and ^{13}C NMR spectra between **7** (Tables 1 and 3) and **6** suggested the close similarity of these compounds. In **7**, an angeloyloxy group (δ_C 165.8 s, 126.9 s, 139.9 d, 15.5 q, 19.7 q) was located at C-6 and a *trans*-cinnamate moiety at C-9, from the HMBC correlations of H-6 with C-1′ (δ_C 165.8) and H-9 with C-1″ (δ_C 165.0), respectively. Accordingly, tiegusanin G (**7**) was determined structurally as shown.

Both tiegusanins H (**8**) and I (**9**) were isolated as white, amorphous powders. Their molecular formulas, $C_{35}H_{38}O_{10}$ and $C_{31}H_{38}O_{10}$, were determined by HRESIMS (*m*/*z* 641.2359 $[M + Na]^+$ and 593.2370 $[M + Na]^+$, respectively). The ^{1}H and ^{13}C NMR spectra (Tables 2 and 4), together with their CD, UV, and IR data, suggested that **8** and **9** are also *S*-biphenyl-configured dibenzocyclooctadiene lignans.[25] Comparison of the spectroscopic data of **8** and **9** with those of **7** revealed the presence of a benzoyloxy group at C-9 in **8** and a propionyl group (δ_C 173.6, 27.1, 8.6) at C-9 in **9**, by analysis of their HMBC spectra. In addition, no hydroxy group occurred at C-7 in either **8** or **9**, consistent with the significant upfield chemical shifts of C-7 and C-17 and the noticeable change of H_3-17 from single peaks to doublets. Furthermore, the orientations of all substituents in **8** and **9** were the same as those in **7**, from the ROESY experiments.

Tiegusanin J (**10**) gave a molecular formula of $C_{33}H_{40}O_{10}$ by HRESIMS at *m*/*z* 619.2522 $[M + Na]^+$ (calcd 619.2519). The NMR data indicated that **10** (Tables 2 and 4) is an analogue of **9** with two tiglyloxy groups substituted at C-6 and C-9. Tiegusanin K (**11**) was shown to differ from **8** by the replacement of the C-9 benzoyloxy group in **8** with a *trans*-cinnamate group, and the C-1 methoxy group in **8** with a hydroxy group. The ROESY experiment

Table 2. ^{1}H NMR Data of Compounds **8**−**13** and **15** [$CDCl_3$, δ_H (J in Hz)]

position	**8**[b]	**9**[b]	**10**[b]	**11**[a]	**12**[b]	**13**[a]	**15**[a]
4	6.84 (1H, s)	6.70 (1H, s)	6.73 (1H, s)	6.61 (1H, s)	6.93 (1H, s)	6.42 (1H, s)	6.69 (1H, s)
6α	5.98[c] (1H, d, 8.0)	5.83 (1H, d, 8.0)	5.89[c] (1H, d 8.0)	5.86[c] (1H, d 9.0)	5.61 (1H, s)	2.43 (1H, dd 17.5, 9.0)	2.65 (1H, dd, 13.5, 7.5)
6β						3.11 (1H, dd 17.5, 2.0)	2.58 (1H, dd, 13.5, 1.5)
7	2.23 (1H, m)	2.21 (1H, m)	2.16 (1H, m)	2.20 (1H, m)	2.10 (1H, m)	2.37 (1H, m)	2.00 (1H, m)
8	2.35 (1H, m)	2.12 (1H, m)	2.26 (1H, m)	2.31 (1H, m)	2.04[c] (1H, m)		1.81 (1H, m)
9	6.06 (1H, d, 3.6)	5.74 (1H, d, 3.2)	5.83 (1H, d, 3.2)	5.79 (1H, d, 3.5)	2.18 (1H, m) 2.02[c] (1H, m)		4.75 (1H, s)
11	6.56 (1H, s)	6.44 (1H, s)	6.49 (1H, s)	6.55 (1H, s)	6.49 (1H, s)	6.66 (1H, s)	6.35 (1H, s)
17	0.87 (3H, d, 6.8)	0.84[c] (3H, d, 6.8)	1.05 (3H, d, 6.8)	1.01 (3H, d, 7.0)	0.80 (3H, d, 6.8)	0.80 (3H, d, 7.5)	0.98 (3H, d, 7.0)
18	1.05 (3H, d, 6.8)	0.93 (3H, d, 6.8)	0.97 (3H, d, 6.8)	1.10 (3H, d, 7.0)	1.01 (3H, d, 6.8)	1.45 (3H, s)	1.17 (3H, d, 7.0)
2′					6.45 (1H, d 16.0)		
3′	5.97[c] (1H, m)	5.95[c] (1H, m)	5.92[c] (1H, m)	5.96[c] (1H, m)	7.63 (1H, d 16.0)		5.92 (1H, q, 7.2)
4′	1.86 (3H, d, 6.8)	1.85[c] (3H, d, 6.8)	1.59 (3H, d, 6.8)	1.87 (3H, d, 7.5)			1.72 (3H, d, 7.2)
5′	1.51 (3H, s)	1.49 (3H, s)	1.48[c] (3H, s)	1.52 (3H, s)	7.52[c] (1H, m)		1.78 (3H, s)
6′					7.38[c] (1H, m)		
7′					7.38[c] (1H, m)		
8′					7.38[c] (1H, m)		
9′					7.52[c] (1H, m)		
2″		1.80[c] (2H, m)		5.84[c] (1H, d 16.0)			
3″	7.34[c] (1H, m)	0.85[c] (3H, t, 6.8)	5.92[c] (1H, m)	7.12 (1H, d 16.0)			
4″	7.26[c] (1H, m)		1.84 (3H, d, 6.8)				
5″	7.45 (1H, m)		1.48[c] (3H, s)	7.36[c] (1H, m)			
6″	7.26[c] (1H, m)			7.35[c] (1H, m)			
7″	7.34[c] (1H, m)			7.37[c] (1H, m)			
8″				7.35[c] (1H, m)			
9″				7.36[c] (1H, m)			
OMe-1	3.10 (3H, s)	3.10 (3H, s)	3.31 (3H, s)		3.56 (3H, s)	3.51 (3H, s)	
OMe-2	3.52 (3H, s)	3.52 (3H, s)	3.82 (3H, s)	3.64 (3H, s)	3.95 (3H, s)	3.86 (3H, s)	3.76 (3H, s)
OMe-3	3.98 (3H, s)	3.98 (3H, s)	3.90 (3H, s)	3.94 (3H, s)		3.83 (3H, s)	3.86 (3H, s)
OMe-12							3.81 (3H, s)
OMe-13							3.78 (3H, s)
OMe-14	3.76 (3H, s)	3.76 (3H, s)	3.75 (3H, s)	3.80 (3H, s)	3.79 (3H, s)	3.87 (3H, s)	3.52 (3H, s)
OCH_2O-12,13	5.97[c] (1H, s) 5.95[c] (1H, s)	5.93[c] (1H, s) 5.93[c] (1H, s)	5.93[c] (1H, s) 5.92[c] (1H, s)	5.96[c] (1H, s) 5.94[c] (1H, s)	5.97 (1H, s) 5.97 (1H, s)	6.04 (1H, s) 6.02 (1H, s)	

