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Lignans and Neolignans from *Sinocalamus affinis* and Their Absolute Configurations

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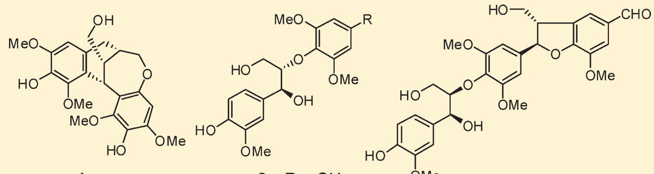
S *Supporting Information*

ABSTRACT: Twenty-two new lignans and neolignans (**1**−**22**), together with 14 known analogues, have been isolated from an ethanolic extract of the stem (with skin removed) of *Sinocalamus affinis*. Their structures were elucidated by spectroscopic and chemical methods. On the basis of systematic NMR and circular dichroism (CD) data analysis, the validity of $J_{7,8}$ and $\Delta\delta_{C8-C7}$ values to distinguish *threo* and *erythro* aryl glycerol units in different neolignans and the CD data [particularly the $Rh_2(OCOCF_3)_4$-induced CD data (the E band)] to determine the absolute configurations at C-8 (C-7) of the aryl glycerol units are discussed. At a concentration of 10 μM, compounds **20** and **22** inhibited NO production in mouse peritoneal macrophages 84.2 ± 5.9% and 71.7 ± 1.0%, respectively. Compounds **19**, **20**, and **22** showed activity against serum deprivation induced PC12 cell damage by increasing the cell viability from 80.7 ± 2.8% to 91.6 ± 6.4%, 107.2 ± 8.0%, and 97.6 ± 8.5%, respectively.



1 **2** R = OH **4**

Sinocalamus affinis (Rendle) McClure (Poaceae) is widely distributed and cultivated in southwestern China.[1] Different parts of the plant, including the stem, leaves, and roots, are used in traditional Chinese medicine.[1] Slices of the stem (with skin removed), named "ci zhu ru" in Chinese, are commonly used to treat various diseases, such as cough and phlegm.[1,2] However, no chemical or pharmacological study of this remedy has been reported.[2,3] As part of a program to study the chemical diversity of traditional Chinese medicines and their biological effects, an ethanol extract of "ci zhu ru" has been investigated. We describe herein the isolation, structure elucidation, and biological assays of 22 new lignans and neolignans (**1**−**22**) and 14 known analogues from the EtOAc-soluble portion of the extract. On the basis of IUPC recommendations for nomenclature of lignans and neolignans,[4] compound **1** is categorized as an unusual 6′,9-epoxy-2,7′-cyclolignane, **2** and **3** are 7′,8′,9′-trinor- and 8′,9′-dinor-8,4-oxyneolignanes, respectively, and **4** is a 8′,9′-dinor-4,8″-oxy-8,3′-sesquineolignane. Though compounds with planar structures identical to sesquineolignans (**10**−**15**),[5−9] dineolignans (**16**−**18**),[9,10] and flavonolignans (**19**−**22**)[11,12] were reported for more than 25 years, configurations for these complex natural products were undetermined with contrary and/or controversial data reported in the literature.[5−12] Extensive NMR and CD data analyses, in combination with chemical transformations, have led to assignments of configuration for **10**−**22**. In addition, by systematic comparison of the spectroscopic data, the validity of $J_{7,8}$ and $\Delta\delta_{C8-C7}$ values to distinguish *threo* and *erythro* arylglycerol units in the different series of neolignans and the CD data [particularly, the $Rh_2(OCOCF_3)_4$-induced CD data (the E band)] to determine the absolute configurations at C-7 of the aryl glycerol units are discussed.

RESULTS AND DISCUSSION

Compound **1** showed IR absorptions for OH (3246 cm^{-1}) and aromatic ring (1612 and 1493 cm^{-1}) groups. The NMR data of **1** (Tables 1 and 2) indicated the presence of two pentasubstituted phenyl, four methoxy, three methylene (two oxygen-bearing), and three methine groups. These data resembled those of the co-occurring (+)-lyoniresinol[13] except that the resonances for the 4′-hydroxy-3′,5′-dimethoxyphenyl in (+)-lyoniresinol were replaced by those attributable to a dimethoxy-dioxyphenyl. This combined with the molecular formula $C_{22}H_{26}O_8$ (HRESIMS) suggested that **1** was an unusual 2,7′-cyclolignane containing an oxy-bridge between the dimethoxy-dioxy-phenyl and C-9 or C-9′. The suggestion was refined by 2D NMR data analysis of **1** (Supporting Information, Figures S6−S8). Particularly, in the HMBC spectrum, correlations for H$_2$-7/C-1, C-2, C-6, C-8, C-8′, and C-9; H-7′/C-1, C-1′, C-2, C-2′, C-3, C-6′, C-8, C-8′, and C-9′; H-5′/C-1′, C-3′, C-4′, and C-6′; O*Me*-2′/C-2′; O*Me*-3/C-3; O*Me*-4′/C-4′; and O*Me*-5/C-5, together with shifts of these resonances, proved that **1** had the basic structure of 3′,4-dihydroxy-2′,3,4′,5-tetramethoxy-2,7′-cyclolignane. HMBC correlations for H$_2$-9/C-6′ revealed the oxy-bridge between C-6′ and C-9. The remaining OH had to be positioned at C-9′ to match the molecular composition and shifts of H$_2$-9′ and C-9′. In the NOE difference spectrum of **1**, irradiation of H-7′ enhanced O*Me*-2′, O*Me*-3, H-8′, and H-9′a, while H-9′b was enhanced upon irradiation of H-8. These enhancements, together with the coupling constant of $J_{7',8'}$ (≈0 Hz), indicated that the torsion

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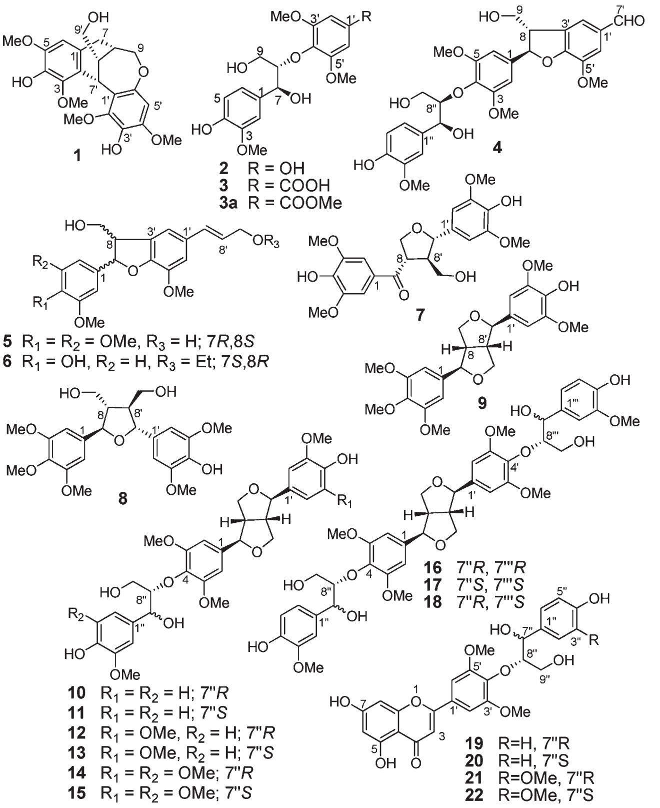

angle between H-7′ and H-8′ was about 90° and revealed that H-8′ was *trans*-oriented to H-7′ and H-8. The CD spectrum of **1** displayed a negative Cotton effect at 284 nm ($\Delta\varepsilon$ −1.03) corresponding to the ^1L_b band of the benzene chromophores. On the basis of the benzene sector and the benzene chirality rules for chiral tetralin derivatives,[14] the 7′*S* configuration was assigned for **1** (Supporting Information, Figure S10). Therefore, compound **1** was (+)-(7′*S*,8*S*,8′*S*)-3′,4-dihydroxy-2′,3,4′,5-tetramethoxy-6′,9-epoxy-2,7′-cyclolignan-9′-ol.

Compound **2**, $C_{18}H_{22}O_8$ (HRESIMS), showed IR absorptions for OH (3405 cm^{-1}) and aromatic ring (1603 and 1512 cm^{-1}) groups. The NMR data (Tables 1 and 2) indicated that there were both guaiacylglycerol-8-yl and 3′,5′-dimethoxy-1′,4′-dioxyphenyl groups in **2**. The chemical shifts of the oxymethines and the coupling constant ($J_{7,8}$ = 7.5 Hz), together with the molecular composition, suggested that **2** was 7,8-*threo*-1′,4-dihydroxy-3,3′,5′-trimethoxy-7′,8′,9′-trinor-8,4′-oxyneoligna-7,9-diol.[15,16] This was confirmed by 2D NMR data analysis of **2** (Supporting Information, Figures S16−S18). The HMBC correlations from H-7 to C-1, C-2, C-6, C-8, and C-9, from H-2′/6′ to C-1′, C-3′/5′, and C-4′, and from O*Me*-3′/5′ to C-3′/5′, together with their shifts, verified the location of the substitutents and the 8,4′-oxy linkage in **2**. A positive Cotton effect at 237 nm in the CD spectrum suggested the 8*S* configuration for **2**.[15−17] On the basis of the bulkiness rule for secondary alcohols,[18] a positive Cotton effect at 351 nm (the E band) in the $Rh_2(OCOCF_3)_4$-induced CD spectrum (Supporting Information, Figure S19) indicated the 7*S*

Table 1. ^{1}H NMR Data (δ) for Compounds 1−3, 3a, and 5−9[a]

no.	1	2	3	3a[b]	5	6[c]	7	8	9
2		7.05 d (2.0)	6.96 brs	6.95 brs	6.75 brs	7.03 d (1.5)	7.34 brs	6.76 brs	6.69 brs
5		6.77 d (8.0)	6.69 d (8.0)	6.68 d (8.4)		6.80 d (8.0)			
6	6.40 s	6.90 dd (8.0, 2.0)	6.82 d (8.0)	6.80 d (8.4)	6.75 brs	6.88 dd (8.0, 1.5)	7.34 brs	6.76 brs	6.69 brs
7a	3.02 dd (17.0, 7.5)	4.94 d (7.5)	4.94 d (7.0)	4.94 d (6.0)	5.59 d (6.5)	5.56 d (6.5)		4.92 d (8.5)	4.70 d (4.2)
7b	2.79 d (17.0)								
8	2.17 m	3.74 m	4.05 m	4.21 m	3.51 m	3.53 m	4.21 m	2.27 m	3.09 m
9a	4.34 dd (12.0, 3.0)	3.59 dd (12.5, 3.5)	3.70 dd (12.0, 3.5)	3.72 dd (12.0, 4.2)	3.91 m	3.88 m	4.18 m	3.72 m	4.24 m
9b	3.71 d (12.0)	3.22 dd (12.5, 2.5)	3.28 (12.0, 2.5)	3.33 dd (12.0, 3.6)	3.85 m	3.82 m	4.14 m	3.64 m	3.85 m
2′		6.21 brs	7.32 brs	7.28 brs	6.96 brs	6.99 brs	6.67 brs	6.75 brs	6.67 brs
5′	6.19 s								
6′		6.21 brs	7.32 brs	7.28 brs	6.95 brs	6.97 brs	6.67 brs	6.75 brs	6.67 brs
7′	4.51 brs				6.52 d (16.0)	6.53 d (16.0)	4.59 d (8.5)	4.90 d (8.5)	4.66 d (4.2)
8′	2.09 m				6.24 dt (16.0, 5.5)	6.17 dt (16.0, 6.0)	2.58 m	2.27 m	3.09 m
9′a	3.56 dd (11.0, 8.0)				4.19 (5.5)	4.05 d (6.0)	3.64 dd (11.5, 4.5)	3.72 m	4.24 m
9′b	3.48 dd (11.0, 7.5)						3.59 dd (11.5, 5.0)	3.64 m	3.85 m
O*Me*-3/5	3.31 s/3.74 s	3.82 s/	3.77 s/	3.77 s/	3.82 s/3.82 s	3.81 s/	3.86 s/3.86 s	3.82 s/3.82 s	3.81 s/3.81 s
O*Me*-4					3.70 s			3.71 s	3.69 s
O*Me*-2′/4′	3.84 s/3.67 s								
O*Me*-3′/5′		3.81 s/3.81 s	3.82 s/3.82 s	3.83 s/3.83 s	/3.88 s	/3.86 s	3.80 s/3.80 s	3.82 s/3.82 s	3.81 s/3.81 s

[a] Data were measured in MeOH-d_4 at 500 MHz for **1**, **3**, and **7** and at 600 MHz for **3a** and in Me_2CO-d_6 for **2**, **5**, **6**, **8**, **9** at 500 or 600 MHz. Coupling constants (*J*) in Hz are given in parentheses. The assignments were based on $^1H-^1H$ COSY, HSQC, and HMBC. [b] Data for COO*Me* in **3a**: δ 3.83 s. [c] Data for OEt in **6**: δ 3.47 q (7.0), 1.15 t (7.0).

