Chemical Constituents from the Leaves and Stems of *Schisandra rubriflora*

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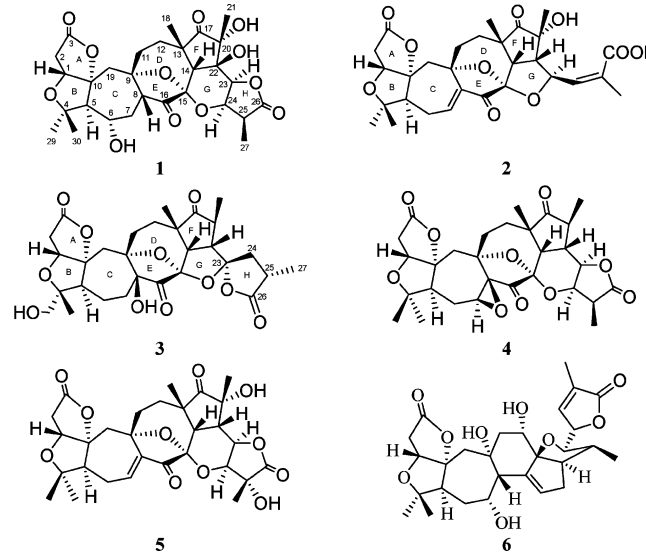
Six new nortriterpenoids, schirubridilactones A−F (**1**−**6**), as well as 14 known compounds, were isolated from the leaves and stems of *Schisandra rubriflora*. The structures of **1**−**6** were elucidated on the basis of spectroscopic methods including HSQC, HMBC, ^{1}H−^{1}H COSY, and ROESY NMR experiments. The relative stereochemistry of **1** was confirmed through single-crystal X-ray analysis. In addition, compounds **1**−**6** showed anti-HIV-1 activity with EC_{50} values in the range 14.3−80.8 μg/mL and selectivity indices in the range 2.2−9.0.

Plants of the genus *Schisandra* are well-known to be economically and medicinally valuable and are reported to contain dibenzocyclooctadiene lignans, lanostane, and cycloartane triterpenes, of which some possess antihepatitis, antitumor, and anti-HIV activities.[1−5] Recent research on *Schisandra* species has led to the characterization of a series of structurally interesting triterpene metabolites, the *Schisandra* nortriterpenoids.[6] On the basis of their structural characterization, *Schisandra* nortriterpenoids may be grouped into different classes including the schisanartane,[6,7] schiartane,[6,8] 18-norschiartane,[6,9,10] 18(13/14)-*abeo*-schiartane,[6,11] preschisanartane,[6,12] and wuweiziartane[6,13] types. Certain of these nortriterpenoids exhibit anti-HIV-1[8,10]and cytotoxic[14,15] activities.

Schisandra rubriflora (Franch.) Rehd. et Wils, a climbing plant mainly distributed in the Yunnan and Sichuan Provinces of the People's Republic of China, has been used as a sedative and tonic agent in traditional Chinese medicine, and its fruits are eaten locally. Therefore, this species has attracted the interest of phytochemists and biologists, which led to the discovery of a series of lignans[16−21] and triterpenoids,[10,22,23] with some showing anti-HIV-1 activities.[10,16,22] So far, only some lignans were reported from the fruits of *S. rubriflora* in Lijiang Prefecture of Yunnan Province.[16] Since *Schisandra* nortriterpenoids are normally found from the leaves and stems of *Schisandra* species,[6] we collected the leaves and stems of *S. rubriflora* from Lijiang Prefecture of Yunnan Province for the current chemical investigation focusing on bioactive triterpenoids. Our research led to the isolation of six new nortriterpenoids, schirubridilactones A−F (**1**−**6**), and eight known nortriterpenoids, including lancifodilactones A, C, and D,[9,24] micrandilactones A and D,[7,25] and henridilactones A−C,[26] together with six known lignans comprising *meso*-dihydroguaiaretic acid,[27] *meso*-monomethyl dihydroguaiaretic acid,[28] 4,4′-(2*R*,3*S*)-2,3-dimethylbutane-1,4-diyl)bis(1,2-dimethoxybenzene),[29] tiegusanin L,[30] (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,[31] and (8*R*,7′*R*,8*R*)-5-hydroxy-4,3′,4′-trimethoxy-2,7′-cyclolignan.[32] The structures of **1**−**6** were identified by interpretation of their spectroscopic data, aided by a single-crystal X-ray diffraction study on **1**. In the present paper, we report the isolation and structural elucidation of compounds **1**−**6** and their biological activities.