[a] 500 MHz. [b] 400 MHz. [c] Overlapped.

revealed that all of the substituents in **11** have the same orientations as those in **9**, except for CH_3-17. Correlations of H-4 with H_3-17 suggested that CH_3-17 should have an α-orientation in **11**. However, H-4 showed no correlations with H_3-17, indicating that CH_3-17 is β-oriented in **9**.

Tiegusanin L (**12**) was obtained as a yellow, amorphous solid. Comparison of the NMR data between **12** and **11** (Tables 2 and 4), in combination with the molecular formula $C_{31}H_{32}O_8$, deduced from HRESIMS at m/z 555.1992 $[M + Na]^+$ (calcd 555.1994), showed that **12** is also a dibenzocyclooctadiene lignan structurally similar to **11**. The main differences found were the positions of substituents of the OH group at C-3 in **12** instead of C-1 in **11** and the *trans*-cinnamate group at C-6 in **12** instead of C-9 in **11**. However, the CD spectrum of **12** showed a negative Cotton effect around 220 nm and a positive value around 250 nm, suggesting that **12** possesses an *R*-biphenyl configuration.[25] The absolute configuration of **12** was determined by means of a ROESY experiment and comparison with that of gomisin A.[25] The ROESY correlations of H-11/H-9α, H-4/H_3-17, and H_3-17/H_3-18 in **12**, instead of H-11/H_3-18 and H-4/H-6β in **11**, indicated that the *trans*-cinnamate group and two methyls are all β-oriented. These were in agreement with a cyclooctadiene lignan with a twisted boat/chair conformation having C-6 (*R*), C-7 (*R*), and C-8 (*R*) absolute configurations.

Tiegusanin M (**13**) was obtained as a brown gum. The ^{1}H and ^{13}C NMR spectra of **13** (Tables 2 and 4) were similar to those of schisanlignone A,[30] except that **13** was observed to have an OCH_2O group in the aromatic ring and an OOH functionality in the cyclooctadiene ring, as supported by a series of characteristic ion peaks at m/z 469 $[M + Na]^+$, 447 $[M + H]^+$, 429 $[M - OH]^+$, and 413 $[M - OOH]^+$ in the ESIMS. The hydroperoxy group was assigned at C-8 because the signals at δ_H 0.99 (3H, d, $J = 6.8$ Hz, δ_C 15.0, q) and δ_H 2.62 (1H, m, δ_C 40.8, d) due to CH_3-18 and CH-8 in schisanlignone A[30] were shifted downfield to δ_H 1.57 (3H, s, δ_C 17.6, q) and δ_C 92.2 (s) in **13**. HMBC correlations of H_3-18 (δ 1.57) with C-7 (δ 37.2), C-8 (δ 92.2), and C-9 (δ 206.9) supported the above assignment. The OCH_2O attached to C-12 and C-13 was confirmed by the correlations of H_2-19 (δ 6.03) with C-12 (δ 148.4) and C-13 (δ 137.1). The CD spectrum of **13** showed a negative Cotton effect around 250 nm and a positive value around 220 nm, suggesting this compound possesses an *S*-biphenyl configuration, the same as those of schisantherin Q and yunnankadsurin A.[33,34] Comparison of the spectroscopic data of **13** and other dibenzocyclooctadiene lignans with a C-6 or C-9 oxo substitution[31−33] revealed that the cyclooctadiene ring possesses a stable twisted boat conformation and that two methyl groups are both α-oriented in **13**. These methyl groups of **13** appeared at δ_C 17.6 and 14.3, which differ from those of dibenzocyclooctadiene lignans possessing a

Table 3. ^{13}C NMR Data of Compounds **1**−**7** ($CDCl_3$)