Table 2. ^{13}C NMR Data (δ) for Compounds 1−3, 3a, and 5−9[a]

no.	1	2	3	3a[b]	5	6[c]	7	8	9
1	127.6	133.8	133.4	133.5	138.5	132.2	128.6	140.0	138.5
2	124.1	111.6	111.8	111.7	104.0	108.3	107.8	104.5	104.1
3	147.5	147.9	148.8	148.7	154.4	146.2	149.2	154.3	154.4
4	138.2	146.8	147.2	147.2	138.5	145.1	142.9	138.3[d]	138.6
5	148.6	115.2	115.9	115.8	154.4	113.5	149.2	154.3	154.4
6	107.4	120.8	121.0	120.8	104.0	117.4	107.8	104.5	104.1
7	30.0	74.1	74.6	74.4	88.3	86.4	200.3	83.8	86.6
8	35.4	90.0	89.1	88.7	54.8	52.6	50.2	56.8	55.3
9	81.6	61.1	61.8	62.0	64.5	62.4	71.6	62.6	72.4
1′	125.7	155.2	123.8	126.6	132.0	129.4	132.9	134.4	133.1
2′	146.9	94.0	108.1	107.9	116.0	114.1	105.3	104.8	104.5
3′	136.8	154.4	153.6	154.1	130.1	128.2	149.2	148.6	148.7
4′	147.9	130.0	139.7	141.9	148.8	147.0	136.3	137.0[d]	136.2
5′	102.3	154.4	153.6	154.1	145.1	143.0	149.2	148.6	148.7
6′	154.0	94.0	108.1	107.9	111.7	109.5	105.3	104.8	104.5
7′	31.4		156.0[d]	168.0	130.3	130.4	85.4	84.1	86.7
8′	45.2				128.4	122.8	55.1	56.8	55.4
9′	65.3				63.3	69.5	61.4	62.7	72.5
O*Me*-3/5	60.0/56.5	56.2/	56.4/	56.4/	56.4/56.4	54.1/	56.9/56.9	56.4/56.4	56.4/56.4
O*Me*-4					60.4			60.5	60.4
O*Me*-2′/4′	61.7/56.5								
O*Me*-3′/5′		56.4/56.4	56.6/56.6	56.8/56.8	/56.3	/54.2	56.8/56.8	56.7/56.7	56.5/56.5
$\Delta\delta_{C8-C7}$		15.9	14.5	14.3					

[a] Data were measured in MeOH-d_4 for **1**, **3**, and **7** at 500 MHz and for **3a** at 600 MHz and in Me_2CO-d_6 for **2**, **5**, **6**, **8**, and **9** at 500 MHz. The assignments were based on ^{1}H−^{1}H COSY, HSQC, and HMBC experiments. [b] Data for COO*Me* in **3a**: δ 52.8. [c] Data for OEt in **6**: δ 63.6, 13.4. [d] Data were obtained from the HMBC spectrum.

configuration for **2**, which was in agreement with that defined by the 7,8-*threo* and 8*S* configurations assigned above. Thus, **2** was (+)-(7*S*,8*S*)-1′,4-dihydroxy-3,3′,5′-trimethoxy-7′,8′,9′-trinor-8,4′-oxyneoligna-7,9-diol.

Compound **3** ($C_{19}H_{22}O_9$) had an additional CO unit. The NMR spectra of **3** (Supporting Information, Figures S23−S25) resembled those of **2**. However, the resonances for H-2′/6′ and C-2′/6′ of **3** were broadened, compared with those of **2**, and deshielded significantly by $\Delta\delta_H$ 1.11 and $\Delta\delta_C$ 14.1 ppm, respectively. This suggested that OH-1′ in **2** was replaced by COOH-1′ in **3** to match the molecular composition, although the ^{13}C NMR spectrum displayed two fewer carbon resonances (C-1′ and C-7′) than those expected from the molecular formula. The presence of COOH-1′ was supported by the 2D NMR data analysis of **3** that amended the 1D NMR data assignments (Tables 1 and 2). This was confirmed by methylation of **3** with CH_3I that produced **3a**. The NMR spectra of **3a** displayed resonances (Tables 1 and 2 and Supporting Information, Figures S31−S33) corresponding to COOMe. The ^{1}H NMR coupling constants of **3** ($J_{7,8}$ = 7.0 Hz) and **3a** ($J_{7,8}$ = 6.0 Hz) and positive Cotton effects in the CD spectra of **3** (258 nm) and **3a** (262 nm) suggested the 7*S*,8*S* configuration (Supporting Information, Figures S29 and S34). This was supported by positive Cotton effects in the $Rh_2(OCOCF_3)_4$-induced CD spectra of **3** (359 nm) and **3a** (356 nm) (Supporting Information, Figures S29 and S34). Therefore, compound **3** was deduced to be (+)-(7*S*,8*S*)-4-hydroxy-3,3′,5′-trimethoxy- 8′,9′-dinor-8,4′-oxyneoligna-7,9-diol-7′-oic acid.

Compound **4** ($C_{29}H_{32}O_{11}$) showed IR absorption bands for OH (3429 cm^{-1}), conjugated carbonyl (1680 cm^{-1}), and aromatic ring (1592 and 1514 cm^{-1}) groups. The NMR data of **4** (Tables 3 and 4) indicated the presence of a symmetric 3,4,5-trisubstituted phenyl, an asymmetric 3′,4′,5′-trisubstituted phenyl, a 3″,4″-disubstituted phenyl, and aldehyde groups. Also evident were four aromatic OCH_3, two oxymethylene, and four methine (three oxygenated) groups. These data suggested that **4** was a dinorsesquineolignane.[6b,10] In the HMBC spectrum of **4**, correlations for H-2 (H-6)/C-1, C-4, and C-7; H-7/C-1, C-2, C-6, C-8, C-9, and C-4′; H-8/C-1, C-7, C-9, C-3′, and C-4′; H-2′/C-4′, C-6′, C-7′, and C-8; O*Me*-5′/C-5′; and O*Me*-3 (O*Me*-5)/C-3 (C-5) revealed the presence of a 4-substituted 3,5,5′-trimethoxy-4′,7-epoxy-8,3′-neolignan-9-ol-7′-al moiety. In addition, HMBC correlations for H-2″ and H-6″/C-4″ and C-7″; H-5″/C-1″ and C-3″; H-7″/C-1″, C-2″, C-6″, C-8″, and C-9″; and O*Me*-3″/C-3″ indicated the presence of a guaiacylglycerol unit in **4**. Although no HMBC correlation for H-8″/C-4 was observed, the connection between C-8″ and C-4 was indicated by the shifts for H-8″ (δ_H 4.19) and C-8″ (δ_C 87.8) and C-4 (δ_C 136.4) and C-3/5 (δ_C 154.4).[10,16,19] In the NOE difference spectrum of **4**, H-2 and/or H-6 were enhanced when H-8 was irradiated, and irradiation of H-7 gave an enhancement of H_2-9. These enhancements combined with the coupling constant ($J_{7,8}$ = 6.5 Hz)[20] indicated the 7,8-*trans* configuration for **4**. The 7″,8″-*erythro* configuration was deduced by the coupling constant $J_{7'',8''}$ (2.0 Hz).[16] In the CD spectrum, a negative Cotton effect at 295 nm ($\Delta\varepsilon$ −0.15) indicated that **4** had a 7*R*,8*S* configuration on the basis of the reversed helicity rule of the ^1L_b band CD for the 7-methoxy-2,3-dihydrobenzo[*b*]furan chromophore[21] (Supporting Information, Figure S45). The 8″*R* configuration was proposed by a

Table 3. ^{1}H NMR Data (δ) for Compounds 4 and 10−15[a]

	4	10		11		12		13		14		15	
no.	Me_2CO-d_6	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6	$CDCl_3$
2	6.83 brs	6.77 brs	6.63 brs	6.76 brs	6.62 brs	6.76 brs	6.63 brs	6.76 brs	6.62 brs	6.77 brs	6.64 brs	6.75 brs	6.70 brs
6	6.83 brs	6.77 brs	6.63 brs	6.76 brs	6.62 brs	6.76 brs	6.63 brs	6.76 brs	6.62 brs	6.77 brs	6.64 brs	6.75 brs	6.70 brs
7	5.75 d (6.5)	4.67 d (4.5)	4.76 d (5.0)	4.68 d (4.0)	4.75 d (5.5)	4.67 d (4.0)	4.75 d (4.5)	4.67 d (3.0)	4.75 d (5.0)	4.68 d (4.0)	4.75 (3.0)	4.67 d (3.5)	4.74 d (5.0)
8	3.70 m	3.11 m	3.13 m	3.12 m	3.13 m	3.11 m	3.11 m	3.10 m	3.09 m	3.11 m	3.12 m	3.10 m	3.09 m
9a	3.92 m	4.24 m	4.32 m	4.24 m	4.29 m	4.25 m	4.31 m	4.25 m	4.30 m	4.25 m	4.32 m	4.25 m	4.30 m
9b	3.92 m	3.85 m	3.93 m	3.85 m	3.91 m	3.86 m	3.94 m	3.85 m	3.90 m	3.84 m	3.94 m	3.86 m	3.91 m
2′	7.52 brs	7.00 brs	6.91 brs	6.98 (1.0)	6.89 (1.0)	6.68 brs	6.59 brs	6.68 brs	6.58 brs	6.68 brs	6.59 brs	6.73 brs	6.62 brs
5′		6.82 d (8.0)	6.90 d (8.0)	6.78 d (8.0)	6.90 d (8.0)								
6′	7.44 brs	6.77 d (8.0)	6.83 d (8.0)	6.83 dd (8.0, 1.0)	6.82 dd (8.0, 1.0)	6.68 brs	6.59 brs	6.68 brs	6.58 brs	6.68 brs	6.59 brs	6.73 brs	6.62 brs
7′	9.84 s	4.73 d (4.5)	4.77 d (5.0)	4.73 d (4.0)	4.76 d (5.5)	4.73 d (3.5)	4.76 d (4.5)	4.73 d (4.0)	4.76 d (5.0)	4.73 d (4.0)	4.76 (3.0)	4.72 d (4.0)	4.75 d (5.0)
8′		3.11 m	3.10 m	3.12 m	3.07 m	3.11 m	3.11 m	3.10 m	3.09 m	3.11 m	3.12 m	3.10 m	3.09 m
9′a		4.24 m	4.28 m	4.24 m	4.27 m	4.25 m	4.31 m	4.25 m	4.30 m	4.25 m	4.32 m	4.25 m	4.30 m
9′b		3.85 m	3.93 m	3.85 m	3.91 m	3.86 m	3.94 m	3.85 m	3.90 m	3.84 m	3.94 m	3.86 m	3.91 m
2″	7.03 d (1.0)	7.03 brs	6.97 brs	7.04 d (1.0)	6.97 brs	6.99 brs	6.96 brs	7.03 brs	6.97 brs	6.65 brs	6.58 brs	6.68 brs	6.58 brs
5″	6.76 d (8.0)	6.82 d (8.0)	6.86 d (8.0)	6.75 d (8.0)	6.88 d (8.0)	6.82 d (8.0)	6.85 d (8.0)	6.75 d (8.0)	6.88 d (8.0)				
6″	6.82 dd (8.0, 1.0)	6.77 d (8.0)	6.75 d (8.0)	6.89 dd (8.0, 1.0)	6.95 d (8.0)	6.76 d (8.0)	6.74 d (8.0)	6.89 d (8.0)	6.96 d (8.0)	6.65 brs	6.58 brs	6.68 brs	6.58 brs
7″	4.97 d (2.0)	4.97 (3.0)	5.00 (3.5)	4.97 d (7.0)	5.02 d (8.5)	4.98 (3.5)	4.99 brs	4.87 d (7.0)	5.02 d (8.5)	4.97 (4.0)	4.98 (3.5)	4.95 d (6.5)	5.01 d (8.5)
8″	4.19 m	4.15 m	4.13 m	3.94 m	3.87[b] m	4.15 m	4.13 m	3.95 m	3.89 m	4.17 m	4.11 m	4.00 m	3.89 m
9″a	3.80 m	3.83 m	3.89 m	3.64 m	3.57 m	3.82 m	3.89 m	3.64 m	3.57 m	3.81 m	3.89 m	3.66 m	3.58 m
9″b	3.45 dd (12.0, 3.0)	3.43 m	3.50 m	3.31 m	3.32 m	3.42 m	3.50 m	3.32 m	3.32 m	3.43 m	3.49 m	3.35 m	3.30 m
OMe-3/5	3.84 s	3.86 s	3.91 s	3.89 s	3.92 s	3.86 s	3.90 s	3.89 s	3.92 s	3.87 s	3.91 s	3.89 s	3.92 s
OMe-3′/5′	3.95 s	3.83 s	3.90 s	3.85 s	3.91 s	3.82 s	3.90 s	3.82 s	3.91 s	3.81 s	3.91 s	3.82 s	3.89 s
OMe-3″/5″	3.81 s	3.82 s	3.90 s	3.83 s	3.89 s	3.80 s	3.87 s	3.80 s	3.89 s	3.80 s	3.88 s	3.79 s	3.88 s

[a] Data were measured for **4** and **10**−**15** at 500 MHz. Coupling constants (J) in Hz are given in parentheses. The assignments were based on ^{1}H−^{1}H COSY, HSQC, and HMBC experiments.

