Four New Cytotoxic Tetrahydrofuranoid Lignans from *Sinopodophyllum emodi*

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Abstract

Four new tetrahydrofuranoid lignans, (−)-tanegool-7′-methyl ether (**1**), (+)-7′-methoxylariciresinol (**2**), sinolignan C (**3**), and epipinoresinol-4,4′-di-*O*-*β*-*D*-glucopyranoside (**4**), were isolated from the roots and rhizomes of *Sinopodophyllum emodi* together with one known lignan (**5**). Their structures and stereochemistry were elucidated on the basis of spectroscopic and mass spectrometric evidence. The isolation of compounds **1**–**5** represents the first report of tetrahydrofuran lignans from the genus *Sinopodophyllum*. The cytotoxic activities of all isolated compounds were evaluated against HeLa and KB cell lines, and compound **1** showed the most potent cytotoxicity with IC_{50} values of 9.7 µM and 4.7 µM, respectively.

Key words
tetrahydrofuranoid lignans · *Sinopodophyllum emodi* · Berberidaceae · cytotoxic activities

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Sinopodophyllum emodi (Wall.) Ying (Berberidaceae) is distributed widely in the southwest of China [1]. The dried roots and rhizomes of *S. emodi*, called "Taoerqi" in Chinese, are used as a folk medicine for the treatment of certain cancers, various verrucoses [1], as a cathartic and anthelminthic [2], as well as against rheumatoid ache [3] and pyogenic infection of the skin tissue [4]. Previous chemical and pharmacological investigations on *S. emodi* revealed the presence of bioactive aryltetralin lignans [1,5–7], and cytotoxic and antiviral properties [4,7]. In a continuation of our search for cytotoxic natural products, five tetrahydrofuranoid lignans (**Fig. 1**) were obtained. We herein described the isolation and structure elucidation of four new lignans (**1**–**4**) and the evaluation of the cytotoxic activity of all isolated compounds, along with their preliminary structure–activity relationships. Compound **5** was identified as lanicepside A by comparison with the literature [8].

Compound **1** was obtained as a sticky oil and possessed a molecular formula $C_{21}H_{26}O_7$, as revealed from its HR-ESI-MS analysis (*m*/*z* 413.1574 $[M + Na]^+$). The ^{1}H-NMR spectrum (**Table 1**) showed proton signals of two ABX systems of aromatic protons at δ_H 6.83, 6.75, 6.70, 6.81, 6.70, and 6.70, two aromatic CH_3O groups at δ_H 3.73 (3H, s) and 3.76 (3H, s), indicating the presence of two trisubstituted benzene rings. Six oxygenated aliphatic protons at δ_H 3.44, 3.49 (2H), 3.54, 3.95, and 4.51, together with two aliphatic protons at δ_H 2.07 and 2.50 were evidence for the presence of a tetrahydrofuranoid lignan skeleton [8], which was supported by ^{13}C-NMR analysis. In the ^{13}C-NMR spectrum, apart from the twelve aromatic and three CH_3O signals, there were six