Results and Discussion

Powdered dried leaves and stems of *S. rubriflora* were extracted with 70% aqueous acetone. The filtrate was concentrated and partitioned between H_2O and EtOAc. The EtOAc fraction was dried under reduced pressure and then submitted to successive chromatographic fractionation and purification steps, to yield six new compounds (**1**−**6**) and 14 known compounds.

Schirubridilactone A (**1**), $[\alpha]_D^{24.5}$ +99.5 (*c* 0.13, CH_3OH), was assigned the molecular formula $C_{29}H_{36}O_{11}$ from the pseudomolecular ion peak at *m*/*z* 599 $[M + Na]^+$ in the ESIMS and HRESIMS (*m*/*z* 599.2201 $[M + Na]^+$), corresponding to 12 degrees of unsaturation. The ^{1}H NMR spectrum displayed signals due to four tertiary methyls and one secondary methyl. The ^{13}C NMR spectrum of **1** showed signals for 29 carbons, including two ester groups, two carbonyl groups, seven quaternary carbons, eight methines (including four oxygenated ones), five methylenes, and five methyls (Tables 1 and 2). The characteristic proton signals at H-1 (δ_H 4.29, d, J = 6.2 Hz) and H-19 (δ_H 2.30 and 2.43, AB d, J = 16.1 Hz) and carbon signals at δ_C 81.4 (C-1), 99.8 (C-15), 220.7 (C-17), 75.8 (C-23), 75.3 (C-24), and 177.6 (C-26) suggested that **1** is a schisanartane nortriterpenoid.[6,7] Comparison of the 1D NMR spectroscopic data of **1** with those of the known compound micrandilactone A[7] suggested that they are structurally similar. Thus, the structure of **1** was determined by comparison with the

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Table 1. ^{13}C NMR Spectroscopic Assignments of Compounds **1**−**6**[a]

position	1	2	3	4	5	6
1	81.4 d	80.6 d	82.0 d	80.0 d	80.3 d	83.0 d
2	35.1 t	35.6 t	35.4 t	35.4 t	35.3 t	35.9 t
3	175.3 s	174.8 s	174.9 s	175.3 s	174.8 s	175.4 s
4	84.7 s	83.0 s	86.7 s	83.6 s	83.2 s	84.4 s
5	67.9 d	57.7 d	56.0 d	54.1 d	57.8 d	52.9 d
6	68.0 d	24.1 t	19.6 t	28.1 t	23.7 t	34.4 t
7	38.5 t	136.7 d	32.3 t	63.9 d	135.5 d	69.6 d
8	49.7 d	137.6 s	83.2 s	61.3 s	137.9 s	51.4 d
9	83.0 s	81.4 s	78.1 s	80.8 s	82.8 s	78.2 s
10	93.9 s	94.7 s	96.5 s	95.7 s	94.7 s	98.6 s
11	41.1 t	38.5 t	36.6 t	36.1 t	39.1 t	42.6 t
12	32.5 t	30.9 t	31.7 t	31.8 t	31.1 t	72.2 d
13	49.4 s	47.7 s	48.9 s	50.7 s	49.7 s	98.2 s
14	54.2 d	61.2 d	61.3 d	46.4 d	45.9 d	140.6 s
15	99.8 s	109.8 s	105.6 s	98.2 s	99.0 s	130.0 s
16	209.9 s	198.8 s	216.2 s	208.0 s	198.4 s	31.9 t
17	220.7 s	220.5 s	220.0 s	220.1 s	220.2 s	45.4 d
18	30.9 q	27.8 q	26.2 q	26.5 q	27.5 q	
19	42.8 t	45.2 t	43.2 t	38.8 t	42.7 t	46.5 t
20	75.5 s	75.5 s	44.6 d	44.8 d	74.7 s	37.7 d
21	18.9 q	26.8 q	17.2 q	14.7 q	25.4 q	12.5 q
22	80.3 s	55.9 d	53.0 d	40.1 d	41.8 d	82.1 d
23	75.8 d	80.5 d	115.3 s	75.0 d	73.4 d	81.2 d
24	75.3 d	144.1 d	44.0 t	68.6 d	75.8 d	146.9 d
25	42.5 d	125.9 s	35.4 d	42.5 d	76.8 s	130.5 s
26	177.6 s	169.6 s	177.8 s	178.1 s	177.5 s	174.4 s
27	8.2 q	20.6 q	14.6 q	8.4 q	18.0 q	10.8 q
29	20.3 q	20.5 q	67.7 t	20.5 q	20.4 q	28.8 q
30	30.4 q	27.6 q	17.0 q	27.5 q	27.5 q	22.7 q