Table 4. ^{13}C NMR Data (δ) for Compounds 4 and 10−15[a]

	4	10		11		12		13		14		15	
no.	Me_2CO-d_6	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6	$CDCl_3$
1	138.1	139.0	137.8	139.2	137.9	139.1	137.7	139.2	137.8	139.1	137.8	139.2	137.9
2	104.3	104.1	102.8	104.0	102.7	104.0	102.7	103.9	102.7	104.8	102.9	104.0	102.7
3	154.4	154.2	153.5	153.8	153.1	154.2	153.3	153.8	153.1	154.1	153.5	153.8	153.5
4	136.4	135.7	134.3	136.1	134.6	135.7	134.2	136.0	134.4	135.8	134.4	136.1	134.4
5	154.4	154.2	153.5	153.8	153.1	154.2	153.3	153.8	153.1	154.1	153.5	153.8	153.5
6	104.3	104.1	102.8	104.0	102.7	104.0	102.7	103.9	102.7	104.8	102.9	104.0	102.7
7	89.6	86.6	86.0	86.6	85.9	86.7	85.9	86.7	86.0	86.7	86.0	86.7	86.0
8	54.0	55.1	54.1	55.1	54.0	55.2	54.2	55.2	54.4	55.2	54.4	55.2	54.3
9	64.2	72.5	72.2	72.5	72.1	72.6	71.9	72.6	72.0	72.6	72.1	72.6	72.0
1′	132.6	134.1	132.7	134.1	132.7	133.7	131.8	133.7	131.9	133.1	131.9	133.1	131.9
2′	121.3	110.9	108.6	110.6	108.6	104.4	102.7	104.4	102.7	104.4	102.8	104.5	102.7
3′	131.0	148.0	146.6	148.3	146.7	148.7	147.2	148.7	147.2	148.7	147.2	148.7	147.2
4′	154.7	146.9	145.3	146.7	145.3	136.2	134.4	136.2	134.6	136.2	134.4	136.2	134.6
5′	145.8	115.5	114.3	115.2	114.2	148.7	147.2	148.7	147.2	148.7	147.2	148.7	147.2
6′	113.5	120.0	118.9	119.6	118.9	104.4	102.7	104.4	102.7	104.4	102.8	104.5	102.7
7′	190.9	86.5	85.7	86.5	85.7	86.6	85.8	86.5	85.8	86.6	86.0	86.5	85.8
8′		55.4	54.5	55.5	54.5	55.4	54.3	55.4	54.5	55.4	54.5	55.4	54.5
9′		72.3	71.5	72.3	71.5	72.4	71.6	72.4	71.7	72.4	71.7	72.4	71.7
1″	133.7	134.0	131.3	133.7	131.9	133.1	131.2	133.0	131.9	133.0	130.4	132.7	131.0
2″	110.9	110.6	108.3	111.3	109.7	110.9	108.5	111.3	109.8	104.1	102.6	105.3	104.0
3″	147.9	148.3	146.7	147.9	146.4	148.0	146.6	147.9	146.5	148.4	147.1	148.3	147.0
4″	146.4	146.4	144.9	146.9	145.4	146.4	144.8	146.7	145.4	133.1	134.0	136.0	134.3
5″	115.2	115.2	114.1	115.5	114.3	115.2	114.2	115.2	114.3	148.4	147.1	148.3	147.0
6″	120.0	119.6	118.7	120.6	120.4	120.0	118.7	120.6	120.3	104.1	102.6	105.3	104.0
7″	73.4	73.4	72.5	73.9	74.1	73.3	72.4	73.9	74.0	73.6	72.7	74.0	74.3
8″	87.8	87.9	87.1	89.6	89.1	87.8	86.9	89.6	89.0	87.9	87.2	89.3	89.1
9″	61.0	61.0	60.6	61.4	60.5	60.9	60.4	61.4	60.5	61.0	60.6	61.5	60.5
OMe-3/5	56.6	56.6	56.2	56.6	56.2	56.6	56.3	56.6	56.5	56.8	56.4	56.6	56.4
OMe-3′/5′	56.4	56.2	56.0	56.2	56.0	56.6	56.2	56.6	56.4	56.8	56.4	56.6	56.3
OMe-3″/5″	56.2	56.2	56.0	56.2	56.0	56.2	55.9	56.2	56.0	56.6	56.3	56.5	56.2
$\Delta\delta_{C8''-C7''}$	14.4	14.5	14.6	15.7	15.0	14.5	14.5	15.7	15.0	14.3	14.5	15.3	14.8

[a] Data were measured for **4** and **10**−**15** at 125 MHz. The assignments were based on ^{1}H−^{1}H COSY, HSQC, and HMBC experiments.

negative Cotton effect at 235 nm.[15−17] The 7″*S* configuration defined by the 7″,8″-*erythro* was supported by a positive Cotton effect at 347 nm (the E band) in the $Rh_2(OCOCF_3)_4$-induced CD spectrum of **4**[18] (Supporting Information, Figure S45). Therefore, compound **4** was (−)-(7*R*,8*S*,7″*S*,8″*R*)-3,3″,5,5′- tetramethoxy-4″-hydroxy-4′,7-epoxy-8′,9′-dinor-4,8″-oxy-8,3′-sesquineolignа-7″,9,9″-triol-7′-al.

Compound **5** exhibited spectroscopic data (Tables 1 and 2 and Experimental Section) almost identical to those of woorenogenin,[22] but with opposite Cotton effects. Comprehensive analysis of the 2D NMR and NOE difference spectra proved that **5** had the same planar structure and relative configuration as woorenogenin. On the basis of the reversed helicity rule of the ^1L_b band CD for the 7-methoxy-2,3-dihydrobenzo[*b*]furan chromophore,[21] a negative Cotton effect at 272 nm in the CD spectrum of **5** indicated that it had a 7*R*,8*S* configuration (Supporting Information, Figure S54), and this was supported by the negative optical rotation (the reported optical rotation of woorenogenin was ambiguous).[23] Thus, compound **5** was (−)-(7*R*,8*S*,7′*E*)-3,4,5,5′-tetramethoxy-4′,7-epoxy-8,3′-neolign-7′-ene-9,9′-diol.

Compound **6** ($C_{22}H_{26}O_6$) had UV, IR, and NMR spectroscopic features similar to those of **5**, except that the NMR resonances of the 3,4,5-trimethoxyphenyl group in **5** were replaced by those attributed to 3-methoxy-4-hydroxyphenyl and ethoxy units in **6** (Tables 1 and 2). In addition, the resonance for C-9′ of **6** was deshielded significantly as compared with that of **5**. This implied that OH-9′ in **5** was substituted by OEt-9′ in **6**, which was confirmed by a correlation for H_2-1‴/C-9′ in the HMBC spectrum of **6** (Supporting Information, Figure S62). The optical rotation and CD data of **6** were opposite of those of **5**, indicating a 7*S*,8*R* configuration for **6**.[21] Accordingly, compound **6** was determined as (+)-(7*S*,8*R*,7′*E*)-4-hydroxy-3,5′-dimethoxy-4′,7-epoxy-8,3′-neolign-7′-ene-9,9′-diol 9′-ethyl ether. The ethyl group in **6** could be an artifact formed during isolation, although the de-ethyl precursor of **6** was not obtained in this study.

Compound **7**, $C_{22}H_{26}O_9$, showed IR absorptions for OH (3473 cm^{-1}), conjugated carbonyl (1661 cm^{-1}), and aromatic ring (1611 and 1518 cm^{-1}) groups. The NMR data (Tables 1 and 2) were similar to those of wikstrone[15] except for substitution of the resonances for the 4′-hydroxy-3′,5′-dimethoxyphenyl moiety in **7** by those for the 4′-hydroxy-3′-methoxyphenyl unit in wikstrone. This was confirmed by 2D NMR data analysis (Supporting Information, Figures S71−S73). The shifts and coupling constants for H-7′ and H-8′ of **7**, similar to those of wikstrone, indicated that H-8′ was oriented opposite H-7′ and H-8. This was verified by enhancements of H-2/H-6 and H-2′/H-6′ (overlapped each pair) when H-8′ was irradiated in the NOE difference spectrum of **7**. In the CD spectrum of **7**, Cotton effects (negative at 324 nm and positive at 286 nm) arising from the exciton coupling of the benzoyl and benzene chromphores (Supporting Information, Figure S75) suggested the 7′*S*,8*S*,8′*R* configuration.[15] Thus, compound **7** was determined to be (−)-(7′*S*,8*S*,8′*R*)-4,4′-dihydroxy-3,3′,5,5′-tetramethoxy-7′,9-epoxylignan-9′-ol-7-one.

Compound **8** had the molecular formula $C_{23}H_{30}O_9$, and the NMR data of **8** (Tables 1 and 2) were similar to those of icariol A_2.[24] However, resonances for an additional OCH_3 were observed in the spectra of **8**. This indicated replacement of OH-4 in icariol A_2 by OMe-4 in **8**, which was proved by 2D NMR analysis. Detailed explanation of the HMBC data (Supporting Information, Figure S83) amended the assignment of the shifts for C-4 and C-4′ that were not observed in the ^{13}C NMR spectrum of **8** due to limitation of the sample amount available. The ^{1}H NMR shifts and coupling constants for H-7, H-7′, H-8, and H-8′ of **8** indicated the *trans*-orientation between each pair of the vicinal protons.[24] The CD spectrum displayed a typical coupled Cotton effect, positive at 243 nm ($\Delta\varepsilon$ +10.9) and negative at 207 nm ($\Delta\varepsilon$ −16.6), indicating exciton coupling between the $\pi \rightarrow \pi^*$ transition of the phenyl chromophores (Supporting Information, Figure S84). The positive chirality revealed the 7*R*,7′*R*,8*S*,8′*S* configuration for **8**,[25] which was supported by the positive optical rotation {$[\alpha]^{20}_D$ +25.5 (*c* 0.04, MeOH)}.[24b,25] Therefore, compound **8** was determined to be (+)-(7*R*,7′*R*,8*S*,8′*S*)-4′-hydroxy-3,3′,4,5,5′-pentamethoxy-7,7′-epoxy lignan-9,9′-diol.

Compound **9**, $C_{23}H_{28}O_8$, displayed spectroscopic data similar to those of (−)-syringaresinol.[26] However, the NMR spectra in Me_2CO-d_6 indicated partial separation of resonances for the two aryl groups and the presence of a phenolic OH and five OCH_3 groups in **9**. This suggested that **9** was 4′-hydroxy-3,3′,4,5,5′-pentamethoxy-7,9′:7′,9-diepoxylignane. 2D NMR data analysis of **9** (Supporting Information, Figures S91−S93) provided unambiguous assignments. The coupling constants of $J_{7,8}$ and $J_{7',8'}$ (4.2 Hz) and the shifts of H-7/H-7′, H-8/H-8′, and C-8/C-8′ indicated that the aryl groups were pseudoequatorial and *cis*-oriented with H-8 and H-8′ in **9**.[20,27] The CD data (negative at 274, 239, and 214 nm) and specific rotation {$[\alpha]^{20}_D$ −45.8 (*c* 0.03, MeOH)} of **9** were consistent with those of (−)-syringaresinol[26] (Supporting Information, Figure S247), but opposite those of (+)-syringaresinol.[28,29] Therefore, compound **9** was (−)-(7*R*,7′*R*,8*S*,8′*S*)-4′-hydroxy-3,3′,4,5,5′-pentamethoxy-7,9′:7′,9-diepoxylignane.

Compound **10** had the molecular formula $C_{31}H_{36}O_{11}$, and comparison of the NMR data between **10** (Tables 3 and 4) and medioresinol[29] indicated that they differed in the presence of resonances attributable to an additional 4″-hydroxy-3″-methoxyphenylglycerol-8″-yl moiety in **10**. The coupling constant for $J_{7'',8''}$ (3.0 Hz) indicated an *erythro* configuration for the aryl glycerol-8″-yloxy moiety,[9] and shifts of resonances for C-8″ (87.9) and C-3/5 (154.2)[10] in Me_2CO-d_6 revealed that the aryl glycerol-8″-yloxy was located at C-4. This suggested that **10** had the same planar structure as hedyotol C[5] and/or buddlenol E.[6] However, hedyotol C, with configuration undetermined, was reported to have contrary optical rotations (positive[5a,b] and negative[5c,d]), and buddlenol E was reported as a mixture of 7″,8″-*erythro* and *threo* isomers.[6a,c] Comparison of the NMR data between **10** and hedyotol C demonstrated that they had the same relative configuration. The relative configuration of **10** was supported by the ^{1}H NMR coupling constants $J_{7,8}$, $J_{7'8'}$, and $J_{7'',8''}$ in the spectrum of the acetonide derivative (**10a**) (Supporting Information, Figure S108 and Table S1). Alkaline hydrolysis of **10** liberated a product having the spectroscopic data including $[\alpha]_D$ identical to (−)-medioresinol. Comparing the CD data of (−)-medioresinol with those of **10** and **10a** (Supporting Information, Figures S106, S110, and S247), a negative ^1L_b Cotton effect at 281 nm in the CD spectra of **10** and **10a** supported the 7*R*,7′*R*,8*S*,8′*S* configuration.[28,30] In addition, a positive Cotton effect at 239 nm indicated the 8″*S* configuration for **10** and **10a**.[15−17] The 7″*R* configuration defined by the 7″,8″-*erythro* was supported by a negative Cotton effect at 353 nm (the E band) in the $Rh_2(OCOCF_3)_4$-induced CD spectrum of **10** since the E band was absent in the $Rh_2(OCOCF_3)_4$-induced CD of **10a** and (−)-medioresinol (Supporting Information, Figure S106). Thus, **10** was (−)-(7*R*,7′*R*,7″*R*,8*S*,8′*S*,8″*S*)-4′,4″-dihydroxy-3,3′,3″,5-tetramethoxy-7,9′:7′,9-diepoxy-4,8″-oxy-8,8′-sesquineolignan-7″,9″-diol.

The spectroscopic data of **11** (Tables 3 and 4 and Experimental Section) were consistent with hedyotol D.[5a,c,d] However, the configuration and $[\alpha]_D$ values (positive[5a] and negative[5c,d]) of hedyotol D were ambiguous. Using the same methods as described for **10** (Supporting Information, Figures S122−126 and Table S1), the 7*R*,7′*R*,7″*S*,8*S*,8′*S*,8″*S* configuration of **11** was elucidated. Particularly, in the $Rh_2(OCOCF_3)_4$-induced CD spectrum, a positive Cotton effect at 348 nm opposite that of **10** (Supporting Information, Figure S122) supported the 7″*S* configuration for **11**.

The spectroscopic data of **12** (Tables 3 and 4 and Experimental Section) were almost identical to those of buddlenol C, which was reported to have controversial configuration.[6a,b,7] The 7*R*,7′*R*,7″*R*,8*S*,8′*S*,8″*S* configuration of **12** was verified by the NMR data of the acetonide product (**12a**) (Supporting Information, Figures S140−142 and Table S1) as well as by alkaline hydrolysis producing (−)-syringaresinol and the CD data of **12** and **12a** including the $Rh_2(OCOCF_3)_4$-induced CD data of **12** (negative at 351 nm) (Supporting Information, Figure S138).