position	**1**[a]	**2**[a]	**3**[b]	**4**[b]	**5**[a]	**6**[b]	**7**[a]
1	141.5 s	141.6 s	151.2 s	151.6 s	151.4 s	151.5 s	151.3 s
2	138.9 s	139.0 s	139.1 s	141.6 s	141.2 s	141.5 s	141.4 s
3	151.3 s	151.3 s	151.5 s	152.2 s	152.0 s	151.8 s	151.8 s
4	113.0 d	113.0 d	113.0 d	110.5 d	110.3 d	110.4 d	110.5 d
5	134.6 s	134.6 s	134.6 s	129.4[c] s	129.4 s	129.4[c] s	129.8 s
6	38.8 t	38.8 t	38.8 t	85.2 d	85.2 d	85.2 d	84.8 d
7	35.3 d	35.2 d	35.2 d	74.2 s	74.0 s	74.0 s	74.0 s
8	43.1 d	43.1 d	42.9 d	43.5 d	43.3 d	43.4 d	43.2 d
9	83.0 d	83.0 d	83.1 d	83.8 d	83.2 d	83.2 d	83.3 d
10	140.8 s	140.6 s	140.8 s	132.5 s	133.6 s	132.6 s	132.5 s
11	106.8 d	106.8 d	106.8 d	102.0 d	101.8 d	101.8 d	102.2 d
12	153.0 s	152.9 s	152.6 s	148.8 s	148.8 s	148.8 s	148.8 s
13	140.4 s	140.4 s	140.3 s	135.8 s	135.5 s	135.6 s	135.7 s
14	151.5 s	151.5 s	141.8 s	140.7 s	140.5 s	140.6 s	140.9 s
15	119.2 s	119.2 s	119.1 s	120.5 s	120.3 s	120.4 s	120.6 s
16	123.0 s	122.9 s	123.0 s	122.2 s	121.9 s	122.2 s	122.2 s
17	15.2 q	15.2 q	15.2 q	28.9 q	28.8 q	28.8 q	28.7 q
18	20.2 q	20.1 q	20.3 q	17.1 q	17.1 q	17.1 q	16.9 q
1′	176.5 s	176.8 s	165.8 s	164.7 s	164.7 s	164.7 s	165.8 s
2′	41.2 d	34.0 d	129.0 s	129.3 s	128.6 s	116.8 d	126.9 s
3′	26.6 t	18.7 q	130.2[c] d	129.4[c] d	129.6[c] d	145.5 d	139.9 d
4′	11.3 q	18.6 q	128.3[c] d	127.9[c] d	127.9[c] d	133.7 s	15.5 q
5′	16.5 q		133.5 d	133.0 d	132.9 d	128.1[c] d	19.7 q
6′			128.3[c] d	127.9[c] d	127.9[c] d	127.9[c] d	
7′			130.2[c] d	129.4[c] d	129.6[c] d	130.6 d	
8′						127.9[c] d	
9′						128.1[c] d	
1″				164.9 s	171.7 s	164.9 s	165.0 s
2″				128.7 s	33.7 t	129.3 s	116.7 d
3″				129.1[c] d	24.1 t	128.9[c] d	145.6 d
4″				128.4[c] d	22.2 t	129.4[c] d	133.7 s
5″				133.5 d	31.0 t	133.0 d	128.1[c] d
6″				128.4[c] d	13.8 q	129.4[c] d	128.8[c] d
7″				129.1[c] d		128.9[c] d	130.6 d
8″							128.8[c] d
9″							128.1[c] d
OMe-1			60.8 q	60.0 q	60.5 q	60.3 q	60.2 q
OMe-2	60.7[c] q	61.1 q	61.3 q	59.9 q	60.4 q	60.4 q	60.3 q
OMe-3	56.0 q	56.0[c] q	56.0 q	56.1 q	56.0 q	56.0 q	55.9 q
OMe-12	56.0 q	56.0[c] q	55.8 q				
OMe-13	61.1 q	60.8 q	60.6 q				
OMe-14	60.7[c] q	60.7 q		58.8 q	58.7 q	58.8 q	59.0 q
OCH_2O-12,13				100.9 t	100.8 t	100.8 t	101.0 t

[a] 125 MHz. [b] 100 MHz. [c] Overlapped.

twisted boat/chair conformation of the cyclooctadiene ring. Commonly, the chemical shifts of two methyl groups in lignans possessing a twisted boat conformation are close, while the analogous values for compounds having a twisted boat/chair conformation have greater differences.[6,33,34] The above analysis indicated that **13** possesses a twisted boat conformation having C-7 (*R*) and C-8 (*S*) absolute configurations. Therefore, the structure of tiegusanin M (**13**) was determined as shown.

Tiegusanin N (**14**) was obtained as a white, amorphous solid. Its molecular formula was determined as $C_{23}H_{32}O_5$ by the HRESIMS at *m*/*z* 411.2155 $[M + Na]^+$ (calcd 411.2147). The functional group signals appearing in the ^1H and ^{13}C NMR spectra included two aromatic rings, five methoxy groups, two methyl groups, two methylene groups, and seven methine groups. The strong IR absorption bands indicated the presence of aromatic rings (1590, 1514, and 1462 cm^{-1}). HMBC correlations found from H-2 and H-6 to C-7 and from H-2′ and H-6′ to C-7′ implied that the two substituted aromatic moieties were not linked directly (Figure 2). Moreover, the HMBC correlations of H_3-9 with C-7, C-8, and C-8′, of H_3-9′ with C-7′, C-8′, and C-8, of H_2-7 with C-1, C-2, C-6, C-8, and C-9, and of H_2-7′ with C-1′, C-2′, C-6′, C-8′, and C-9′, together with the spin systems of H-7/H-8/H-8′/H-7′, H-8/H-9, and H-8′/H-9′ in the $^1H-^1H$ COSY spectrum, suggested that **14** is a substituted 1,4-biphenyl-2,3-dimethylbutane-type lignan (Figure 2).[35] The correlations from the protons of five methoxy groups to C-3, C-4, C-3′, C-4′, and C-5′ were used to locate these groups at C-3, C-4, C-3′, C-4′, and C-5′, respectively. Since the C−C bonds can rotate randomly, the relative configuration of **14** could not be determined on the basis of ROESY spectra. Thus, the structure of tiegusanin N (**14**) was established as shown.

The lignans from *S. propinqua* var. *sinensis* were tested for their ability to prevent the cytopathic effects of HIV-1 in C8166 cells, and their cytotoxicity was measured in parallel with the determination of antiviral activity, using AZT as a positive control (Table 6). Among the compounds tested, **7** exhibited the most potent anti-HIV-1 activity, with an EC_{50} of 7.9 μM, a CC_{50} value of more than 200 μM, and therefore a TI of greater than 25. Compounds **8**, **12**, **15**, and **17** and the epimeric diastereomers **22** and **23** (1:1) showed weak to moderate anti-HIV activity (Table 6). Compounds **2**, **11**, **13**, and **26** were not tested for their bioactivity due to the limited amounts available.