[a] Spectra were recorded in C_5D_5N, and chemical shifts (δ) are in ppm.

NMR spectroscopic data of micrandilactone A and analysis of the two-dimensional NMR data of **1**. Differences found between **1** and micrandilactone A may be rationalized as the hydroxy group being at C-6 in **1** rather than at C-7. This deduction was further confirmed by HMBC correlations of H-6 (δ_H 4.10, m) with C-4 (δ_C 84.7), C-5 (δ_C 67.9), and C-8 (δ_C 49.7) and $^1H-^1H$ COSY correlations of H-5/H-6/H-7/H-8 (Figure 1). The HMBC correlations of CH_3-21 (δ_H 1.77, s) with C-17 (δ_C 220.7), C-20 (δ_C 75.5), and C-22 (δ_C 80.3) indicated that C-20 and C-22 are oxygenated carbons. Thus, the planar structure of **1** was established as shown.

The relative configuration of **1** was determined by analysis of a ROESY NMR experiment and by X-ray crystallographic analysis (Figure 2). The ROESY correlations of H-6 with H-5, H-8, and CH_3-30 were used to establish H-6 as being β-oriented. Accordingly, the 6-hydroxy group was α-oriented. The ROESY correlations of CH_3-18/CH_3-21, CH_3-18/H-14, and CH_3-18/H-22 showed that CH_3-21, H-14, and H-22 are located on the same side of the molecule as CH_3-18. They were further determined to be β-oriented by the X-ray diffraction experiment. In addition, according to the IUPAC sequence rule,[33] based on the chiral center with the lowest locant, the relative configurations of carbons C-9, C-10, and C-15 were deduced as *S**, *R**, and *R**, respectively.

Compound **2** gave a quasi-molecular ion peak at *m*/*z* 565 $[M + Na]^+$ in its positive ESIMS and was assigned a molecular formula of $C_{29}H_{34}O_{10}$, which was confirmed by its HRESIMS (found $[M + Na]^+$ 565.2160, calcd 565.2152) and NMR data. Evident in the ^1H NMR spectrum were five tertiary methyl signals. The ^{13}C NMR and DEPT spectra of **1** exhibited signals for 29 carbons, including four carbonyl carbons (of which two were ketones), eight quaternary carbons (five oxygenated and two olefinic), seven methines (two oxygenated and two olefinic), four methylenes, and five methyls. This suggested that compound **2** is a highly oxygenated nortriterpene containing seven rings. Analysis of the ^1H and ^{13}C NMR data of **2** revealed it has similar values to those reported for henridilactone A,[26] which was also isolated in our present study. A combination of the 1D NMR data comparison of these two compounds and analysis of the HMBC and $^1H-^1H$ COSY spectra of **2** indicated the nature of rings A−F in **2** (Figure 1).

The NMR data for the remaining portion of the molecule of **2** were quite distinctive from those of henridilactone A. HMBC correlations from H-23 (δ_H 6.50) to C-14 and C-15 indicated the presence of an oxygen bridge between C-15 and C-14 to form the five-membered ring G. HMBC correlations of H-23 with carbon signals at δ_C 144.1 (C-24) and 125.9 (C-25) indicated a double bond between C-24 and C-25, which connected directly with C-23. HMBC correlations of the methyl protons at δ_H 2.04 (C-27, s) with C-24, C-25, and a carbonyl carbon at δ_C 169.6 (C-26) established that both C-26 and C-27 are directly attached to C-25.