Compound **13** was the 7″,8″-*threo* isomer of **12** possessing a 7″*S* configuration, as indicated by the spectroscopic data (Tables 3 and 4 and Experimental Section) and confirmed by the same procedures as described above (Supporting Information, Figures S153−155 and Table S1). 7″,8″-*threo*-Buddlenol C was reported to have UV, IR, MS, and NMR data identical to **13**, but with ambiguous configuration[6a,b,7] and $[\alpha]_D$ value (positive[7f]).

The spectroscopic data of **14** (Tables 3 and 4 and Experimental Section) were in agreement with those of buddlenol D, which was assigned ambiguous configuration.[6a,7c,7e,8] Using the same methods as above (Supporting Information, Figures S167−S171 and Table S1), compound **14** was (−)-(7*R*,7′*R*,7″*R*,8*S*,8′*S*,8″*S*)-4′,4″-dihydroxy-3,3′,3″,5,5′,5″-hexamethoxy-7,9′:7′,9-diepoxy-4,8″-oxy-8,8′-sesquineolignan-7″,9″-diol.

Differences of the spectroscopic data between **15** and **14** (Tables 3 and 4 and Experimental Section) were similar to those between **11** and **10** and between **13** and **12**. This demonstrated that **15** was the 7″,8″-*threo* isomer of **14**. The 7*R*,7′*R*,7″*S*,8*S*,8′*S*,8″*S* configuration of **15** was substantiated also as described above (Supporting Information, Figures S179−S183 and Table S1).

Compound **16** had the molecular formula $C_{42}H_{50}O_{16}$ (HRESIMS), and the NMR data (Table 5) resembled those of hedyotisol A, having conflicting configuration and $[\alpha]_D$ values (optical inactive[7h,9] and negative[10]). The 7″,8″:7‴,8‴-di-*erythro*

Table 5. NMR Data (δ) for Compounds 16−18[a]

	16		17		18			16		17		18	
no.	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	no.	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1		138.9		139.1		139.0	1″		133.7		133.7		133.7
2	6.76 brs	104.0	6.76 brs	104.0	6.76 brs	104.1	2″	7.03 d (1.5)	110.9	7.03 d (1.5)	111.3	7.03 brs	110.9
3		154.1		153.9		154.2	3″		147.9		147.9		147.9
4		135.6		136.1		135.5	4″		146.4		146.7		146.5
5		154.1		153.9		154.2	5″	6.76 d (8.4)	115.2	6.75 d (8.5)	115.2	6.75 d (8.0)	115.2
6	6.76 brs	104.0	6.76 brs	104.0	6.76 brs	104.1	6″	6.82 dd (8.4, 1.5)	120.0	6.89 dd (8.5, 1.5)	120.6	6.82 d (8.0)	120.0
7	4.74 d (3.3)	86.4	4.74 d (3.0)	86.5	4.74 d (3.0)	86.4	7″	4.97 brs	73.3	4.98 d (7.0)	73.9	4.97 brs	73.4
8	3.12 m	55.3	3.12 m	55.4	3.12 m	55.3	8″	4.16 m	87.7	3.94 m	89.6	4.15 m	87.8
9a	4.28 m	72.6	4.28 m	72.6	4.28 m	72.6	9″a	3.85 m	60.9	3.64 m		3.84 m	61.0
9b	3.91 m		3.89 m		3.91 m		9″b	3.45 m		3.31 m	61.4	3.45 m	
1′		138.9		139.1		139.1	1‴		133.7		133.7		133.8
2′	6.76 brs	104.0	6.76 brs	104.0	6.76 brs	104.0	2‴	7.03 d (1.5)	110.9	7.03 d (1.5)	111.3	7.03 brs	111.3
3′		154.1		153.9		153.9	3‴		147.9		147.9		148.0
4′		135.6		136.1		135.7	4‴		146.4		146.7		146.7
5′		154.1		153.9		153.9	5‴	6.76 d (8.4)	115.2	6.75 d (8.5)	115.2	6.75 d (8.0)	115.2
6′	6.76 brs	104.0	6.76 brs	104.0	6.76 brs	104.0	6‴	6.82 dd (8.4, 1.5)	120.0	6.89 dd (8.5, 1.5)	120.6	6.89 d (8.0)	120.6
7′	4.74 d (3.3)	86.4	4.74 d (3.0)	86.5	4.74 d (3.0)	86.5	7‴	4.97 brs	73.3	4.98 d (7.0)	73.9	4.97 (7.0)	73.9
8′	3.12 m	55.3	3.12 m	55.4	3.12 m	55.3	8‴	4.16 m	87.7	3.94 m	89.6	3.94 m	89.6
9′a	4.28 m	72.6	4.28 m	72.6	4.28 m	72.6	9‴a	3.85 m	60.9	3.64 m	61.4	3.64 m	61.4
9′b	3.91 m		3.89 m		3.89 m		9‴b	3.45 m		3.31 m		3.31 m	
OMe-3/5	3.85s	56.6	3.89 s	56.6	3.86 s	56.6	OMe-3‴/5‴	3.81 s	56.2	3.80 s	56.2	3.80 s	56.2
OMe-3′/5′	3.85s	56.6	3.89 s	56.6	3.89 s	56.6	$\Delta\delta_{C8''-C7''}$		14.4		15.7		14.4
OMe-3″/5″	3.81 s	56.2	3.80 s	56.2	3.82 s	56.2	$\Delta\delta_{C8'''-C7'''}$		14.4		15.7		15.7

[a] ^{1}H NMR data were measured in Me_2CO-d_6 at 300 MHz for 16 and at 500 MHz for 17 and 18, respectively. Proton coupling constants (J) in Hz are given in parentheses. ^{13}C NMR data were measured in Me_2CO-d_6 at 125 MHz for 16−18. The assignments were based on ^{1}H−^{1}H COSY, HSQC, and HMBC experiments.

configuration of **16** was indicated by the coupling constant of $J_{7'',8''}/J_{7''',8'''}$ (≈0 Hz) and the shifts of H-8″/8‴, H_2-9″/9‴, and C-8″/8‴. Alkaline hydrolysis of **16** generated (−)-syringaresinol, suggesting the 7*R*,7′*R*,8*S*,8′*S* configuration. This was supported by a negative ^1L_b Cotton effect at 287 nm[28,30] in the CD spectrum of **16**. In addition, the 8″*S*,8‴*S* configuration was proposed by a positive Cotton effect at 234 nm[15−17] and supported by a negative Cotton effect at 351 nm (the E band) in the $Rh_2(OCOCF_3)_4$-induced CD spectrum of **16** (Supporting Information, Figure S190).

The spectroscopic data of **17** (Table 5 and Experimental Section) indicated that it was the 7″,8″:7‴,8‴-di-*threo* isomer of **16**. Application of the same methods as described for **16** resulted in the assignment of a 7*R*,7′*R*,7″*S*,7‴*S*,8*S*,8′*S*,8″*S*,8‴*S* configuration for **17**. Particularly, in the $Rh_2(OCOCF_3)_4$-induced CD spectrum, a positive Cotton effect at 350 nm (Supporting Information, Figure S197) substantiated the 7″*R*,7‴*R* configuration for **17**. It was reported that hedyotisol C had MS and NMR data identical to **17**, but it also had ambiguous configuration (optically inactive[9a,d,f]).

Compound **18** was another isomer of **16**, as indicated by the spectroscopic data (Table 5 and Experimental Section). However, the NMR resonances for the two disubstituted aryl glycerol units were partially separated. Analysis of the 1D and 2D NMR data of **18** indicated that the resonances for one aryl glycerol unit [H-8″, H_2-9″, and C-8″] were identical to those of **10**, **12**, **14**, and **16**, whereas the resonances for another aryl glycerol unit [H-8‴, H_2-9‴, and C-8‴] were identical with those of **11**, **13**, **15**, and **17**. These data indicated that **18** was the 7″,8″-*erythro*-7‴,8‴-*threo* stereoisomer of **16** and **17**. In the CD spectrum of **18**, a positive Cotton effect at 235 nm with intensity similar to those of **16** and **17** suggested that they had the same 8″*S*,8‴*S* configuration. The 7″*R*,7‴*S* configuration defined by the 7″,8″-*erythro*-7‴,8‴-*threo* configuration was supported by comparison of the $Rh_2(OCOCF_3)_4$-induced CD of **18** with **16** and **17**. The $Rh_2(OCOCF_3)_4$-induced CD spectrum of **18** gave a diminished positive Cotton effect with the intensity representing deduction of the half-intensity of the Cotton effect for the 7″*R*,7‴*R*-isomer (**16**) from that for the 7″*S*,7‴*S*-isomer (**17**). Accordingly, **18** was (+)-(7*R*,7′*R*,7″*R*,7‴*S*,8*S*,8′*S*,8″*S*,8‴*S*)-4″,4‴-dihydroxy-3,3′,3″,3‴,5,5′-hexamethoxy-7,9′:7′,9-diepoxy-4,8″:4′,8‴-bisoxy-8,8′-dineolignan-7″,7‴,9″,9‴-tetraol. Hedyotisol B was reported to have spectroscopic data similar to those of **18**; however, its configuration had not been determined (optical inactive[9a,b,d,f]).

Compound **19** had spectroscopic data (Table 6 and Experimental Section) similar to those of calquiquelignans D, having undetermined absolute configuration.[11] The relative configuration for the glycerol unit in **19** could not be deduced from the $J_{7'',8''}$ value since H-7″ appeared as a broad singlet in the ^{1}H NMR spectrum in DMSO-d_6.[12b] However, in the acetonide derivative (**19a**) (Supporting Information, Figure S219 and Table S2), the $J_{7'',8''}$ value (9.4 Hz) proved the 7″,8″-*erythro* configuration for **19**.[16,31] The CD spectrum of **19** displayed a typical coupled Cotton effect arising from exciton coupling between the transition moments of the flavone and benzene chromophores, negative at 362 nm ($\Delta\varepsilon$ −0.13) and positive at 322 nm ($\Delta\varepsilon$ +0.09) (Supporting Information, Figure S217). On the basis of the CD exciton chirality method,[32] the negative chirality CD suggested the 7″*R*,8″*S* configuration for **19**. The 7″*R* configuration defined by the 7″,8″-*erythro* was supported by a negative Cotton effect at 356 nm (the E band) in the $Rh_2(OCOCF_3)_4$-induced CD spectrum (Supporting Information, Figure S218). Hence, **19** was (−)-(7″*R*,8″*S*)-4″,5,7-trihydroxy-3′,5′-dimethoxy-4′,8″-oxyflavonolignan-7″,9″-diol.

The spectroscopic data of **20** (Table 6 and Experimental Section) resembled those of calquiquelignans E {$[\alpha]^{20}_D$ +27.0 (c 0.48,

Table 6. NMR Data (δ) for Compounds 19−22[a]

	19		20		21		22	
no.	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
2		163.0		163.0		162.9		162.7
3	7.05 s	104.8	7.04 s	104.8	7.02 s	104.7	7.01 s	104.7
4		181.8		181.9		181.8		181.5
5		161.4		161.4		161.4		161.3
6	6.20 d (1.8)	98.9	6.20 brs	99.0	6.18 brs	99.1	6.17 brs	99.3
7		164.4		164.4		164.3		164.3
8	6.56 d (1.8)	94.3	6.56 brs	94.3	6.53 brs	94.3	6.52 brs	94.5
9		157.4		157.4		157.4		157.5
10		103.8		103.8		103.6		103.7
1′		125.2		125.3		125.2		125.4
2′	7.30 brs	104.2	7.30 brs	104.3	7.30 brs	104.2	7.30 brs	104.2
3′		153.0		152.9		152.9		152.9
4′		139.4		139.9		139.4		139.8
5′		153.0		152.9		152.9		152.9
6′	7.30 brs	104.2	7.30 brs	104.3	7.30 brs	104.2	7.30 brs	104.2
1″		132.5		132.3		133.2		133.0
2″	7.15 d (8.4)	127.9	7.18 d (8.4)	127.8	6.92 brs	110.9	6.96 d (1.5)	111.0
3″	6.68 d (8.4)	114.4	6.67 d (8.4)	114.4		147.0		146.9
4″		156.2		156.2		145.4		145.4
5″	6.68 d (8.4)	114.4	6.67 d (8.4)	114.4	6.68 d (8.1)	114.7	6.68 d (8.0)	114.6
6″	7.15 d (8.4)	127.9	7.18 d (8.4)	127.8	6.74 d (8.1)	119.4	6.79 d (8.0, 1.5)	119.1
7″	4.77 brs	72.0	4.84 brs	71.5	4.78 brs	72.1	4.83 brs	71.6
8″	4.30 m	86.4	4.21 m	87.0	4.34 m	86.5	4.24 m	87.0
9″a	3.71 m	60.1	3.63 m	60.4	3.71 m	60.1	3.63 m	60.4
9″b	3.47 m		3.22 m		3.47 m		3.24 m	
O*Me*-3′/5′	3.86 s	56.3	3.85 s	56.4	3.87 s	56.4	3.85 s	56.4
O*Me*-3″					3.73 s	55.5	3.72 s	55.5
$\Delta\delta_{C8''-C7''}$		14.4		15.5		14.4		15.4

[a] ^{1}H NMR data were measured in DMSO-d_6 at 300 MHz for **19** and **21**, at 600 MHz for **20**, and at 500 MHz for **22**, respectively. Proton coupling constants (J) in Hz are given in parentheses. ^{13}C NMR data were measured in DMSO-d_6 at 125 MHz for **19** and **22** and at 150 MHz for **20** and **21**, respectively. The assignments were based on ^{1}H−^{1}H COSY, HSQC, and HMBC experiments.