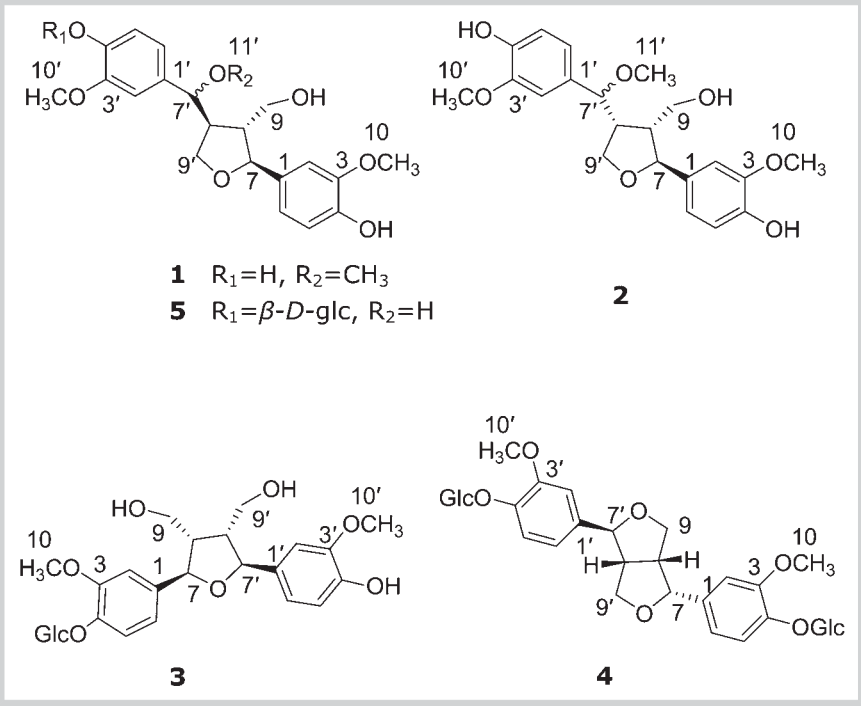

Fig. 1 Compounds **1**–**5** isolated from *S. emodi*.

Table 1 ^{1}H NMR data (300 MHz, δ in ppm, J in Hz) of compounds **1**–**4** in DMSO-d_6.

No.	1	2	3	4
2	6.81 (1H, brs)	6.85 (1H, brs)	7.02 (1H, d, 1.7)	6.94 (1H, d, 1.8)
5	6.70 (1H, m)	6.71 (1H, m)	7.06 (1H, d, 8.4)	7.04 (1H, d, 8.4)
6	6.70 (1H, m)	6.72 (1H, m)	6.90 (1H, dd, 8.4, 1.7)	6.83 (1H, dd, 8.4, 1.8)
7	4.51 (1H, d, 7.4)	4.50 (1H, d, 7.1)	4.69 (1H, d, 6.2)	4.79 (1H, d, 5.9)
8	2.07 (1H, m)	1.60 (1H, m)	2.38 (1H, m)	3.37 (1H, m)
9	3.49 (2H, m)	3.05 (1H, m), 2.89 (1H, m)	3.65 (1H, m), 3.49 (1H, m)	3.74 (1H, m), 3.07 (1H, m)
2′	6.83 (1H, brs)	6.75 (1H, brs)	6.96 (1H, d, 1.7)	6.95 (1H, d, 1.8)
5′	6.75 (1H, d, 8.0)	6.71 (1H, d, 8.0)	6.75 (1H, d, 8.0)	7.03 (1H, d, 8.4)
6′	6.70 (1H, m)	6.62 (1H, brd, 8.0)	6.81 (1H, dd, 8.0, 1.7)	6.86 (1H, dd, 8.4, 1.8)
7′	3.95 (1H, d, 8.9)	3.90 (1H, d, 9.3)	4.64 (1H, d, 6.5)	4.37 (1H, d, 6.8)
8′	2.50 (1H, m)	2.41 (1H, m)	2.38 (1H, m)	2.84 (1H, m)
9′	3.54 (1H, m), 3.44 (1H, m)	4.03 (1H, dd, 4.0, 8.8) 3.79 (1H, brd, 8.2)	3.65 (1H, m) 3.49 (1H, m)	4.08 (1H, m) 3.75 (1H, m)
10	3.73 (3H, s)	3.73 (3H, s)	3.75 (3H, s)	3.76 (3H, s)
10′	3.76 (3H, s)	3.76 (3H, s)	3.75 (3H, s)	3.76 (3H, s)
11′	3.02 (3H, s)	3.05 (3H, s)		
1′′			4.88 (1H, d, 7.3)	4.88 (1H, d, 7.1)
2′′			3.24 (1H, m)	3.24 (1H, m)
3′′			3.25 (1H, m)	3.26 (1H, m)
4′′			3.14 (1H, m)	3.14 (1H, m)
5′′			3.28 (1H, m)	3.27 (1H, m)
6′′			3.44 (1H, m), 3.69 (1H, m)	3.44 (1H, m), 3.66 (1H, m)
1′′′				4.87 (1H, d, 7.0)
2′′′				3.24 (1H, m)
3′′′				3.26 (1H, m)
4′′′				3.14 (1H, m)
5′′′				3.27 (1H, m)
6′′′				3.44 (1H, m), 3.66 (1H, m)