The relative configuration of **2** was established by analysis of its ROESY NMR data and chemical shift comparison with those of henridilactone A. The ROESY correlation of H-24 with H-14 indicated a β-orientation of C-24 and the α-orientation of H-23. ROESY correlations of CH_3-21 with H-14 and H-14 with CH_3-18 suggested CH_3-21 to be β-oriented and OH-20 therefore α-oriented. The ROESY correlation of H-24 with CH_3-27 was used to determine the double bond as being in a *Z* configuration (Figure 3). Therefore, compound **2** was established as shown and has been accorded the trivial name schirubridilactone B.

Compound **3** was isolated as white crystals, and the molecular formula, $C_{29}H_{36}O_{11}$, was established by HRESIMS (found *m*/*z* $[M + Na]^+$ 583.2263, calcd 583.2258) and from its ^{13}C NMR spectrum. The ^{13}C NMR data of **3** were very close to those of a known compound, schigrandilactone A,[15] which was also isolated from *Schisandra* species, and its structure was established by an X-ray experiment. A side-by-side comparison of the ^1H and ^{13}C NMR spectroscopic data of **3** and schigrandilactone A showed that the proton and carbon atom shifts of rings A−G are closely comparable in both compounds. Differences observed were the chemical shifts of C-23, C-24, and C-27 at δ_C 118.3, 38.0, and 17.1 in schigrandilactone A to δ_C 115.3, 44.0, and 14.6, respectively. These differences can be rationalized by the change of the relative configuration of C-23 from *R** in schigrandilactone A to *S** in **3**, i.e., C-24 is β-oriented in **3**. This deduction was confirmed by the ROESY correlation of H-24 with H-14 (Figure 3). Therefore, the structure of **3** (schirubridilactone C) was determined as shown.

Compound **4** was isolated as white crystals and was determined to have the molecular formula $C_{29}H_{34}O_{10}$ from its HRESIMS and ^{13}C NMR spectra. The ^1H and ^{13}C NMR data of **4** were closely comparable to those of lancifodilactone C,[24] except for the presence of one methine (C-7, δ_C 69.0) and one quaternary carbon (C-8, δ_C 61.3) and the absence of two low-field signals at δ 135.5 and 138.2. The carbon signals at δ_C 69.0 (d, C-7) and 61.3 (s, C-8) indicated an epoxy group between C-7 and C-8,[24] which was in accord with the molecular formula. The H-7 proton was deduced to be α-oriented by the ROESY correlation of H-5 with H-7. Accordingly, the epoxy group was assigned as β-oriented, and the structure of **4** (schrubridilactone D) determined as shown.

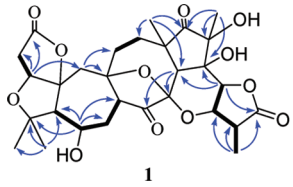
Compound **5** was isolated as white crystals, and HRESIMS analysis demonstrated a molecular formula of $C_{29}H_{34}O_{11}$, 16 mass units more than henridilactone A.[26] Comparison of the ^1H and ^{13}C NMR data of these compounds showed that a structural difference could be rationalized by the replacement of a methine in henridilactone A by an oxygenated quaternary carbon (C-25) in **5**. This was confirmed by HMBC cross-peaks from CH_3-27 (δ_H 2.10, s) to C-24 (δ_C 75.8), C-25 (δ_C 76.8), and C-26 (δ_C 177.5). The configuration of CH_3-27 in **5** was determined to be β-oriented by comparison of the chemical shifts with those of lancifodilactone D[24] and the lack of a ROESY correlation observed either between CH_3-27 and H-23 or between CH_3-27 and H-24. Thus, the structure of **5** (schirubridilactone E) was established as shown.