MeOH)};[11] however, the optical rotation of **20** {$[\alpha]^{20}_D$ −20.0 (c 0.02, MeOH)} was opposite. The 7″,8″-*threo* configuration for **20** was verified by the ^{1}H NMR spectrum of the acetonide derivative (**20a**) showing $J_{7'',8''} \approx 0.0$ Hz (Supporting Information, Figure S229 and Table S2).[16,31] The 7″*S*,8″*S* configuration of **20** was also indicated by a typical coupled Cotton effect [negative at 353 nm ($\Delta\varepsilon$ −0.07) and positive at 318 nm ($\Delta\varepsilon$ +0.08)] similar to that of **19**, as well as by the $Rh_2(OCOCF_3)_4$-induced positive Cotton effect at 362 nm (the E band) opposite that of **19** (Supporting Information, Figures S227 and S228).

Compound **21** exhibited spectroscopic data (Table 6 and Experimental Section) similar to those of salcolin B.[12] However, the absolute configuration of salcolin B was not determined, and it was assigned to be tricin 4′-*O*-(*erythro*-β-guaiacylglyceryl) ether,[12c−e] having a positive optical rotation opposite that of **21** {$[\alpha]_D$ −18.3 (c 0.03, MeOH)}. The 7″,8″-*erythro* configuration for **21** was substantiated by the $J_{7'',8''}$ value (9.0 Hz) displayed in the ^{1}H NMR spectrum of the acetonide derivative (**21a**).[16,31] Although it was reported that the CD spectrum of salcolin A did not exhibit any Cotton effect presumably due to conformational mobility,[12d] the CD spectrum of **21** in MeCN showed Cotton effects similar to those of **19** (Supporting Information, Figure S234). The similarity of the CD and $Rh_2(OCOCF_3)_4$-induced CD data between **21** and **19** (Supporting Information, Figure S235) indicated that these analogues had the same 7″*R*,8″*S* configuration. Therefore, compound **21** was determined to be (−)-(7″*R*,8″*S*)-4″,5,7-trihydroxy-3′,3″,5′-trimethoxy-4′,8″-oxyflavonolignan-7″,9″-diol.

The spectroscopic data of **22** (Table 6 and Experimental Section) resembled those of salcolin A,[12a,c−e] which was reassigned as tricin 4′-*O*-(*threo*-β-guaiacylglyceryl) ether,[12b] indicating that it was the 7″,8″-*threo* isomer of **21**. The 7″,8″-*threo* configuration for **22** was proved by the $J_{7'',8''}$ value (≈0.0 Hz) in the ^{1}H NMR spectrum of the acetonide derivative (**22a**). The 7″*S*,8″*S* configuration of **22** was suggested by Cotton effects [negative at 348 nm ($\Delta\varepsilon$ −0.06) and positive at 318 nm ($\Delta\varepsilon$ +0.07)] in the CD spectrum and a positive Cotton effect at 366 nm (the E band) in the $Rh_2(OCOCF_3)_4$-induced CD spectrum (Supporting Information, Figures S241 and S242).

The known compounds were identified by comparison of spectroscopic data with those reported in the literature as (−)-syringaresinol,[26] (−)-medioresinol,[33] (−)-(7*R*,8*S*)-guaiacylglycerol, (+)-(7*S*,8*S*)-guaiacylglycerol,[16] tricin,[34] 7-methoxytricin,[35]

(−)-5′-methoxyisolariciresinol,[36] (+)-lyoniresinol,[13] (+)-brugunin A,[37] (+)-(7*S*,8*S*)-guaiacylglycerol-*β*-vanillic acid ether,[38] (+)-(7′*E*,7*S*,8*R*)-4,7,9,9′-tetrahydroxy-3,3′,5′-trimethoxy-8,4′-oxyneolign-7′-ene,[15] (−)-(7′*E*,7*R*,8*S*)-3,4,5′-trimethoxy-4′,7-epoxy-8,3′-neolign-7′-ene-9,9′-diol,[21b] (+)-(7*S*,8*R*,8′*R*)-5,5′-dimethoxylariciresinol,[39] and (+)-5′-methoxylariciresinol.[40]

The isolation of 7,9′:7′,9-diepoxy-4,8″-oxy-8,8′-sesquineolignan-7″,9″-diol derivatives from the hydrolysate of hardwood lignin of *Fraxinus mandshurica*,[7a] 7,9′:7′,9-diepoxy-4,8″:4′,8‴-bisoxy-8,8′-dineolignan-7″,7‴,9″,9‴-tetraol from the MeOH extract of dried leaves of *Hedyotis lawsoniae*,[9a] and 4′,8″-oxyflavonolignan-7″,9″-diol from the extract of *Aegilops ovata*[41] was reported more than 25 years ago. However, the configuration of both the 7,9′:7′,9-diepoxylignane and arylglycerol moieties in the molecules had not been substantiated due to some contrary and controversial data reported in the literature. By comparing the NMR and CD data of **2**−**4** and **10**−**22**, in combination with a literature survey, several points concerning the configuration of the aryl glycerol units in these compounds could be summarized. Our previous investigation indicated that coupling constants ($J_{7,8}$) distinct for the deshielded benzylic proton (H-7) resonance in the ^{1}H NMR spectra of 8,4′-oxyneolignanes varied in different solvents due to possible dynamic conformational changes.[16] Therefore, direct application of the $J_{7,8}$ values was ambiguous to differentiate *erythro* and *threo* 8,4′-oxyneolignans with the exception of aglycone acetonides ($J_{7,8} > 7.0$ Hz for *erythro* and $J_{7,8} < 2.0$ Hz for *threo*) and glycoside acetates ($J_{7,8} \leq 5.3$ Hz for *erythro* and $J_{7,8} \geq 6.3$ Hz for *threo*) in $CDCl_3$, as well as aglycones in $CDCl_3$ ($J_{7,8} \leq 5.0$ Hz for *erythro* and $J_{7,8} \geq 7.0$ Hz for *threo*).[16] In addition, the $\Delta\delta_{C8-C7}$ values eliminating the effect of systematic errors [$\Delta\delta_{C8-C7}(threo) > \Delta\delta_{C8-C7}(erythro)$] were also applicable to differentiate *threo* and *erythro* aryl glycerols without substituent(s) at C-7 or/and C-8 of the glycerol moiety[42] as well as the *erythro* and *threo* 8,4′-oxyneolignane isomers[16] when the data were obtained in the same solvent. Inspection of the NMR data obtained in Me_2CO-d_6 and/or $CDCl_3$ (Tables 1−5) indicated that the coupling constants for the *erythro* aryl glycerol moieties ($J_{7'',8''}$ for **4**, **10**, **12**, **14**, **16**, and **18**; $J_{7''',8'''}$ for **16**; <4.0 Hz) were smaller than those for *threo* isomers ($J_{7,8}$ for **2**, **3**, and **3a**; $J_{7'',8''}$ for **11**, **13**, **15**, and **17**; and $J_{7''',8'''}$ for **17** and **18**; >6.0 Hz). Meanwhile, chemical shift differences for the *erythro* aryl glycerol moieties ($\Delta\delta_{C8''-C7''}$ for **4**, **10**, **12**, **14**, **16**, and **18**; $\Delta\delta_{C8'''-C7'''}$ for **16**; <14.6 ppm) were smaller than those for the *threo* moieties ($\Delta\delta_{C8''-C7''}$ for **11**, **13**, **15**, and **17**; $\Delta\delta_{C8'''-C7'''}$ for **17** and **18**; >14.8 ppm). Although the $J_{7'',8''}$ values for **19**−**22** in DMSO-d_6 (Table 6) and pyridine-d_5 were indistinguishable[12b] and it was reported that the data ($J_{7'',8''}$) in CD_3OD and CD_3CN for the *erythro* forms (**19** and **21**) were smaller than those for the *threo* forms (**20** and **22**),[12] the $\Delta\delta_{C8''-C7''}$ values in the different solvents for the *erythro* analogues were consistently smaller than those for the *threo* derivatives. This was fully consistent with our previous reports,[16,42] supporting the validity of direct application of $\Delta\delta_{C8-C7}$ values to distinguish *threo* and *erythro* arylglycerol units in the different neolignans. This was confirmed by the coupling constants in the ^{1}H NMR spectra of the corresponding acetonide derivatives ($J_{7'',8''}$ for **4a**, **10a**, **12a**, **14a**, **16a**, **18a**, **19a**, and **21a** and $J_{7''',8'''}$ for **16a** > 9.0 Hz, whereas $J_{7,8}$ for **2a**, $J_{7'',8''}$ for **11a**, **13a**, **15a**, **17a**, **20a**, and **22a**, and $J_{7''',8'''}$ for **17a** and **18a** < 2.0 Hz).

Detailed analysis of the CD data of compounds **2**, **4**, **10**−**18**, and **10a**−**15a** and our previous investigation,[16] together with literature surveys,[15,17,20] indicated that the ^1L_a Cotton effects at around 235 ± 5 nm could be validated for the configuration assignment at C-8 (positive for 8*S* and negative for 8*R*) of the aryl glycerol units in the aryl glycerols, neolignans[15−17] including sesquineolignans (**10**−**15**), and dineolignans (**16**−**18**), although substitution of OH and/or OMe group(s) on the aryl ring(s) and acetonation at C-7 and C-9 of the glycerol units varied wavelengths and intensities of the Cotton effect bands in the CD spectra. For the sesquineolignans and dineolignans, the Cotton effects should be contributed by both the aryl glycerol and 7,9′:7′,9-diepoxylignane chromaphores in the molecules. However, it was dominated by the aryl glycerol moiety. This was supported by comparison of the CD spectra of **10**−**18** and acetonide derivatives (**10a**−**15a**) with those of aryl glycerols [(−)-(7*R*,8*S*)-guaiacylglycerol and (+)-(7*S*,8*S*)-guaiacylglycerol)] and 7,9′:7′,9-diepoxy lignanes [**9**, (−)-syringaresinol, and (−)-medioresinol)] (Supporting Information, Figures S244−S247) as well as the related derivatives in the literature.[20] Differing from those of **2**, **4**, and **10**−**18**, the CD spectra of **19**−**22** exhibited typical coupled Cotton effects (negative at 355 ± 10 nm and positive at 320 ± 5 nm, Supporting Information, Figure S248). Therefore, the exciton chirality method[32] should be applicable to determine the configurations at C-8 of the glycerol units in **19**−**22**. A convenient bulkiness rule for the $Rh_2(OCOCF_3)_4$-induced CD data (the E band) was demonstrated to be useful to determine the absolute configuration of chiral secondary and tertiary alcohols[18] including the secondary benzylic alcohols.[18b] Application of the method to **2**−**4** and **10**−**22** indicated that the absolute configurations at C-7 of the glycerol units (355 ± 10 nm, positive for 7*S* and negative for 7*R*, predicted by the bulkiness rule) (Supporting Information, Figures S249−S250) were consistent with those elucidated by a combination of the NMR data (determining 7,8-*threo* or *erythro* relative configurations) and the CD data (predicting C-8 configurations). This was supported further by measurement of the $Rh_2(OCOCF_3)_4$-induced CD spectra of (−)-syringaresinol and tricin (Supporting Information, Figures S249−S250), which did not show any Cotton effect.

The inhibitory effects of the isolates against nitric oxide (NO) production in mouse peritoneal macrophages were examined. Compounds **20** and **22** inhibited NO elevation by 84.2 ± 5.9% and 71.7 ± 1.0%, respectively, at a concentration of 10 μM, while the positive control dexamethasone gave an inhibitory rate of 61.6 ± 1.3% at the same concentration. The other compounds showed inhibitory rates less than 30%. The protective activities of the compounds against neurotoxicity induced by serum deprivation in PC12 cells were investigated by the MTT method. The results showed that serum deprivation induced significant inhibition of MTT reduction, at a concentration of 10 μM. Compounds **19**, **20**, and **22** increased cell viability from 80.7 ± 2.8% to 91.6 ± 6.4%, 107.2 ± 8.0%, and 97.6 ± 8.5%, respectively, indicating that they may be effective in neurodegenerative disorders. The isolates were also assessed for their activities against HIV-1 replication,[43] Fe^{2+}-cystine-induced rat liver microsomal lipid peroxidation,[44] and DL-galactosamine-induced WB-F344 cell damage[45] as well as cytotoxicity against several human cancer cell lines,[46] but were inactive at a concentration of 10 μM.

■ EXPERIMENTAL SECTION

General Experimental Procedures. Optical rotations were measured on a Rudolph Research Autopol III automatic polarimeter. UV spectra were measured on a Cary 300 spectrometer. CD spectra were recorded on a JASCO J-815 CD spectrometer. IR spectra were recorded on a Nicolet 5700 FT-IR microscope instrument (FT-IR microscope transmission). NMR spectra were obtained at 300, 500, or 600 MHz for ^{1}H and 125 or 150 MHz for ^{13}C, respectively, on Varian Mecury-300 MHz or INOVA 500 MHz or SYS 600 MHz spectrometers with solvent peaks being used as references. ESIMS data were measured with a Q-Trap LC/MS/MS (Turbo Ionspray Source) spectrometer. HRESIMS data were measured using an Agilent Technologies 6520 Accurate Mass Q-ToF LC/MS spectrometer. Column chromatography was performed using silica gel (200−300 mesh, Qingdao Marine Chemical Inc., China) and Sephadex LH-20 (Pharmacia Biotech AB, Uppsala Sweden). HPLC separation was performed on an instrument consisting of a Waters 600 controller, a Waters 600 pump, and a Waters 2487 dual λ absorbance detector with an Alltima (250 × 10 mm) preparative column packed with C_{18} (5 μm). TLC was carried out on precoated silica gel GF_{254} plates. Spots were visualized under UV light (254 or 356 nm) or by spraying with 7% H_2SO_4 in 95% EtOH followed by heating.