sp^3 C-atoms, including two oxymethines at δ_C 83.3 and 85.7 and two oxymethylenes at δ_C 61.5 and 69.1. The 8, 8′-linked tetrahydrofuran skeleton between two propanyl groups was certified by connectivities of H-8 with H-7, H-9, and H-8′, and of H-8′ with H-7′, H-9′, and H-8 in the ^{1}H-^{1}H COSY experiment. The above data suggested that **1** was tanegool methyl ether [9], which was supported by the HMBC spectrum. The remaining CH_3O group was located at C-7′, based on the HMBC correlation between CH_3O group protons at δ_H 3.02 (3H, s) and C-7′ (δ_C 85.7). The relative configuration in the tetrahydrofuran ring was determined by the H-7 chemical shift and NOESY experiment. For a *cis*-orientation of substituents at C-7 and C-8, the signal of H-7 was at around 5.5 ppm, while for a *trans*-orientation, the signal of H-7 upfield shifted to around 4.7 ppm [10]. According to a signal of H-7 at δ_H 4.51, the orientation of H-7/H-8 of compound **1** was determined to be *trans*. All *trans* orientation of H-7/H-8/H-8′ was determined by the cross-peak of H-7/H-9, H-7/H-8′, H-8/H-7′, H-9/H-8′ in the NOESY spectrum. There were no definitive conclusions on the relationships between the absolute configuration and circular dichroism (CD) in this series of tetrahydrofuranoid lignans [11, 12]. Although the CD spectrum of **1** showed the positive absorption peaks at 228 and 284 nm, the absolute configuration was not determined. Thus, the structure of **1** was determined as (7*S**,8*R**,8′*S**)-3,3′,7′-trimethoxy-4,9,4′-trihydroxy-8.8′,7.O.9′-lignan and named (−)-tanegool-7′-methyl ether.

Compound **2** was obtained as a sticky oil and possessed a molecular formula of $C_{21}H_{26}O_7$, derived from its HR-ESI-MS analysis (m/z 413.1562 [M + Na]$^+$). The ^{1}H-NMR and ^{13}C-NMR data of **2** were similar with those of compound **1**. The COSY, HSQC, and HMBC spectra of **2** also showed similar cross-peaks with those of **1**. Due to apparent differences of the NOESY correlations in **1** and **2**, it was reasonably assumed that **2** was a stereoisomer of **1**. The relative configuration between H-7 and H-8 was determined as *trans* on the basis of H-7 at δ_H 4.50 [10]. The relative configuration between H-8′ and H-8 was deduced as *cis* due to the absence of a cross-peak of H-7/H-8′ in the NOESY spectrum, which was supported by the chemical shift of H-9 in compound **2** [13]. H-9 of compound **2** shifted upfield to δ_H 3.05 (1H, *m*) and 2.89 (1H, *m*) due to the influence of the 7′-OCH_3, while H-9 of compound **1** gave a downfield signal at δ_H 3.49 (2H, *m*). Thus, the structure of **2** was determined as (7*S**,8*R**,8′*R**)-3,3′,7′-trimethoxy-4,9,4′-trihydroxy-8.8′,7.O.9′-lignan, and named (+)-7′-methoxylariciresinol.

Compound **3** was isolated as amorphous powder. Its molecular formula was established as $C_{26}H_{34}O_{12}$, derived from HR-ESI-MS analysis (m/z 561.1945 [M + Na]$^+$). The ^{1}H-NMR spectrum showed proton signals of two aromatic CH_3O groups at δ_H 3.75 (6H, s), two ABX systems of aromatic protons at δ_H 7.02 (1H, *d*, J = 1.7 Hz), 6.90 (1H, *dd*, J = 1.7, 8.4 Hz), 7.06 (1H, *d*, J = 8.4 Hz), 6.96 (1H, *d*, J = 1.7 Hz), 6.81 (1H, *dd*, J = 1.7, 8.0 Hz), and 6.75 (1H, *d*, J = 8.0 Hz), six oxygenated aliphatic protons at δ_H 3.65 (2H), 3.49 (2H), 4.64, 4.69, and two aliphatic protons at δ_H 2.38 (2H), indicating the presence of a tetrahydrofuranoid lignan skeleton. The 7.O.7′ oxygen bridge of the tetrahydrofuran ring moiety was established based on ^{13}C-NMR and HMBC analyses. The ^{13}C-NMR spectrum revealed four O-bearing C-atoms at δ_c 82.0, 81.7, 58.7,

Table 2 ^{13}C NMR data (75 MHz, δ in ppm) of compounds **1–4** in DMSO-d_6.