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. CD spectra were measured on a JASCO J-810 spectropolarimeter. A Tenor 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. Unless otherwise specified, chemical shifts (δ) are expressed in ppm with reference to the solvent signals. HRESIMS was performed on an API QSTAR time-

Table 4. ^{13}C NMR Data of Compounds **8**−**13** and **15** ($CDCl_3$)

position	**8**[a]	**9**[b]	**10**[b]	**11**[a]	**12**[a]	**13**[b]	**15**[a]
1	151.8 s	151.6 s	151.7 s	147.5 s	151.5 s	151.9 s	141.4 s
2	140.5 s	141.2 s	140.8[c] s	134.8 s	139.9 s	141.4 s	138.8 s
3	152.1 s	151.8 s	151.8 s	150.3 s	149.5 s	152.1 s	151.1 s
4	110.6 d	110.4 d	110.3 d	107.2 d	110.6 d	111.1 d	112.8 d
5	131.1 s	131.2 s	131.0 s	131.5 s	135.0 s	131.1 s	134.4 s
6	80.7 d	80.7[c] d	80.6 d	80.9 d	77.2 d	34.4 t	38.7 t
7	38.4 d	38.6[c] d	38.1 d	38.8[c] d	41.9 d	37.2 d	35.1 d
8	39.5 d	38.6[c] d	38.4 d	38.8[c] d	40.4 d	92.2 s	42.9 d
9	82.0 d	80.7[c] d	81.3 d	80.9 d	36.1 t	206.9 s	82.9 d
10	136.2 s	133.2 s	133.6 s	133.9 s	139.0 s	135.5 s	140.7 s
11	102.6 d	102.3 d	102.6 d	102.8 d	104.8 d	99.6 d	106.6 d
12	148.7 s	148.6 s	148.6 s	148.8 s	150.7 s	148.4 s	152.7 s
13	136.8 s	135.9 s	135.7 s	136.2 s	137.0 s	137.1 s	140.2 s
14	141.8 s	141.7 s	142.6[c] s	142.4 s	142.5 s	140.8 s	151.3 s
15	121.3 s	121.1 s	121.1 s	120.0 s	121.4 s	118.5 s	119.3 s
16	119.8 s	123.1 s	124.0 s	116.2 s	122.3 s	122.0 s	123.1 s
17	15.6[c] q	8.6[c] q	8.9 q	15.6[c] q	10.0 q	14.3 q	15.0 q
18	19.9[c] q	15.6[c] q	19.8 q	22.3 q	23.3 q	17.6 q	20.1[c] q
1′	166.8 s	166.7 s	166.8 s	166.8 s	167.0 s		167.0 s
2′	127.8 s	127.8 s	127.6[c] s	127.8 s	120.0 d		127.1 s
3′	139.0 d	138.4 d	138.2[c] d	138.4 d	146.1 d		138.6 d
4′	15.6[c] q	15.6[c] q	14.2 q	15.6[c] q	135.9 s		15.2 q
5′	19.9[c] q	19.8 q	11.7[c] q	19.9 q	129.5[c] d		20.1[c] q
6′					130.3[c] d		
7′					131.6 d		
8′					130.3[c] d		
9′					129.5[c] d		
1″	165.8 s	173.6 s	167.2 s	165.9 s			
2″	133.7 s	27.1 t	127.6[c] s	117.8 d			
3″	129.6[c] d	8.6[c] q	138.2[c] d	144.3 d			
4″	128.1[c] d		15.6 q	134.4 s			
5″	133.0 d		11.7[c] q	128.7[c] d			
6″	128.1[c] d			128.0[c] d			
7″	129.6[c] d			130.1 d			
8″				128.0[c] d			
9″				128.7[c] d			
OMe-1	59.8 q	60.2 q	59.4 q		61.4 q	60.6 q	
OMe-2	60.2 q	60.5 q	59.7 q	60.5 q	62.4 q	59.9 q	60.8 q
OMe-3	56.1 q	56.0 q	55.9 q	55.8 q		55.8 q	55.8 q
OMe-12							55.8 q
OMe-13							60.5[c] q
OMe-14	59.4 q	59.2 q	60.5 q	59.5 q	61.6 q	61.1 q	60.5[c] q
OCH_2O-12,13	101.1 t	101.0 t	101.0 t	101.1 t	102.4 t	101.4 t	

[a] 125 MHz. [b] 100 MHz. [c] Overlapped.

of-flight mass spectrometer. Semipreparative 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 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 Si gel plates sprayed with 5% H_2SO_4 in EtOH.