Plant Material. The skin-removed stems of *S. affinis* were collected at Pingle Town, Sichuang Province, China, in August 2008. Plant identification was verified by Dr. Yan Ren (Chengdu University of TCM, Sichuan 610075, China). A voucher specimen (no. ID-S-2326) was deposited at the Herbarium of the Department of Medicinal Plants, Institute of Materia Medica, Beijing 100050, China.

Extraction and Isolation. Air-dried slices of the skin-removed stem of *S. affinis* (6 kg) were powdered and extracted with 95% EtOH (3 × 40 L) at rt for 3 × 72 h. The EtOH extract was evaporated under reduced pressure to yield a dark brown residue (330 g). The residue was suspended in H_2O (2500 mL) and then partitioned with EtOAc (6 × 2500 mL). After removing the solvent, the EtOAc fraction (120 g) was applied to a silica gel column. Successive elution with a gradient of increasing acetone (0−100%) in petroleum ether afforded 10 fractions (F_1−F_{10}) based on TLC analysis. F_5 (8.5 g) was subjected to RP flash CC (40−95% MeOH in H_2O) to give subfractions $F_{5\text{-}1}$−$F_{5\text{-}5}$. Separation of $F_{5\text{-}2}$ (1.1 g) with Sephadex LH-20 (petroleum ether−$CHCl_3$−MeOH, 5:5:1) and RP semipreparative HPLC (50% MeOH in H_2O), successively, yielded **9** (4 mg). $F_{5\text{-}3}$ (4.57 g) was fractioned via silica gel (30−100% EtOAc in petroleum ether) and Sephadex LH-20 (petroleum ether−$CHCl_3$−MeOH, 5:5:1) followed by RP semipreparative HPLC (55% MeOH in H_2O) purification to yield **5** (8 mg) and **6** (11 mg). Eluting with a step gradient of 30−95% MeOH in H_2O, F_6 (21.0 g) was separated by flash chromatography over MCI gel, to give subfractions $F_{6\text{-}1}$−$F_{6\text{-}5}$. $F_{6\text{-}2}$ (6.0 g) was purified via silica gel (5−40% acetone in $CHCl_3$) followed by RP semipreparative HPLC (40% MeOH in H_2O) to yield **1** (6 mg), **2** (6 mg), **3** (7 mg), **7** (87 mg), and **8** (5 mg). $F_{6\text{-}3}$ (2.0 g) was subjected to Sephadex LH-20, successively using petroleum ether−$CHCl_3$−MeOH (2:2:1) and $CHCl_3$−MeOH (1:1) as mobile phases, to afford **19** (260 mg), **20** (145 mg), **21** (21 mg), and **22** (18 mg). $F_{6\text{-}4}$ (4.6 g) was fractioned by RP flash chromatography (30−70% MeOH in H_2O) to give $F_{6\text{-}4\text{-}1}$−$F_{6\text{-}4\text{-}6}$. $F_{6\text{-}4\text{-}2}$ (0.5 g) and $F_{6\text{-}4\text{-}3}$ (0.7 g) were subjected separately to RP semipreparative HPLC (55% MeOH in H_2O) to yield **14** (150 mg) and **15** (147 mg) from $F_{6\text{-}4\text{-}2}$ and **12** (217 mg) and **13** (150 mg) from $F_{6\text{-}4\text{-}3}$. $F_{6\text{-}4\text{-}4}$ (1.2 g) was separated successively by chromatography over Sephadex LH-20 ($CHCl_3$−MeOH, 1:1) and RP semipreparative HPLC (60% MeOH in H_2O) to afford **10** (146.0 mg), **11** (85 mg), and **17** (3 mg). Separation of $F_{6\text{-}4\text{-}4}$ (0.6 g) by RP semipreparative HPLC (45% CH_3CN in H_2O) yielded **4** (5 mg), **16** (150 mg), and **18** (180 mg).

(+)-(7′S,8S,8′S)-3′,4-Dihydroxy-2′,3,4′,5-tetramethoxy-6′,9-epoxy-2,7′-cyclolignan-9′-ol (**1**): white, amorphous powder; $[\alpha]^{20}_D$ +43.3 (*c* 0.12, MeOH); UV (MeOH) λ_{max} (log ε) 207 (4.28), 235 (3.68), 282 (3.24) nm; CD (MeOH) 226 ($\Delta\varepsilon$ −2.23), 247 ($\Delta\varepsilon$ +0.78) nm, 284 ($\Delta\varepsilon$ −1.03) nm; IR ν_{max} 3432, 3246, 2963, 2935, 2897, 1612, 1493, 1451, 1437, 1305, 1235, 1195, 1125, 1091, 1033, 919, 872, 809 cm^{-1}; ^{1}H NMR (MeOH-d_4, 500 MHz) data, see Table 1; ^{13}C NMR (MeOH-d_4, 125 MHz) data, see Table 2; (+)-ESIMS *m/z* 419 [M + H]$^+$, 441 [M + Na]$^+$, 457 [M + K]$^+$; (+)-HRESIMS *m/z* 441.1532 [M + Na]$^+$ (calcd for $C_{22}H_{26}O_8Na$, 441.1520).

(+)-(7S,8S)-1′,4-Dihydroxy-3,3′,5′-trimethoxy-7′,8′,9′-trinor-8,4′-oxyneolignan-7,9-diol (**2**): white, amorphous powder; $[\alpha]^{20}_D$ +3.5 (*c* 0.10, MeOH); UV (MeOH) λ_{max} (log ε) 204 (4.30), 234 (3.64), 280 (3.10) nm; CD (MeOH) 207 ($\Delta\varepsilon$ +1.32), 224.5 ($\Delta\varepsilon$ +0.20), 237 ($\Delta\varepsilon$ +0.41) nm; $Rh_2(OCOCF_3)_4$ -induced CD (CH_2Cl_2) 319 ($\Delta\varepsilon$ −0.01), 329 ($\Delta\varepsilon$ −0.04), 351 ($\Delta\varepsilon$ +0.08) nm; IR ν_{max} 3405, 2939, 2849, 1603, 1512, 1481, 1434, 1368, 1274, 1217, 1032, 996, 821, 632 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 500 MHz) data, see Table 1; ^{13}C NMR (Me_2CO-d_6, 125 MHz) data, see Table 2; (+)-ESIMS *m/z* 389 [M + Na]$^+$, 405 [M + K]$^+$, 755 [2 M + Na]$^+$; (+)-HRESIMS *m/z* 389.1208 [M + Na]$^+$ (calcd for $C_{18}H_{22}O_8Na$, 389.1207).

(+)-(7S,8S)-4-Hydroxy-3,3′,5′-trimethoxy-8′,9′-dinor-8,4′-oxyneolignan-7,9-diol-7′-oic acid (**3**): white, amorphous powder; $[\alpha]^{20}_D$ +13.4 (*c* 0.13, MeOH); UV (MeOH) λ_{max} (log ε) 204 (4.15), 256 (3.37), 284 (3.08) nm; CD (MeOH) 227 ($\Delta\varepsilon$ −0.22), 258 ($\Delta\varepsilon$ +0.50) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 319.5 ($\Delta\varepsilon$ −0.15), 359 ($\Delta\varepsilon$ +0.06), 429 ($\Delta\varepsilon$ −0.01) nm; IR ν_{max} 3423, 2941, 2845, 1564, 1519, 1459, 1404, 1224, 1124, 1031, 789, 767 cm^{-1}; ^{1}H NMR (MeOH-d_4, 500 MHz) data, see Table 1; ^{13}C NMR (MeOH-d_4, 125 MHz) data, see Table 2; ESIMS *m/z* 417 [M + Na]$^+$, 393 [M − H]$^-$; (+)-HRESIMS *m/z* 417.1164 [M + Na]$^+$ (calcd for $C_{19}H_{22}O_9Na$, 417.1156).

Methylation of 3. A solution of compound **3** (2.0 mg) in dry acetone (3 mL) was treated with $NaHCO_3$ (1.5 mg) and CH_3I (2.5 mg) at 50 °C for 8 h. The reaction mixture was evaporated under reduced pressure to give a residue. The residue was partitioned between H_2O (10 mL) and EtOAc (10 mL). The EtOAc extract was evaporated, and then purified by preparative TLC using $CHCl_3$−MeOH (15:1) to afford **3a** (1.3 mg): white, amorphous powder; $[\alpha]^{20}_D$ +2.7 (*c* 0.10, MeOH); UV (MeOH) λ_{max} (log ε) 202 (4.31), 217 (4.01), 270 (3.55) nm; CD (MeOH) 243 ($\Delta\varepsilon$ +0.26), 262 ($\Delta\varepsilon$ +0.41) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 320 ($\Delta\varepsilon$ +0.06), 356 ($\Delta\varepsilon$ +0.02) nm; ^{1}H NMR (MeOH-d_4, 600 MHz) data, see Table 1; ^{13}C NMR (MeOH-d_4, 150 MHz) data, see Table 2; (+)-ESIMS *m/z* 431 [M + Na]$^+$.

(−)-(7R,8S,7′′S,8′′R)-3,3′′,5,5′-Tetramethoxy-4′′-hydroxy-4′,7-epoxy-8′,9′-dinor-4,8′′-oxy-8,3′-sesquineolignan-7′′,9,9′′-triol-7′-al (**4**): white, amorphous powder; $[\alpha]^{20}_D$ −3.0 (*c* 0.07, CH_2Cl_2); UV (MeOH) λ_{max} (log ε) 205 (4.22), 235 (3.77), 286 (3.44), 310 (3.35) nm; CD (MeOH) 212 ($\Delta\varepsilon$ +1.41), 236 ($\Delta\varepsilon$ −0.47), 280 ($\Delta\varepsilon$ +0.03), 295 ($\Delta\varepsilon$ −0.15), 320 ($\Delta\varepsilon$ +0.06) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 313.5 ($\Delta\varepsilon$ +0.01), 327.5 ($\Delta\varepsilon$ −0.02), 347.5 ($\Delta\varepsilon$ +0.06), 397 ($\Delta\varepsilon$ +0.01) nm; IR ν_{max} 3429, 2939, 2844, 1680, 1592, 1514, 1462, 1426, 1325, 1225, 1127, 1031, 949, 830 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 500 MHz) data, see Table 3; ^{13}C NMR (Me_2CO-d_6, 125 MHz) data, see Table 4; (+)-ESIMS *m/z* 579 [M + Na]$^+$; (−)-ESIMS *m/z* 555 [M − H]$^-$; (+)-HRESIMS *m/z* 579.1845 [M + Na]$^+$ (calcd for $C_{29}H_{32}O_{11}Na$, 579.1837).

(−)-(7R,8S,7′E)-3,4,5,5′-Tetramethoxy-4′,7-epoxy-8,3′-neolign-7′-ene-9,9′-diol (**5**): white, amorphous powder; $[\alpha]^{20}_D$ −7.8 (*c* 0.10, MeOH); UV (MeOH) λ_{max} (log ε) 206 (4.26), 275 (3.71) nm; CD (MeOH) 203 ($\Delta\varepsilon$ +7.58), 220 ($\Delta\varepsilon$ −0.37), 234 ($\Delta\varepsilon$ +3.76), 272 ($\Delta\varepsilon$ −2.89) nm; IR ν_{max} 3397, 2937, 1595, 1499, 1463, 1420, 1330, 1237, 1126, 965, 834, 616 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 500 MHz) data, see Table 1; ^{13}C NMR (Me_2CO-d_6, 125 MHz) data, see Table 2; (+)-ESIMS *m/z* 425 [M + Na]$^+$, 441 [M + K]$^+$; (+)-HRESIMS *m/z* 403.1741 [M + H]$^+$ (calcd for $C_{22}H_{27}O_7$ 403.1751).

(+)-(7S,8R,7′E)-4-Hydroxy-3,5′-dimethoxy-4′,7-epoxy-8,3′-neolign-7′-ene-9,9′-diol 9′-ethyl ether (**6**): white, amorphous powder; $[\alpha]^{20}_D$ +11.8 (*c* 0.10, MeOH); UV (MeOH) λ_{max} (log ε) 204 (4.16), 278 (3.67) nm; CD (MeOH) 211 ($\Delta\varepsilon$ +2.82), 238 ($\Delta\varepsilon$ −0.88), 261 ($\Delta\varepsilon$ +1.74), 282.5 ($\Delta\varepsilon$ +3.30) nm; IR ν_{max} 3365, 2970, 2928, 2852, 1603, 1517, 1497, 1464, 1331, 1274, 1212, 1144, 1033, 967, 856, 816 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 500 MHz) data, see Table 1; ^{13}C NMR (Me_2CO-d_6,

125 MHz) data, see Table 2; (+)-ESIMS m/z 409 [M + Na]$^+$, 425 [M + K]$^+$; (+)-HRESIMS m/z 409.1622 [M + Na]$^+$ (calcd for $C_{22}H_{26}O_6Na$, 409.1622).

*(−)-(7′S,8S,8′R)-4,4′-Dihydroxy-3,3′,5,5′-tetramethoxy-7′,9-epoxylignan-9′-ol-7-one (**7**):* white, amorphous powder; $[\alpha]^{20}_D$ −1.5 (c 0.20, MeCN); UV (MeOH) λ_{max} (log ε) 208 (4.18), 233 (3.73), 303 (3.47) nm; CD (MeOH) 209 ($\Delta\varepsilon$ −0.36), 225 ($\Delta\varepsilon$ −0.55), 255 ($\Delta\varepsilon$ +0.27), 273 ($\Delta\varepsilon$ +0.05), 286 ($\Delta\varepsilon$ +0.14), 324 ($\Delta\varepsilon$ −0.16) nm; IR ν_{max} 3473, 3285, 2940, 1661, 1611, 1518, 1463, 1425, 1325, 1218, 1116, 1033, 842, 715 cm^{-1}; ^{1}H NMR (MeOH-d_4, 500 MHz) data, see Table 1; ^{13}C NMR (MeOH-d_4, 125 MHz) data, see Table 2; (+)-ESIMS m/z 435 [M + H]$^+$, 457 [M + Na]$^+$, 473 [M + K]$^+$; (−)-ESIMS m/z 433 [M − H]$^-$; (+)-HRESIMS m/z 457.1472 [M + Na]$^+$ (calcd for $C_{22}H_{26}O_9Na$, 457.1469).