No.	1	2	3	4
1	133.6 (*s*)	133.6 (*s*)	136.7 (*s*)	132.5 (*s*)
2	110.4 (*d*)	110.4 (*d*)	110.8 (*d*)	110.0 (*d*)
3	147.5 (*s*)	147.5 (*s*)	148.9 (*s*)	148.7 (*s*)
4	145.7 (*s*)	145.7 (*s*)	145.8 (*s*)	145.5 (*s*)
5	115.1 (*d*)	115.2 (*d*)	115.2 (*d*)	114.9 (*d*)
6	118.8 (*d*)	118.7 (*d*)	118.5 (*d*)	117.7 (*d*)
7	83.3 (*d*)	82.7 (*d*)	81.7 (*d*)	81.9 (*d*)
8	53.8 (*d*)	52.2 (*d*)	51.4 (*d*)	49.4 (*d*)
9	61.5 (*t*)	60.4 (*t*)	58.7 (*t*)	69.1 (*t*)
10	55.6 (*q*)	55.6 (*q*)	55.6 (*q*)	55.7 (*q*)
1′	131.3 (*s*)	130.9 (*s*)	133.5 (*s*)	135.3 (*s*)
2′	111.0 (*d*)	111.0 (*d*)	110.7 (*d*)	110.5 (*d*)
3′	147.7 (*s*)	147.7 (*s*)	147.5 (*s*)	149.0 (*s*)
4′	146.3 (*s*)	146.2 (*s*)	145.9 (*s*)	146.0 (*s*)
5′	115.2 (*d*)	115.2 (*d*)	115.2 (*d*)	115.3 (*d*)
6′	120.4 (*d*)	120.5 (*d*)	118.9 (*d*)	118.2 (*d*)
7′	85.7 (*d*)	85.4 (*d*)	82.0 (*d*)	86.7 (*d*)
8′	48.3 (*d*)	48.0 (*d*)	51.2 (*d*)	54.1 (*d*)
9′	69.1 (*t*)	70.4 (*t*)	58.6 (*t*)	70.4 (*t*)
10′	55.7 (*q*)	55.7 (*q*)	55.6 (*q*)	55.7 (*q*)
11′	55.8 (*q*)	55.8 (*q*)		
1′′			100.2 (*d*)	100.2 (*d*)
2′′			73.3 (*d*)	73.3 (*d*)
3′′			76.9 (*d*)	77.0 (*d*)
4′′			69.7 (*d*)	69.8 (*d*)
5′′			77.1 (*d*)	77.1 (*d*)
6′′			60.8 (*t*)	60.8 (*t*)
1′′′				100.2 (*d*)
2′′′				73.3 (*d*)
3′′′				77.0 (*d*)
4′′′				69.8 (*d*)
5′′′				77.1 (*d*)
6′′′				60.8 (*t*)