The molecular formula of **6** was deduced as $C_{28}H_{36}O_9$ from its HRESIMS and ^{13}C NMR data. The ^{13}C NMR data indicated that **6** possesses two ester groups, six quaternary carbons, including two

Table 2. ^{1}H NMR Spectroscopic Assignments of Compounds **1**−**6**[a]

position	1	2	3	4	5	6
1	4.29 (d, 6.2)	4 0.11 (d, 6.6)	4.25 (d, 6.1)	4.21 (d, 5.9)	4.09 (d, 6.0)	4.18 (d, 4.6)
2α	2.78 (d, 14.6)	2.57 (d, 18.4)	2.53 (br d, 18.2)	2.77 (d, 18.5)	2.60 (d, 18.8)	2.63 (d, 18.0)
2*β*	2.96 (dd, 6.4, 14.6)	2.78 (dd, 6.6, 18.4)	2.95 (overlapped)	3.15 (dd, 5.9, 18.5)	2.71 (dd, 6.0, 18.8)	2.98 (dd, 4.6, 18.0)
5	2.57 (d, 10.8)	2.11 (m)	2.90 (m)	2.40 (dd, 2.4, 14.4)	2.12 (dd, 2.0, 14.2)	3.23 (dd, 4.3, 13.5)
6α	4.10 (m)	2.20 (overlapped)	2.21 (m)	2.20 (m)	2.18 (m)	1.50 (m)
6*β*		2.28 (m)	1.69 (m)	1.42 (m)	2.18 (m)	2.03 (overlapped)
7α	2.51 (m)	7.27 (t, 7.7)	2.32 (m)	3.89 (t, 6.3)	7.13 (t, 7.5)	4.88 (br s)
7*β*	2.70 (m)		2.00 (m)			
8	3.05 (dd, 4.9, 12.5)					2.63 (br s)
11α	1.94 (overlapped)	2.40 (overlapped)	2.02 (m)	1.88 (m)	1.80 (m)	2.18 (dd, 2.5, 15.4)
11*β*	1.67 (overlapped)	1.85 (m)	2.35 (m)	1.95 (m)	2.25 (overlapped)	2.37 (dd, 2.5, 15.4)
12α	1.93 (overlapped)	1.90 (m)	1.91 (m)	1.69 (m)	1.67 (m)	5.11 (br s)
12*β*	1.52 (m)	1.65 (m)	1.74 (m)	1.98 (m)	1.97 (m)	
14	3.28 (s)	3.12 (d, 7.2)	3.22 (d, 7.8)	2.68 (d, 7.2)	2.90 (d, 8.0)	
15						6.25 (br s)
16						2.35 (m)
17						2.98 (m)
18	1.60 (s)	1.14 (s)	0.97 (s)	0.91 (s)	1.05 (s)	
19α	2.30 (AB d, 16.1)	2.25 (AB d, 16.5)	2.32 (AB d, 15.9)	2.24 (AB d, 16.0)	2.35 (AB d, 15.8)	1.99 (AB d, 15.4)
19*β*	2.43 (AB d, 16.1)	2.40 (AB d, 16.5)	2.53 (AB d, 15.9)	2.14 (AB d, 16.0)	2.22 (AB d, 15.8)	2.03 (overlapped)
20			3.60 (m)	2.55 (m)		2.38 (m)
21	1.77 (s)	1.74 (s)	1.11(d, 6.5)	1.17 (d, 7.0)	1.57 (s)	0.93 (d, 6.8)
22		3.05 (br d, 7.2)	2.90 (m)	2.85 (m)	3.23 (d, 8.0)	3.66 (dd, 4.0, 10.0)
23	4.93 (br s)	6.50 (m)		4.58 (br s)	5.65 (br s)	5.14 (br s)
24α	5.43 (br s)	6.55 (d, 8.4)	2.80 (dd, 14.5, 9.2)	5.04 (br s)	4.88 (br s)	7.25 (br s)
24*β*			2.15 (br d, 14.5)			
25	3.29 (m)		3.00 (m)	3.23 (m)		
27	1.31 (d, 7.1)	2.04 (s)	1.09 (d, 7.5)	1.66 (d, 7.1)	2.10 (s)	1.83 (s)
29	1.36 (s)	0.98 (s)	3.60 (d, 11.5)	0.95 (s)	1.00 (s)	0.95 (s)
			3.74 (d, 11.5)			
30	1.68 (s)	1.21 (s)	1.16 (s)	1.22 (s)	1.20 (s)	1.20 (s)

[a] Spectra were recorded in C_5D_5N, and chemical shifts (δ) are in ppm and J in Hz.