Plant Material. The aerial parts of *S. propinqua* var. *sinensis* were collected in the Erlang Mountain area of Sichuan Province, People's Republic of China, in September 2007. The sample was identified by Prof. Xi-Wen Li, and a voucher specimen (KIB-07-09-23) has been deposited in the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation. The air-dried and powdered aerial parts of *S. propinqua* var. *sinensis* (17 kg) were extracted four times with 70% aqueous Me_2CO (4 × 50 L) at room temperature and filtered to yield a filtrate, which was evaporated under reduced pressure and partitioned with EtOAc (4 × 10 L). The EtOAc partition (320 g) was applied to silica gel (200−300 mesh) column chromatography eluting with $CHCl_3$−MeOH (1:0−0:1 gradient system), to give four fractions, 1−4. Fraction 1 was decolorized on MCI gel, eluted with 90% MeOH−H_2O, to yield a brown gum (86 g). The gum was subjected to silica gel column chromatography, eluted with petroleum ether−acetone (9:1−1:1), and yielded fractions 1.1−1.7. Fraction 1.1 (9.5 g) was applied to a Sephadex LH-20 column, using $CHCl_3$−MeOH (1:1) as eluant, to afford fractions 1.1.1−1.1.5. Fraction 1.1.1 (292 mg) provided **12** (4 mg) after being chromatographed over RP-18 (60%−80% MeOH−H_2O gradient system) and normal-phase silica gel (petroleum ether−EtOAc, 15:1−2:1 gradient system). Further purification by semipreparative HPLC with 75% MeOH−H_2O yielded **1** (4 mg), **2** (1 mg), **3** (5 mg), and **15** (93 mg). Fraction 1.1.2 (1.8 g) was further separated (fractions 1.1.2.1−1.1.2.3) using a RP-18 column (50%−100% MeOH−H_2O gradient system). Fraction 1.1.2.1 (62 mg) was purified over silica gel (petroleum ether−Me_2CO, 6:1) to furnish **18** (31 mg) and **25** (1 mg). Fraction 1.1.2.2 (32 mg) was chromatographed by semipreparative HPLC with 70% MeOH−H_2O to yield **16** (3 mg) and **26** (2 mg). Compound **25** (608 mg) was precipitated from fraction 1.1.2.3 (731 mg), and the mother liquor was passed over a silica gel column, eluted with petroleum ether−Me_2CO (4:1), and then purified by semipreparative HPLC with 68% MeOH−H_2O, to obtain **8** (2 mg), **12** (3 mg), and **15** (16 mg). Fraction 1.1.3 (1.1 g) was applied to RP-18, eluted with a 50%−100% MeOH−H_2O gradient system, to afford fractions 1.1.3.1−1.1.3.3. Fractions 1.1.3.1 (14 mg) and 1.1.3.2 (51 mg) gave **13** (1 mg) and **24** (21 mg), respectively, after being chromatographed over silica gel developed with petroleum ether−EtOAc (7:3). Compounds **20** (6 mg) and **25** (3 mg) were obtained from fractions 1.1.3.3 by semipreparative HPLC with 78% MeOH−H_2O. Fraction A2 (2.4 g) was subjected to Sephadex LH-20 column chromatography using $CHCl_3$−MeOH (1:1) for elution to afford fractions 1.2.1−1.2.6. Fraction 1.2.1 (522 mg) was further separated into eight fractions, 1.2.1.1−1.2.1.8, using RP-18 eluted with a 50%−100% MeOH−H_2O gradient system. Compounds **5** (10 mg), **16** (35 mg), and **17** (35 mg) were obtained from fractions 1.2.1.2, 1.2.1.4, and 1.2.1.6, respectively, by evaporating the eluant under reduced pressure. Fraction 1.2.1.1 (47 mg) was purified over silica gel (petroleum

Table 5. ^{1}H (400 MHz) and ^{13}C NMR (125 MHz) Data of Compound **14** ($CDCl_3$)

position	δ_H (J in Hz)	δ_C
1		134.4 s
2	6.65 (1H, s)	112.3 d
3		148.8 s
4		147.1 s
5	6.78 (1H, d, 7.9)	111.1 d
6	6.70 (1H, d, 7.9)	121.0 d
7	2.74[a] (1H, dd, 13.2, 4.9)	38.9 t
	2.33 (1H, dd, 13.2, 9.2)	
8	1.80 (1H, m)	39.0 d
9	0.85 (3H, d, 9.6)	16.2 q
1′		137.7 s
2′	6.34[a] (1H, s)	106.0[a] d
3′		153.0[a]s
4′		136.0 s
5′		153.0[a] s
6′	6.34[a] (1H, s)	106.0[a] d
7′	2.74[a] (1H, dd, 13.2, 4.9)	39.6 t
	2.28 (1H, dd, 13.2, 8.6)	
8′	1.80 (1H, m)	39.2 d
9′	0.85 (3H, d, 9.6)	16.3 q
OMe-3	3.85[a] (3H, s)	55.8 q
OMe-4	3.85[a] (3H, s)	55.9 q
OMe-3′	3.83[a] (3H, s)	56.0[a] q
OMe-4′	3.82 (3H, s)	60.9 q
OMe-5′	3.83[a] (3H, s)	56.0[a] q

[a] Overlapped.

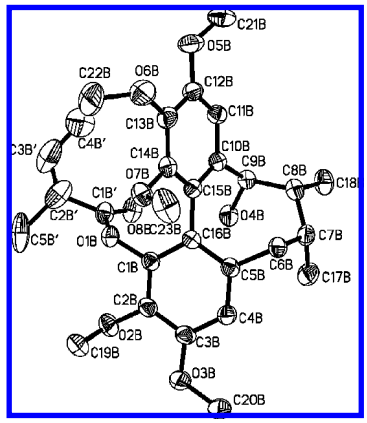


Figure 1. X-ray crystal structure of compound **15**.

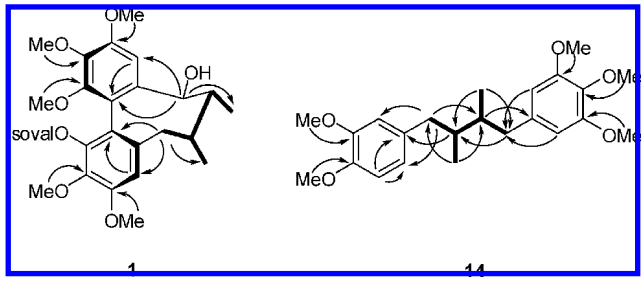


Figure 2. Selected HMBC (→) and ^{1}H−^{1}H COSY (—) correlations of **1** and **14**.