*(+)-(7R,7′R,8S,8′S)-4′-Hydroxy-3,3′,4,5,5′-pentamethoxy-7,7′-epoxylignan-9,9′-diol (**8**):* white, amorphous powder; $[\alpha]^{20}_D$ +25.5 (c 0.04, MeOH); UV (MeOH) λ_{max} (log ε) 207 (4.48), 241 (3.72), 277 (3.03) nm; CD (MeOH) 207 ($\Delta\varepsilon$ −16.55), 221.5 ($\Delta\varepsilon$ +0.87), 226 ($\Delta\varepsilon$ +0.28), 243 ($\Delta\varepsilon$ +10.94), 277 ($\Delta\varepsilon$ −0.56) nm; IR ν_{max} 3381, 2936, 1595, 1514, 1462, 1424, 1329, 1236, 1124, 834, 718 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 500 MHz) data, see Table 1; ^{13}C NMR (Me_2CO-d_6, 125 MHz) data, see Table 2; (+)-ESIMS m/z 473 [M + Na]$^+$, 489 [M + K]$^+$; (+)-HRESIMS m/z 473.1784 [M + Na]$^+$ (calcd for $C_{23}H_{30}O_9Na$, 473.1782).

*(−)-(7R,7′R,8S,8′S)-4′-Hydroxy-3,3′,4,5,5′-pentamethoxy-7,9′:7′,9-diepoxylignane (**9**):* white, amorphous powder; $[\alpha]^{20}_D$ −45.8 (c 0.03, MeOH); UV (MeOH) λ_{max} (log ε) 207 (4.27), 236 (3.55), 272 (2.86) nm; CD (MeCN) 214 ($\Delta\varepsilon$ −3.79), 230.5 ($\Delta\varepsilon$ −0.62), 239 ($\Delta\varepsilon$ −0.86), 254 ($\Delta\varepsilon$ +0.09), 274 ($\Delta\varepsilon$ −0.72) nm; IR ν_{max} 3370, 2935, 2850, 1593, 1510, 1460, 1421, 1329, 1234, 1122, 1005, 830, 701 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 600 MHz) data, see Table 1; ^{13}C NMR (Me_2CO-d_6, 125 MHz) data, see Table 2; (+)-EIMS m/z 432 [M]$^+$; (+)-HRESIMS m/z 455.1677 [M + Na]$^+$ (calcd for $C_{23}H_{28}O_8Na$, 455.1676).

*(−)-(7R,7′R,7″R,8S,8′S,8″S)-4′,4″-Dihydroxy-3,3′,3″,5-tetramethoxy-7,9′:7′,9-diepoxy-4,8″-oxy-8,8′-sesquineolignan-7″,9″-diol (**10**):* white, amorphous powder; $[\alpha]^{20}_D$ −4.0 (c 0.10, MeCN); UV (MeOH) λ_{max} (log ε) 204 (4.35), 233 (3.71), 280 (3.12) nm; CD (MeCN) 207 ($\Delta\varepsilon$ −0.19), 215.5 ($\Delta\varepsilon$ −0.98), 225 ($\Delta\varepsilon$ +0.25) nm, 230 ($\Delta\varepsilon$ −0.10), 238.5 ($\Delta\varepsilon$ +1.08), 247.5 ($\Delta\varepsilon$ −0.10), 267 ($\Delta\varepsilon$ +0.80), 281 ($\Delta\varepsilon$ −0.33), 293 ($\Delta\varepsilon$ −0.42) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 327 ($\Delta\varepsilon$ −0.07), 340 ($\Delta\varepsilon$ −0.01), 353 ($\Delta\varepsilon$ −0.04) nm; IR ν_{max} 3421, 2939, 1593, 1517, 1463, 1426, 1274, 1232, 1125, 1033, 823 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 500 MHz and $CDCl_3$, 500 MHz) data, see Table 3; ^{13}C NMR (Me_2CO-d_6, 125 MHz and $CDCl_3$, 125 MHz) data, see Table 4; (+)-ESIMS m/z 607 [M + Na]$^+$; (−)-ESIMS m/z 583 [M − H]$^-$; (+)-HRESIMS m/z 607.2155 [M + Na]$^+$ (calcd for $C_{31}H_{36}O_{11}Na$, 607.2150).

*(−)-(7R,7′R,7″S,8S,8′S,8″S)-4′,4″-Dihydroxy-3,3′,3″,5-tetramethoxy-7,9′:7′,9-diepoxy-4,8″-oxy-8,8′-sesquineolignan-7″,9″-diol (**11**):* white, amorphous powder; $[\alpha]^{20}_D$ −4.8 (c 0.10, MeCN); UV (MeOH) λ_{max} (log ε) 204 (4.33), 232 (3.73), 280 (3.20) nm; CD (MeCN) 208 ($\Delta\varepsilon$ −1.61), 214.5 ($\Delta\varepsilon$ −0.30), 218.5 ($\Delta\varepsilon$ −0.69) nm, 226 ($\Delta\varepsilon$ +0.11), 239.5 ($\Delta\varepsilon$ +0.58), 249 ($\Delta\varepsilon$ −0.36), 266.5 ($\Delta\varepsilon$ +0.85), 279 ($\Delta\varepsilon$ −0.16), 291 ($\Delta\varepsilon$ −0.55) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 336 ($\Delta\varepsilon$ −0.01), 348 ($\Delta\varepsilon$ +0.06) nm; IR ν_{max} 3447, 2940, 1593, 1517, 1463, 1426, 1274, 1233, 1124, 1033, 824 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 500 MHz and $CDCl_3$, 500 MHz) data, see Table 3; ^{13}C NMR (Me_2CO-d_6, 125 MHz and $CDCl_3$, 125 MHz) data, see Table 4; (+)-ESIMS m/z 607 [M + Na]$^+$; (−)-ESIMS m/z 583 [M − H]$^-$; (+)-HRESIMS m/z 607.2143 [M + Na]$^+$ (calcd for $C_{31}H_{36}O_{11}Na$, 607.2150).

*(−)-(7R,7′R,7″R,8S,8′S,8″S)-4′,4″-Dihydroxy-3,3′,3″,5,5′-pentamethoxy-7,9′:7′,9-diepoxy-4,8″-oxy-8,8′-sesquineolignan-7″,9″-diol (**12**):* white, amorphous powder; $[\alpha]^{20}_D$ −3.0 (c 0.05, MeCN); UV (MeOH) λ_{max} (log ε) 205 (4.38), 235 (3.71), 277 (3.09) nm; CD (MeCN) 214.5 ($\Delta\varepsilon$ −1.44), 223 ($\Delta\varepsilon$ +0.54) nm, 230 ($\Delta\varepsilon$ −1.12), 240 ($\Delta\varepsilon$ +0.77), 251 ($\Delta\varepsilon$ −0.24), 269 ($\Delta\varepsilon$ +0.78), 279 ($\Delta\varepsilon$ −0.24), 288 ($\Delta\varepsilon$ −0.21) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 334 ($\Delta\varepsilon$ +0.03), 351 ($\Delta\varepsilon$ −0.04), 364 ($\Delta\varepsilon$ −0.02), 374 ($\Delta\varepsilon$ −0.03) nm; IR ν_{max} 3303, 2962, 1593, 1518, 1463, 1262, 1224, 1113, 1028, 803 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 500 MHz and $CDCl_3$, 500 MHz) data, see Table 3; ^{13}C NMR (Me_2CO-d_6, 125 MHz and $CDCl_3$, 125 MHz) data, see Table 4; (+)-ESIMS m/z 637 [M + Na]$^+$; (−)-ESIMS m/z 613 [M − H]$^-$; (+)-HRESIMS m/z 637.2263 [M + Na]$^+$ (calcd for $C_{32}H_{38}O_{12}Na$, 637.2255).

*(−)-(7R,7′R,7″S,8S,8′S,8″S)-4′,4″-Dihydroxy-3,3′,3″,5,5′-pentamethoxy-7,9′:7′,9-diepoxy-4,8″-oxy-8,8′-sesquineolignan-7″,9″-diol (**13**):* white, amorphous powder; $[\alpha]^{20}_D$ −6.0 (c 0.10, MeCN); UV (MeOH) λ_{max} (log ε) 206 (4.21), 238 (3.50), 277 (2.81) nm; CD (MeCN) 214.5 ($\Delta\varepsilon$ −0.95), 223.5 ($\Delta\varepsilon$ +0.86), 231 ($\Delta\varepsilon$ −0.17), 238.5 ($\Delta\varepsilon$ +0.66), 246 ($\Delta\varepsilon$ −0.16), 255 ($\Delta\varepsilon$ +0.54), 260 ($\Delta\varepsilon$ +0.40), 267 ($\Delta\varepsilon$ +0.77), 278 ($\Delta\varepsilon$ −0.19), 290.5 ($\Delta\varepsilon$ −0.30) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 336 ($\Delta\varepsilon$ −0.11), 353 ($\Delta\varepsilon$ +0.09), 394 ($\Delta\varepsilon$ +0.01) nm; IR ν_{max} 3450, 2940, 2842, 1593, 1518, 1463, 1425, 1368, 1328, 1273, 1221, 1121, 1059, 1033, 826, 702 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 500 MHz and $CDCl_3$, 500 MHz) data, see Table 3; ^{13}C NMR (Me_2CO-d_6, 125 MHz and $CDCl_3$, 125 MHz) data, see Table 4; (+)-ESIMS m/z 637 [M + Na]$^+$; (−)-ESIMS m/z 613 [M − H]$^-$; (+)-HRESIMS m/z 637.2257 [M + Na]$^+$ (calcd for $C_{32}H_{38}O_{12}Na$, 637.2255).

*(−)-(7R,7′R,7″R,8S,8′S,8″S)-4′,4″-Dihydroxy-3,3′,3″,5,5′,5″-hexamethoxy-7,9′:7′,9-diepoxy-4,8″-oxy-8,8′-sesquineolignan-7″,9″-diol (**14**):* white, amorphous powder; $[\alpha]^{20}_D$ −3.0 (c 0.05, MeCN); UV (MeOH) λ_{max} (log ε) 206 (4.29), 238 (3.59), 277 (2.93) nm; CD (MeCN) 213 ($\Delta\varepsilon$ −2.61), 223 ($\Delta\varepsilon$ +0.08), 229.5 ($\Delta\varepsilon$ −0.58), 239 ($\Delta\varepsilon$ +1.11), 249 ($\Delta\varepsilon$ −0.33), 269 ($\Delta\varepsilon$ +0.53), 279 ($\Delta\varepsilon$ −0.17), 290.5 ($\Delta\varepsilon$ −0.15) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 335.5 ($\Delta\varepsilon$ −0.05), 344 ($\Delta\varepsilon$ −0.01), 353.5 ($\Delta\varepsilon$ −0.03), 364 ($\Delta\varepsilon$ −0.01) nm; IR ν_{max} 3346, 2939, 2841, 1614, 1519, 1462, 1425, 1326, 1218, 1118, 829, 702 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 500 MHz and $CDCl_3$, 500 MHz) data, see Table 3; ^{13}C NMR (Me_2CO-d_6, 125 MHz and $CDCl_3$, 125 MHz) data, see Table 4; (+)-ESIMS m/z 667 [M + Na]$^+$; (−)-ESIMS m/z 643 [M − H]$^-$; (+)-HRESIMS m/z 667.2365 [M + Na]$^+$ (calcd for $C_{33}H_{40}O_{13}Na$, 637.2361).

*(−)-(7R,7′R,7″S,8S,8′S,8″S)-4′,4″-Dihydroxy-3,3′,3″,5,5′,5″-hexamethoxy-7,9′:7′,9-diepoxy-4,8″-oxy-8,8′-sesquineolignan-7″,9″-diol (**15**):* white, amorphous powder; $[\alpha]^{20}_D$ −5.0 (c 0.10, MeCN); UV (MeOH) λ_{max} (log ε) 207 (4.22), 240 (3.47), 274 (2.65) nm; CD (MeCN) 209.5 ($\Delta\varepsilon$ −2.98), 223 ($\Delta\varepsilon$ +1.09), 230.5 ($\Delta\varepsilon$ −0.35), 237.5 ($\Delta\varepsilon$ +0.97), 244 ($\Delta\varepsilon$ +0.31), 253.5 ($\Delta\varepsilon$ +0.70), 261.5 ($\Delta\varepsilon$ +0.07), 268.5 ($\Delta\varepsilon$ +0.62), 283 ($\Delta\varepsilon$ −0.27), 296 ($\Delta\varepsilon$ −0.37) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 335 ($\Delta\varepsilon$ −0.12), 354 ($\Delta\varepsilon$ +0.07), 383 ($\Delta\varepsilon$ +0.05) nm; IR ν_{max} 3441, 2939, 2842, 1613, 1519, 1462, 1326, 1218, 1119, 830, 702 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 500 MHz and $CDCl_3$, 500 MHz) data, see Table 3; ^{13}C NMR (Me_2CO-d_6, 125 MHz and $CDCl_3$, 125 MHz) data, see Table 4; (+)-ESIMS m/z 667 [M + Na]$^+$; (−)-ESIMS m/z 643 [M − H]$^-$; (+)-HRESIMS m/z 667.2368 [M + Na]$^+$ (calcd for $C_{33}H_{40}O_{13}Na$, 637.2361).