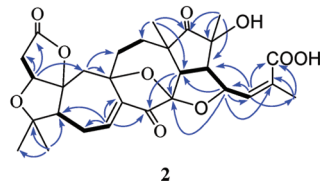


Figure 1. Selected HMBC (→) and ^{1}H−^{1}H COSY (—) correlations of **1** and **2**.

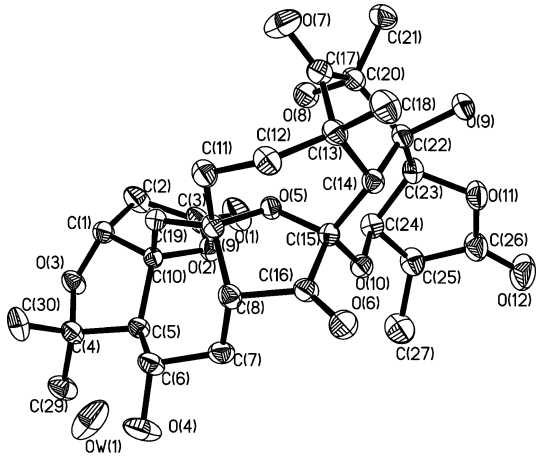


Figure 2. ORTEP drawing of **1**.

olefinic carbons and four oxygenated carbons, 11 methines including two olefinic carbons and five oxygenated carbons, five methylenes, and four methyls, which suggested a highly oxygenated C_{28} triterpene skeleton. Its ^{1}H and ^{13}C NMR spectra were similar to those of lancifodilactone A,[6,9] except for the absence of signals for the acetate group in **6**. Analysis of the 2D NMR data of **6**, including HSQC, HMBC, ^{1}H−^{1}H COSY, and ROESY experiments,

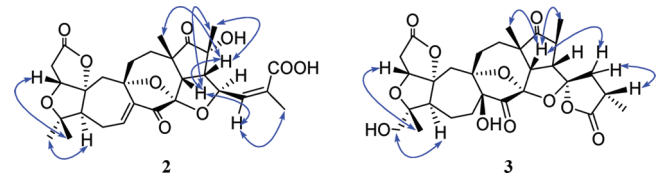


Figure 3. Selected ROESY correlations of **2** and **3**.

and comparison of the chemical shifts with those of lancifodilactone A were used to establish the structure of **6** (schirubridilactone F) as shown.

Compounds **1**−**6** 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 (EC_{50} 0.0045 μg/mL and CC_{50} > 200 μg/mL).[34] Compounds **1**−**6** displayed EC_{50} values of 30.1, 15.2, 14.3, 80.8, 66.8, and 50.1 μg/mL and a selectivity index of 5.1, 9.0, 8.7, 2.2, 3.1, and 3.5, respectively. In addition, compounds **1**, **2**, and **4**−**6** were further evaluated for their cytotoxicity against two human tumor cell lines, K562 and HepG2, using a bioassay method previously described, with cisplatin as the positive control (IC_{50} 0.40 and 0.59 μg/mL, respectively),[35] but showed no obvious inhibitory activities with IC_{50} values of >5 μg/mL. Compound **3** was not tested for cancer cell line cytotoxicity due to the limited amount available.

Experimental Section

General Experimental Procedures. Melting points were obtained on a XRC-1 micro melting point apparatus and are uncorrected. Optical rotations were measured on a Horiba SEPA-300 polarimeter. UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. 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. Unless otherwise specified, chemical shifts (δ) are expressed in ppm with reference to the solvent signals. Mass spectra were performed on a VG Autospec-3000

spectrometer at 70 eV. Column chromatography was performed using silica gel (200−300 mesh, Qing-dao Marine Chemical, Inc., Qingdao, People's Republic of China). Semipreparative HPLC was performed on an Agilent 1100 liquid chromatograph with a Zorbax SB-C_{18} 9.4 mm × 25 cm column. Preparative HPLC was performed on a Shimadzu LC-8A preparative liquid chromatograph with a Shimadzu PRC-ODS (K) column. Fractions were monitored by TLC, and spots were visualized by heating the silica gel plates sprayed with 10% H_2SO_4 in EtOH.