ether−Me_2CO, 4:1) to give **17** (10 mg). After being chromatographed by semipreparative HPLC (70% MeOH−H_2O), fraction 1.2.1.5 (54 mg) gave **7** (5 mg), **9** (9 mg), and **14** (2 mg) and fraction 1.2.1.7 (48 mg) provided **21** (4 mg). Fraction 1.2.2 (1.0 g) was subjected to passage over a reversed-phase column (RP-18), eluting with MeOH−H_2O (30%−90%), to afford compound **20** (20 mg). The remaining portion of this fraction was purified over silica gel (petroleum ether−Me_2CO, 4:1), then by semipreparative HPLC with 65% MeOH−H_2O, to yield **19** (10 mg), **20** (20 mg), and **27** (2 mg). After repeated column chromatography (silica gel, petroleum ether−Me_2CO, 9:1−2:1 gradient system), followed by a reversed-phase column chromatography (RP-18), eluting with MeOH−H_2O (40%−90%), fraction 1.2.3 (932 mg) afforded **19** (123 mg) and **25** (5 mg). Compounds **22** and **23** (5.2 g) were crystallized as a pair of epimeric diastereomers from fraction 1.3 (6.8 g), and the mother liquor was passed through a silica gel column, eluted with a gradient system (petroleum ether−2-propanol, 10:1−2:1), to yield **23** (20 mg), with the remainder purified by semipreparative HPLC (60% MeOH−H_2O), to give compounds **4** (11 mg), **6** (6 mg), **10** (5 mg), and **11** (2 mg).

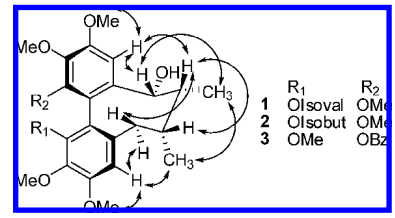


Figure 3. Key ROESY correlations of compounds **1**−**3**.

Table 6. Anti-HIV-1 Activities of Lignans from *S. propinqua* var. *sinensis*

compound	CC_{50}[a] (μM)	EC_{50}[b] (μM)	TI (CC_{50}/EC_{50})
1	>200	29.8	>6.7
3	>200	18.5	>10.8
4	>200	22.9	>8.7
5	118.7	28.7	4.1
6	>200	51.4	>3.9
7	>200	7.9	>25.2
8	78.2	15.4	5.1
9	109.0	14.8	7.4
10	63.5	9.1	7.0
12	74.1	7.3	10.2
14	24.5	9.4	2.6
15	>200	15.7	>12.7
16	>200	79.1	>2.5
17	>200	9.9	>20.2
18	>200	20.4	>9.8
19	24.9	4.0	6.2
20	17.2	2.9	5.8
21	28.8	14.8	2.0
22	43.4	7.7	5.6
22 + **23**[c]	107.7	10.0	10.8
24	19.9	6.8	2.9
25	104.4	15.5	6.7
27	30.0	4.5	6.7
AZT	>1000	1.95×10^{-3}	>500 000

[a] Cytotoxicity against C8166 cells. [b] Inhibition assay for the cytopathic effects of HIV-1_{IIIB}. [c] Epimeric diastereomers **22** and **23** (1:1).

Tiegusanin A (1): white powder; $[\alpha]^{26.7}_D$ 0 (*c* 0.12, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ε) 242 (3.90), 227 (3.58), 208 (3.48), 200 (3.49) nm; CD (MeOH) λ_{max} nm ($\Delta\varepsilon$) 248 (−45.06), 236 (−54.33), 217 (+72.62); IR (KBr) ν_{max} 3499, 2964, 2936, 2874, 1726, 1597, 1496, 1457, 1415, 1386, 1320, 1248, 1198, 1128, 1099, 1009, 989, 930, 849 cm^{-1}; ^{1}H and ^{13}C NMR data, Tables 1 and 2, respectively; HRESIMS (positive ion mode) *m/z* 525.2445 $[M + Na]^+$ (calcd 525.2464 for $C_{28}H_{38}O_8Na$).

Tiegusanin B (2): white powder; $[\alpha]^{26.1}_D$ +24.0 (*c* 0.12, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ε) 241 (3.87), 233 (3.53), 227 (3.54), 223 (3.53), 210 (3.46), 201 (3.47), 198 (3.48) nm; CD (MeOH) λ_{max} nm ($\Delta\varepsilon$) 249 (−31.97), 236 (−35.41), 217 (+50.61); IR (KBr) ν_{max} 3490, 3441, 2964, 2932, 2876, 2854, 1736, 1613, 1597, 1495, 1459, 1407, 1354, 1320, 1267, 1238, 1195, 1125, 1100, 1026, 1009, 989, 932, 849 cm^{-1}; ^{1}H and ^{13}C NMR data, Tables 1 and 2, respectively; HRESIMS (positive ion mode) *m/z* 511.2325 $[M + Na]^+$ (calcd 511.2307 for $C_{27}H_{36}O_8Na$).

Tiegusanin C (3): white powder; $[\alpha]^{28.0}_D$ −57.9 (*c* 0.22, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ε) 241 (4.10), 229 (3.65), 224 (3.64), 208 (3.56), 205 (3.56), 201 (3.57), 199 (3.57), 195 (3.58) nm; CD (MeOH) λ_{max} nm ($\Delta\varepsilon$) 249 (−30.92), 235 (−40.63), 216 (+41.24); IR (KBr) ν_{max} 3504, 2958, 2928, 2873, 2854, 1718, 1598, 1495, 1453, 1408, 1354, 1322, 1278, 1235, 1195, 1126, 1109, 1027, 1006, 990, 931, 848 cm^{-1}; ^{1}H and ^{13}C NMR data, Tables 1 and 2, respectively; HRESIMS (positive ion mode) *m/z* 545.2148 $[M + Na]^+$ (calcd 545.2151 for $C_{30}H_{34}O_8Na$).