*(+)-(7R,7′R,7″R,7‴R,8S,8′S,8″S,8‴S)-4″,4‴-Dihydroxy-3,3′,3″,3‴,5,5′-hexamethoxy-7,9′:7′,9-diepoxy-4,8″:4′,8‴-bisoxy-8,8′-dineolignan-7″,7‴,9″,9‴-tetraol (**16**):* white, amorphous powder; $[\alpha]^{20}_D$ +1.2 (c 0.25, MeCN); UV (MeOH) λ_{max} (log ε) 204 (4.44), 232 (3.81), 278 (3.20) nm; CD (MeCN) 209 ($\Delta\varepsilon$ −1.31), 215 ($\Delta\varepsilon$ −1.71), 234 ($\Delta\varepsilon$ +0.94), 249 ($\Delta\varepsilon$ −0.93), 272 ($\Delta\varepsilon$ +0.38), 287 ($\Delta\varepsilon$ −0.46) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 329 ($\Delta\varepsilon$ +0.03), 351 ($\Delta\varepsilon$ −0.07), 378 ($\Delta\varepsilon$ −0.02) nm; IR ν_{max} 3442, 2970, 2938, 1592, 1517, 1463, 1423, 1231, 1125, 1035, 825, 702 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 300 MHz) data, see Table 5; ^{13}C NMR (Me_2CO-d_6, 125 MHz) data, see Table 5; (+)-ESIMS m/z 833 [M + Na]$^+$; (−)-ESIMS m/z 809

$[M - H]^-$; (+)-HRESIMS m/z 833.2984 $[M + Na]^+$ (calcd for $C_{42}H_{50}O_{16}Na$, 833.2991).

*(+)-(7R,7′R,7″S,7‴S,8S,8′S,8″S,8‴S)-4″,4‴-Dihydroxy-3,3′,3″,3‴,5,5′-hexamethoxy-7,9′:7′,9-diepoxy-4,8″:4′,8‴-bisoxy-8,8′-dineolignan-7″,7‴,9″,9‴-tetraol (**17**):* white, amorphous powder; $[\alpha]^{20}_D$ +1.2 (*c* 0.10, MeCN); UV (MeOH) λ_{max} (log ε) 205 (4.39), 234 (3.77), 278 (3.20) nm; CD (MeCN) 210.5 ($\Delta\varepsilon$ +0.24), 219 ($\Delta\varepsilon$ −1.66), 234.5 ($\Delta\varepsilon$ +1.14), 254 ($\Delta\varepsilon$ −0.46), 266.5 ($\Delta\varepsilon$ +0.60), 278 ($\Delta\varepsilon$ −0.44) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 350 ($\Delta\varepsilon$ +0.13), 385 ($\Delta\varepsilon$ +0.02) nm; IR ν_{max} 3354, 2924, 2851, 1593, 1516, 1463, 1423, 1273, 1231, 1124, 1033, 825 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 500 MHz) data, see Table 5; ^{13}C NMR (Me_2CO-d_6, 125 MHz) data, see Table 5; (+)-ESIMS m/z 833 $[M + Na]^+$; (−)-ESIMS m/z 809 $[M - H]^-$; (+)-HRESIMS m/z 833.3001 $[M + Na]^+$ (calcd for $C_{42}H_{50}O_{16}Na$, 833.2991).

*(+)-(7R,7′R,7″R,7‴S,8S,8′S,8″S,8‴S)-4″,4‴-Dihydroxy-3,3′,3″,3‴,5,5′-hexamethoxy-7,9′:7′,9-diepoxy-4,8″:4′,8‴-bisoxy-8,8′-dineolignan-7″,7‴,9″,9‴-tetraol (**18**):* white, amorphous powder; $[\alpha]^{20}_D$ +2.1 (*c* 0.10, MeCN); UV (MeOH) λ_{max} (log ε) 204 (4.43), 233 (3.79), 278 (3.18) nm; CD (MeCN) 208 ($\Delta\varepsilon$ −0.24), 217 ($\Delta\varepsilon$ −0.85), 235 ($\Delta\varepsilon$ +0.67), 245 ($\Delta\varepsilon$ +0.33), 257 ($\Delta\varepsilon$ −0.68), 269 ($\Delta\varepsilon$ +0.30), 283 ($\Delta\varepsilon$ −0.15) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 349 ($\Delta\varepsilon$ +0.04); IR ν_{max} 3476, 2933, 2850, 1592, 1517, 1463, 1423, 1273, 1231, 1124, 1032, 824, 703 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 500 MHz) data, see Table 5; ^{13}C NMR (Me_2CO-d_6, 125 MHz) data, see Table 5; (+)-ESIMS m/z 833 $[M + Na]^+$; (−)-ESIMS m/z 809 $[M - H]^-$; (+)-HRESIMS m/z 833.2997 $[M + Na]^+$ (calcd for $C_{42}H_{50}O_{16}Na$, 833.2991).

Alkali Hydrolysis of 10−18. To a solution of compound **10** (8.0 mg) in dioxane (5 mL) was added 2 mol/L NaOH (0.5 mL). The reaction mixture was stirred at rt for 5 days. After neutralization with diluted HCl the reaction solution was partitioned between H_2O (25 mL) and CH_2Cl_2 (25 mL). The CH_2Cl_2 phase was evaporated under reduced pressure to give a residue that was separated by PTLC using $CHCl_3$−MeOH (30:1) to afford a product (0.9 mg): $[\alpha]^{20}_D$ −6.1 (*c* 0.20, MeCN); CD (MeCN) 230 ($\Delta\varepsilon$ −0.01), 241 ($\Delta\varepsilon$ −0.21), 257 ($\Delta\varepsilon$ +0.18), 274.5 ($\Delta\varepsilon$ −0.22) nm. These data and the ^{1}H NMR ($CDCl_3$, 300 MHz) and ESIMS data of the product were completely consistent with those of the co-occurring (−)-medioresinol.[33] Similarly, **11** (7.6 mg) was hydrolyzed to afford (−)-medioresinol (0.8 mg). Compounds **12**−**18** were hydrolyzed using the same procedure to produce a colorless gum: $[\alpha]^{20}_D$ −7.0 (*c* 0.10, MeCN); CD (MeCN) 209 ($\Delta\varepsilon$ −1.54), 232 ($\Delta\varepsilon$ 0.00), 241 ($\Delta\varepsilon$ −0.07), 254 ($\Delta\varepsilon$ +0.12), 270 ($\Delta\varepsilon$ −0.12) nm. These data, and the ^{1}H NMR (Me_2CO-d_6, 300 MHz) and ESIMS data of the product, were identical to those of the co-occurring (−)-syringaresinol.[26]

*(−)-(7″R,8″S)-4″,5,7-Trihydroxy-3′,5′-dimethoxy-4′,8″-oxyflavonolignan-7″,9″-diol (**19**):* yellow, amorphous powder; $[\alpha]^{20}_D$ −61.1 (*c* 0.03, MeOH); UV (MeOH) λ_{max} (log ε) 209 (4.19), 270 (3.70), 345 (3.89) nm; CD (MeCN) 239 ($\Delta\varepsilon$ −0.44), 266 ($\Delta\varepsilon$ +0.07), 283 ($\Delta\varepsilon$ −0.03), 322 ($\Delta\varepsilon$ +0.09), 362 ($\Delta\varepsilon$ −0.13) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 323 ($\Delta\varepsilon$ −0.08), 356 ($\Delta\varepsilon$ −0.04), 386 ($\Delta\varepsilon$ −0.01), 410 ($\Delta\varepsilon$ −0.02), 435 ($\Delta\varepsilon$ 0.00), 469 ($\Delta\varepsilon$ −0.03); IR ν_{max} 3436, 2923, 1653, 1615, 1505, 1461, 1355, 1263, 1160, 1118, 838 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz) data, see Table 6; ^{13}C NMR (DMSO-d_6, 125 MHz) data, see Table 6; (−)-ESIMS m/z 495 $[M - H]^-$.

*(−)-(7″S,8″S)-4″,5,7-Trihydroxy-3′,5′-dimethoxy-4′,8″-oxyflavonolignan-7″,9″-diol (**20**):* yellow, amorphous powder; $[\alpha]^{20}_D$ −20.0 (*c* 0.02, MeOH); UV (MeOH) λ_{max} (log ε) 202 (4.17), 272 (3.30), 334 (3.11) nm; CD (MeCN) 221 ($\Delta\varepsilon$ +0.21), 246 ($\Delta\varepsilon$ −0.19), 268 ($\Delta\varepsilon$ +0.05), 286 ($\Delta\varepsilon$ −0.01), 318 ($\Delta\varepsilon$ +0.08), 353 ($\Delta\varepsilon$ −0.07) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 308 ($\Delta\varepsilon$ −0.19), 362 ($\Delta\varepsilon$ +0.07), 424 ($\Delta\varepsilon$ +0.01), 452 ($\Delta\varepsilon$ +0.06), 469 ($\Delta\varepsilon$ +0.05); IR ν_{max} 3204, 2947, 1657, 1618, 1594, 1500, 1454, 1365, 1242, 1165, 1120, 1050, 839 cm^{-1}; ^{1}H NMR (DMSO-d_6, 600 MHz) data, see Table 6; ^{13}C NMR (DMSO-d_6, 150 MHz) data, see Table 6; (−)-ESIMS m/z 495 $[M - H]^-$.

*(−)-(7″R,8″S)-4″,5,7-Trihydroxy-3′,3″,5′-trimethoxy-4′,8″-oxyflavonolignan-7″,9″-diol (**21**):* yellow, amorphous powder; $[\alpha]^{20}_D$ −18.3 (*c* 0.03, MeOH); UV (MeOH) λ_{max} (log ε) 203 (4.15), 271 (3.56), 337 (3.56) nm; CD (MeCN) 207 ($\Delta\varepsilon$ +0.79), 232 ($\Delta\varepsilon$ −0.45), 271 ($\Delta\varepsilon$ +0.19), 294 ($\Delta\varepsilon$ 0.00), 320 ($\Delta\varepsilon$ +0.12), 356 ($\Delta\varepsilon$ −0.12) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 331 ($\Delta\varepsilon$ −0.07), 353.5 ($\Delta\varepsilon$ −0.03), 377 ($\Delta\varepsilon$ 0.00), 404 ($\Delta\varepsilon$ −0.01); IR ν_{max} 3421, 2924, 1655, 1618, 1592, 1498, 1460, 1357, 1248, 1165, 1126, 839 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz) data, see Table 6; ^{13}C NMR (DMSO-d_6, 150 MHz) data, see Table 6; (−)-ESIMS m/z 525 $[M - H]^-$.

*(−)-(7″S,8″S)-4″,5,7-Trihydroxy-3′,3″,5′-trimethoxy-4′,8″-oxyflavonolignan-7″,9″-diol (**22**):* yellow, amorphous powder; $[\alpha]^{20}_D$ −11.2 (*c* 0.03, MeOH); UV (MeOH) λ_{max} (log ε) 203 (4.18), 279 (3.62), 336 (3.51) nm; CD (MeCN) 221 ($\Delta\varepsilon$ +0.24), 241 ($\Delta\varepsilon$ −0.37), 267 ($\Delta\varepsilon$ +0.27), 298 ($\Delta\varepsilon$ −0.02), 318 ($\Delta\varepsilon$ +0.07), 348 ($\Delta\varepsilon$ −0.06) nm; $Rh_2(OCOCF_3)_4$-induced CD (CH_2Cl_2) 325 ($\Delta\varepsilon$ −0.13), 366 ($\Delta\varepsilon$ +0.05), 452 ($\Delta\varepsilon$ +0.01) nm; IR ν_{max} 3381, 2941, 1654, 1614, 1505, 1463, 1355, 1263, 1160, 1117, 835 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) data, see Table 6; ^{13}C NMR (DMSO-d_6, 125 MHz) data, see Table 6; (−)-ESIMS m/z 525 $[M - H]^-$.

Preparation of Acetonide Derivatives of 10a−15a and 18a−22a. A solution of **10** (5.0 mg) in dry acetone (5 mL) was treated with 2,2-dimethoxypropane (8.0 mL) and (1*S*)-(+)-camphorsulforic acid (CSA) (0.5 mg), and the mixture was stirred at rt for 4 h. The reaction mixture was quenched by addition of triethylamine and then evaporated under reduced pressure to give a crude product that was purified by PTLC using $CHCl_3$−MeOH (20:1) to afford acetonide **10a** (4.1 mg). Similarly, **11** (5.6 mg), **12** (4.3 mg), **13** (8.4 mg), **14** (5.0 mg), **15** (4.7 mg), **18** (5.0 mg), **19** (4.5 mg), **20** (4.0 mg), **21** (4.4 mg), and **22** (4.5 mg) yielded acetonide derivatives **11a** (4.0 mg), **12a** (3.2 mg), **13a** (6.9 mg), **14a** (4.3 mg), **15a** (3.3 mg), **18a** (3.8 mg), **19a** (3.2 mg), **20a** (2.4 mg), **21a** (3.5 mg), and **22a** (3.0 mg), respectively. ^{1}H NMR (Me_2CO-d_6, 500 MHz) data of **10a**−**15a**, see Supporting Information, Table S1; ^{13}C NMR (Me_2CO-d_6, 125 MHz) data of **10a**−**15a**, see Supporting Information, Table S1; ^{1}H NMR data (DMSO-d_6, 500 MHz) data of **19a**−**22a**, see Supporting Information, Table S2.

■ ASSOCIATED CONTENT

Supporting Information. Copies of IR, MS, 1D and/or 2D NMR, and CD spectra for compounds **1**−**22**. NMR spectra of compounds **3a** and acetonide derivatives of **10**−**22** (**10a**−**22a**). Table S1, NMR data (δ) for **10a**−**15a**. Table S2, ^{1}H NMR data (δ) for **19a**−**22a**. This can be accessed free of charge via the Internet at http://pubs.acs.org.

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