Plant Material. The leaves and stems of *S. rubriflora* were collected in Lijiang Prefecture, Yunnan Province, People's Republic of China, in August 2006. The specimen was identified by Prof. Xi-Wen Li, and a voucher specimen (no. KIB 2006-08-13) has been deposited at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation. The plant material of *S. rubriflora* (3.7 kg) was powdered and extracted exhaustively with 70% aqueous Me_2CO at room temperature. The solvent was evaporated in vacuo, and the crude extract (210 g) was partitioned between H_2O and EtOAc. The EtOAc extract (91 g) was chromatographed on a silica gel column eluting with $CHCl_3$−Me_2CO (1:0, 9:1, 8:2, 2:1, 1:1, and 0:1) to afford fractions I−V. Fraction II (15.1 g) was applied to a glass column containing RP-18, eluted with a 45%−100% MeOH−H_2O gradient system, to afford six fractions. Fraction II-2 (1.2 g) gave henridilactone B (5 mg) and (8*R*,7′*R*,8*R*)-5-hydroxy-4,3′,4′-trimethoxy-2,7′-cyclolignan (30 mg), after being chromatographed over silica gel developed with petroleum ether−EtOAc (6:4). Fraction II-3 (1.5 g) was purified over silica gel (petroleum ether−Me_2CO, 6:1) to furnish henridilactone C (6 mg) and 4,4′-(2*R*,3*S*)-2,3-dimethylbutane-1,4-diyl)bis(1,2-dimethoxybenzene) (10 mg). Fraction II-4 was subjected to semipreparative HPLC (MeOH−H_2O, 60:40) to yield compounds tiegusanin L (15 mg) and (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 (5 mg). Fraction III (18.9 g) was chromatographed on a silica gel column eluting with $CHCl_3$−MeOH (20:1 10:1, 5:1, 2:1, 1:1) to afford five fractions. Fraction III-2 (3.1 g) was purified by crystallization and repeated chromatography over silica gel, RP-18, and Sephadex LH-20 (MeOH), followed by semipreparative and preparative HPLC (CH_3CN−H_2O, 35:65, and MeOH−CH_3CN−H_2O, 10:33:57), to yield compounds **1** (10 mg), **3** (3 mg), **4** (7 mg), lancifodilactone A (20 mg), and henridilactone A (22 mg). Fraction III-3 (4.4 g) was repeatedly chromatographed on silica gel (200−300 mesh) and Sephadex LH-20, and finally by semipreparative HPLC (MeOH−H_2O, 45:55, and MeOH−CH_3CN−H_2O, 15:33:52), to yield compounds **2** (7 mg), **5** (4 mg), lancifodilactone C (15 mg), micrandilactone A (9 mg), and *meso*-dihydroguaiaretic acid (21 mg). Similarly, fraction III-4 (2.9 g) was also purified using the chromatographic methods mentioned above to yield compounds **6** (10 mg), lancifodilactone D (13 mg), micrandilactone D (5 mg), and *meso*-monomethyl dihydroguaiaretic acid (5 mg).

Schirubridilactone A (1): white crystals; mp 182−183 °C; $[\alpha]_D^{25.5}$ +99.5 (*c* 0.13, CH_3OH); UV (CH_3OH) λ_{max} (log ε) 207 (3.45) nm; IR (KBr) ν_{max} 3443, 2938, 1769, 1747, 1638, 1445, 1387, 1165, 1004, 589 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; positive ESIMS *m*/*z* 599 $[M + Na]^+$; HRESIMS *m*/*z* 599.2201 $[M + Na]^+$ (calcd for $C_{29}H_{36}O_{12}Na$, 599.2207).

Schirubridilactone B (2): white powder; mp 185−186 °C; $[\alpha]_D^{24.3}$ +71.5 (*c* 0.23, MeOH); UV (MeOH) λ_{max} (log ε) 212 (3.69) nm; IR (KBr) ν_{max} 3446, 2970, 2912, 2831, 1744, 1633, 1458, 1215, 1911, 1007, 921, 859 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; positive ESIMS *m*/*z* $[M + Na]^+$ 565; HRESIMS *m*/*z* $[M + Na]^+$ 565.2160 (calcd for $C_{29}H_{34}O_{10}Na$, 565.2152).