Tiegusanin D (4): white, amorphous powder; $[\alpha]^{20.9}_D$ −200.0 (*c* 0.22, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ε) 241 (4.24), 226 (3.74), 223 (3.73), 207 (3.70), 200 (3.72) nm; CD (MeOH) λ_{max} nm ($\Delta\varepsilon$) 242 (−45.75), 225 (+1.22); IR (KBr) ν_{max} 3510, 3453, 2975, 2939, 2910, 2838, 1726, 1699, 1623, 1599, 1502, 1463, 1452, 1412, 1371, 1336, 1317, 1255, 1197, 1149, 1104, 1026, 1009, 975, 936, 847 cm^{-1}; ^1H and ^{13}C NMR data, Tables 1 and 2, respectively; HRESIMS (positive ion mode) *m/z* 679.2136 $[M + Na]^+$ (calcd 679.2155 for $C_{37}H_{36}O_{11}Na$).

Tiegusanin E (5): pale yellow, amorphous powder; $[\alpha]^{26.4}_D$ −108.4 (*c* 0.63, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ε) 241 (4.05), 231 (3.57), 226 (3.57), 219 (3.56), 212 (3.53) nm; CD (MeOH) λ_{max} nm ($\Delta\varepsilon$) 244 (−26.70), 225 (+8.54); IR (KBr) ν_{max} 3567, 3428, 2943, 2873, 1742, 1722, 1620, 1598, 1501, 1466, 1412, 1376, 1336, 1274, 1255, 1150, 1107, 1072, 1046, 1012, 974, 938, 713 cm^{-1}; ^1H and ^{13}C NMR data, Tables 1 and 2, respectively; HRESIMS (positive ion mode) *m/z* 673.2614 $[M + Na]^+$ (calcd 673.2624 for $C_{36}H_{42}O_{11}Na$).

Tiegusanin F (6): white powder; $[\alpha]^{21.2}_D$ −180.6 (*c* 0.25, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ε) 399 (1.85), 355 (1.92), 282 (4.04), 240 (4.15), 232 (3.96), 227 (3.96), 221 (3.95), 201 (3.95), 198 (3.96), 195 (3.96) nm; CD (MeOH) λ_{max} nm ($\Delta\varepsilon$) 247 (−21.54), 224 (+2.41); IR (KBr) ν_{max} 3570, 3434, 2978, 2940, 2844, 1720, 1635, 1598, 1501, 1478, 1466, 1452, 1427, 1411, 1372, 1336, 1314, 1272, 1253, 1201, 1151, 1107, 1043, 1011, 979, 937, 852, 769, 712 cm^{-1}; ^1H and ^{13}C NMR data, Tables 1 and 2, respectively; HRESIMS (positive ion mode) *m/z* 705.2328 $[M + Na]^+$ (calcd 705.2311 for $C_{39}H_{38}O_{11}Na$).

Tiegusanin G (7): white powder; $[\alpha]^{21.7}_D$ −47.5 (*c* 0.20, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ε) 283 (3.97), 262 (3.97), 240 (4.13), 210 (3.88), 205 (3.88), 200 (3.88), 194 (3.90), 192 (3.90) nm; CD (MeOH) λ_{max} nm ($\Delta\varepsilon$) 254 (−17.70), 223 (+13.16); IR (KBr) ν_{max} 3571, 3432, 2974, 2940, 2855, 2844, 1718, 1636, 1597, 1501, 1478, 1465, 1412, 1372, 1336, 1272, 1252, 1231, 1201, 1149, 1106, 1070, 1046, 1012, 976, 938, 844, 769 cm^{-1}; ^1H and ^{13}C NMR data, Tables 1 and 2, respectively; HRESIMS (positive ion mode) *m/z* 683.2456 $[M + Na]^+$ (calcd 683.2468 for $C_{37}H_{40}O_{11}Na$).

Tiegusanin H (8): white, amorphous powder; $[\alpha]^{27.0}_D$ −2.7 (*c* 0.18, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ε) 241 (4.12), 230 (3.67), 225 (3.66), 222 (3.66), 214 (3.62), 197 (3.62) nm; CD (MeOH) λ_{max} nm ($\Delta\varepsilon$) 242 (−13.02), 225 (+13.57); IR (KBr) ν_{max} 3430, 2933, 2880, 2854, 1717, 1621, 1598, 1500, 1478, 1463, 1427, 1410, 1372, 1332, 1276, 1252, 1232, 1199, 1151, 1106, 1067, 1043, 967, 936, 845, 714 cm^{-1}; ^1H and ^{13}C NMR data, Tables 3 and 4, respectively; HRESIMS (positive ion mode) *m/z* 641.2359 $[M + Na]^+$ (calcd 641.2362 for $C_{35}H_{38}O_{10}Na$).

Tiegusanin I (9): white powder; $[\alpha]^{22.0}_D$ +55.9 (*c* 0.44, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ε) 241 (4.04), 227 (3.60), 197 (3.56) nm; CD (MeOH) λ_{max} nm (log ε) 245 (−7.70), 224 (+17.01); IR (KBr) ν_{max} 3447, 2973, 2941, 2880, 1737, 1712, 1647, 1622, 1598, 1502, 1478, 1463, 1427, 1412, 1385, 1354, 1334, 1272, 1254, 1232, 1195, 1152, 1106, 1064, 1044, 1017, 968, 936, 843, 765 cm^{-1}; ^1H and ^{13}C NMR data, Tables 3 and 4, respectively; HRESIMS (positive ion mode) *m/z* 593.2370 $[M + Na]^+$ (calcd 593.2362 for $C_{31}H_{38}O_{10}Na$).

Tiegusanin J (10): white powder; $[\alpha]^{26.8}_D$ −3.9 (*c* 0.26, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ε) 241 (4.03), 226 (3.62), 214 (3.58), 199 (3.59), 195 (3.60), 192 (3.61) nm; CD (MeOH) λ_{max} nm (log ε) 244 (−21.62), 226 (+8.65); IR (KBr) ν_{max} 3435, 2965, 2937, 2879, 1708, 1650, 1622, 1597, 1502, 1478, 1462, 1411, 1385, 1333, 1274, 1252, 1232, 1199, 1138, 1106, 1065, 1042, 1017, 971, 940, 842, 734 cm^{-1}; ^1H and ^{13}C NMR data, Tables 3 and 4, respectively; HRESIMS (positive ion mode) *m/z* 619.2522 $[M + Na]^+$ (calcd 619.2519 for $C_{33}H_{40}O_{10}Na$).

Tiegusanin K (11): white powder; $[\alpha]^{21.6}_D$ +14.6 (*c* 0.10, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ε) 281 (4.05), 261 (4.00), 240 (4.08), 230 (3.94), 219 (3.92), 197 (3.92) nm; CD (MeOH) λ_{max} nm (log ε) 253 (−16.08), 232 (+5.12), 207 (+14.93); IR (KBr) ν_{max} 3437, 2927, 2878, 2854, 1710, 1638, 1614, 1478, 1462, 1428, 1367, 1336, 1272, 1251, 1231, 1202, 1160, 1108, 1063, 1036, 1013, 978, 938, 849, 769 cm^{-1}; ^1H and ^{13}C NMR data, Tables 3 and 4, respectively; HRESIMS (positive ion mode) *m/z* 653.2345 $[M + Na]^+$ (calcd 653.2362 for $C_{36}H_{38}O_{10}Na$).

Tiegusanin L (12): yellow, amorphous solid; $[\alpha]^{26.8}_D$ −68.2 (*c* 0.40, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ε) 280 (4.02), 236 (3.88), 229 (3.86), 221 (3.85), 206 (3.84), 202 (3.84) nm; CD (MeOH) λ_{max} nm ($\Delta\varepsilon$) 248 (+13.97), 232 (+17.48), 213 (−18.95); IR (KBr) ν_{max} 3429, 2954, 2934, 2892, 2877, 1710, 1637, 1621, 1582, 1496, 1476, 1464, 1452, 1419, 1370, 1333, 1308, 1270, 1205, 1172, 1161, 1092, 1067, 1049, 992, 936, 864, 769 cm^{-1}; ^1H and ^{13}C NMR data, Tables 3 and 4, respectively; HRESIMS (positive ion mode) *m/z* 555.1992 $[M + Na]^+$ (calcd 555.1994 for $C_{31}H_{32}O_8Na$).

Tiegusanin M (13): brown gum; $[\alpha]^{21.3}_D$ −83.3 (*c* 0.07, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ε) 241 (3.82), 222 (3.52), 207 (3.48), 197 (3.49) nm; CD (MeOH) λ_{max} nm (log ε) 248 (−6.82), 225 (+12.11); IR (KBr) ν_{max} 3432, 2928, 2853, 1710, 1609, 1601, 1500, 1462, 1404, 1364, 1329, 1274, 1238, 1197, 1144, 1106, 1040, 978, 929 cm^{-1}; ^1H and ^{13}C NMR data, Tables 3 and 4, respectively; HRESIMS (positive ion mode) *m/z* 469.1463 $[M + Na]^+$ (calcd 469.1474 for $C_{23}H_{26}O_9Na$).

Tiegusanin N (14): white, amorphous solid; $[\alpha]^{27.1}_D$ 0 (*c* 0.12, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ε) 279 (3.22), 241 (3.70), 232 (3.26), 228 (3.25), 224 (3.26), 209 (3.22), 206 (3.24), 193 (3.29) nm; IR (KBr) ν_{max} 3425, 2957, 2933, 2875, 1732, 1590, 1514, 1462, 1419, 1378, 1333, 1262, 1238, 1194, 1155, 1129, 1106, 1030, 1012, 977, 927, 830, 766 cm^{-1}; ^1H and ^{13}C NMR data, Table 5; HRESIMS (positive ion mode) *m/z* 411.2155 $[M + Na]^+$ (calcd 411.2147 for $C_{23}H_{32}O_5Na$).

X-ray Crystallographic Analysis of 15. $C_{28}H_{36}O_8$; $M = 500.7$; monoclinic crystalline system; space group: $P2_1$; $a = 9.1176(1)$ Å, $b = 23.0376(3)$ Å, $c = 13.1994(2)$ Å, $\beta = 95.226(1)°$, $V = 2760.98(6)$ $Å^3$, $Z = 4$, crystal dimensions 0.10 × 0.10 × 0.30 mm. The total number of independent reflections measured was 5874, of which 5713 were observed ($|F|^2 \geq 2\sigma|F|^2$). The final indices were $R_1 = 0.0477$, $wR_2 = 0.1257$ ($w = 1/\sigma|F|^2$), $S = 1.033$. Crystal structure measurements were made by using a MAC DIP-2030 K diffractometer with graphite-monochromated Mo Kα radiation. The data were collected by using the $\omega-2\theta$ scan technique to a maximum 2θ value of 114.0°. The crystal structures were solved by direct methods using SHELXS-97,[36] expanded by using difference Fourier techniques, and refined by the program and method NOMCSDP and full-matrix least-squares calculations.[37] The non-hydrogen atoms were refined anisotropically, and hydrogen atoms were included at their calculated positions. Drawing of the molecule was achieved with ORTEP. Crystallographic data for the structure of **15** have been deposited in the Cambridge Crystallographic Data Centre (deposition number CCDC 720855). Copies of the data can be obtained free of charge via www.ccdc.acm.ac.Uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

Anti-HIV-1 Assay. The cytotoxicity assay against C8166 cells (CC_{50}) was assessed using the MTT method, and anti-HIV-1 activity was evaluated by the inhibition assay for the cytopathic effects of HIV-1 (EC_{50}).[38]

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Supporting Information Available: ^1H, ^{13}C, and DEPT NMR spectra of tiegusanins A−N (**1**−**14**) and methyl schisantherin F (**15**), UV, IR, HRESIMS, and 2D NMR spectra of tiegusanin A (**1**), and CD spectra of tiegusanins A−M (**1**−**13**) and methyl schisantherin F (**15**). This material is available free of charge via the Internet at http://pubs.acs.org.

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