Schirubridilactone C (3): white powder; mp 192−193 °C; $[\alpha]_D^{25.5}$ +86.1 (*c* 0.19, CH_3OH); UV (CH_3OH) λ_{max} (log ε) 202 (3.31) nm; IR (KBr) ν_{max} 3430, 2965, 1773, 1701, 1641, 1449, 1433, 1350, 1281, 1080, 595 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; positive ESIMS *m*/*z* 583 $[M + Na]^+$; HRESIMS *m*/*z* 583.2263 $[M + Na]^+$ (calcd for $C_{29}H_{36}O_{11}Na$, 583.2258).

Schirubridilactone D (4): white crystals; mp 180−181 °C; $[\alpha]_D^{24.5}$ +56.5 (*c* 0.33, MeOH); UV (MeOH) λ_{max} (log ε) 201 (3.18) nm; IR (KBr) ν_{max} 2927, 2854, 1779, 1458, 1378, 1236, 1206, 1097, 1009, 926, 590 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; positive ESIMS *m*/*z* $[M + Na]^+$ 565; HRESIMS *m*/*z* $[M + Na]^+$ 565.2159 (calcd for $C_{29}H_{34}O_{10}Na$, 565.2152).

Schirubridilactone E (5): white crystals; mp 190−191 °C; $[\alpha]_D^{24.7}$ +84.6 (*c* 0.31, MeOH); UV (MeOH) λ_{max} (log ε) 203 (3.40) nm; IR (KBr) ν_{max} 3521, 3443, 2979, 2933, 1770, 1755, 1704, 1460, 1380, 1233, 1219, 1103, 1066, 982, 594 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; positive ESIMS *m*/*z* $[M + Na]^+$ 581; HRESIMS *m*/*z* $[M + Na]^+$ 581.2045 (calcd for $C_{29}H_{34}O_{11}Na$, 581.2050).

Schirubridilactone F (6): white crystals; mp 199−200 °C; $[\alpha]_D^{23.9}$ −38.5 (*c* 0.18, CH_3OH); UV (MeOH) λ_{max} (log ε) 205 (2.68) nm; IR (KBr) ν_{max} 3508, 2984, 2918, 1779, 1746, 1653, 1628, 1609, 1459, 1380, 1239, 1065, 930, 876 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; positive ESIMS *m*/*z* $[M + Na]^+$ 539; HRESIMS *m*/*z* 539.2252 $[M + Na]^+$ (calcd for 539.2257, $C_{28}H_{36}NaO_9$).

X-ray Crystal Structure of Schirubridilactone A (1). A crystal, $C_{29}H_{26}O_{12}$, $M = 576$, monoclinic, space group $P2_1$, $a = 9.715(2)$ Å, $b = 13.320(3)$ Å, $c = 11.249(2)$ Å, $\beta = 97.65(3)°$, $V = 1442.7(5)$ Å^3, $Z = 2$, $d = 1.348$ g/cm^3, crystal dimensions 0.15 × 0.20 × 0.40 mm, was used for measurements on a MAC DIP-2030K diffractometer with a graphite monochromator (ω−2θ scans, $2\theta_{max} = 50.0°$), Mo Kα radiation. The total number of independent reflections measured was 2750, of which 2548 were observed ($|F|^2 \geq 2\sigma|F|^2$). Final indices: $R_1 = 0.0492$, $wR_2 = 0.1309$, $S = 1.149$. The crystal structure of **1** was solved by direct methods using SHELX-86[36] and expanded using difference Fourier techniques, refined by the program and method NOMCSDP[37] and full-matrix least-squares calculations. The CIF file of X-ray data of **1** has been deposited in the Cambridge Crystallographic Data Centre (deposition number 759827). 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 depost@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}).[34] Cytotoxicity against human tumor cell lines, K562 and HepG2, was evaluated by a bioassay method previously described.[35]

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Supporting Information Available: 1D and 2D NMR spectra and crystallographic data of schirubridilactone A (**1**). These materials are available free of charge via the Internet at http://pubs.acs.org.

References and Notes

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