and 58.6, which were characteristic of a 7.O.7′-tetrahydrofuranoid lignan. In the HMBC spectrum, the cross-peaks of H-7 at δ_H 4.69 (δ_C 81.7) with C-9 (δ_C 58.7), C-7′ (δ_C 82.0), C-8′ (δ_C 51.2), and of H-7′ at δ_H 4.64 (δ_C 82.0) with C-9′ (δ_C 58.6), C-7 (δ_C 81.7), C-8 (δ_C 51.4) further supported the proposed structure. Two characteristic downfield CH groups at δ_H 4.69 (1H, *d, J* = 6.2 Hz), 4.64 (1H, *d, J* = 6.5 Hz) and six characteristic aliphatic C-atom signals at δ_C 81.7 (CH), 51.4 (CH), 58.7 (CH_2), 82.0 (CH), 51.2 (CH), and 58.6 (CH_2) suggested that the planar structure of the aglycone of compound **3** was the same as (+)-neo-olivil [14]. The chemical shifts of H-7 (δ_H 4.69) and H-7′ (δ_H 4.64) indicated that each $HOCH_2$ group was situated in a *trans*-relation to the vicinal aryl group [15]. The configuration of the aglycone was thus concluded to be either the all *trans* form or the *meso* form. The *cis*-orientation between H-7 and H-7′ was determined by the cross-peak of H-7/H-7′ in the NOESY spectrum. Furthermore, compound **3** showed no Cotton effect (220–350 nm), but known compounds with all *trans*-configuration did so in CD spectra [16, 17]. Thus, the configuration for **3** was the *meso* form. The presence of a *β*-glucopyranosyl moiety in the molecule was indicated by the carbon signals at δ_C 100.2, 73.3, 76.9, 69.7, 77.1, 60.8 and an anomeric proton signal at δ_H 4.88 (1H, *d, J* = 7.3 Hz). On acid hydrolysis, **3** afforded D-glucose. The anomeric proton at δ_H 4.88 showed a long range correlation with the aromatic carbon signals at δ_C 145.8 which was assigned to the C-4. On the basis of the above evidences, the structure of **3** was determined as (7*R**,8*S**,8′*R**,7′*S**)-3,3′-dimethoxy-9,4′,9′-trihydroxy-8.8′,7.O.7′-lignan-4-*O*-*β*-*D*-glucoside and named sinolignan C.

Compound **4** was obtained as amorphous powder. Its molecular formula was established as $C_{32}H_{42}O_{16}$ by HR-ESI-MS analysis (*m/z* 705.2370 $[M + Na]^+$). The ^1H-NMR and ^{13}C-NMR signals were assigned by the ^1H-^1H COSY, HSQC, and HMBC analysis (**Tables 1** and **2**), indicating the presence of two guaiacyl and two glucosyl groups. Two characteristic downfield CH signals at δ_H 4.79 (1H, d, *J* = 5.9 Hz), 4.37 (1H, *d, J* = 6.8 Hz) and six characteristic aliphatic carbon signals at δ_C 81.9 (CH), 49.4 (CH), 69.1 (CH_2), 86.7 (CH), 54.1 (CH), and 70.4 (CH_2) suggested that compound **4** was a ditetrahydrofuranoid lignan. The 8, 8′-linkage was certified by connectivities of H-8 with H-7, H-9, and H-8′, and of H-8′ with H-7′, H-9′, and H-8 in the ^1H-^1H COSY experiment. In the HMBC spectrum, the cross-peaks of H-7 at δ_H 4.79 (δ_C 81.9) with C-9 (δ_C 69.1), C-8′ (δ_C 54.1), and C-9′ (δ_C 70.4) and of H-7′ at δ_H 4.37 (δ_C 86.7) with C-9′ (δ_C 70.4), C-8 (δ_C 49.4), and C-9 (δ_C 69.1) supported 7.O.9′ and 7′.O.9 oxygen bridges in the ditetrahydrofuran ring moiety. The relative and absolute configurations of the aglycone of compound **4** were determined by comparison of NMR data and CD spectrum of known analogous compounds [18–21] and the combined NOESY experiment. Due to an epi-diepoxy system in compound **4**, the signals for the benzylic protons H-7 and H-7′ were not identical and appeared as doublets at δ_H 4.79 (1H, *d, J* = 5.9 Hz) and 4.37 (1H, *d, J* = 6.8 Hz), respectively [19]. The ^{13}C NMR spectrum was important in establishing the orientation of the aryl groups. For an equatorial guaiacyl group, C-1 appeared in downfield at around δ_C 133.0 in $CDCl_3$, while for an axial guaiacyl group in upfield at around δ_C 130.6 [18–20]. Thus, considering the solvent effect and glycosidation shift on the aryl

Table 3 Cytotoxic activities of compounds **1**–**5** against HeLa and KB cell lines.

Compound	IC_{50}[a] (μM)		Compound	IC_{50}[a] (μM)	
	HeLa	KB		HeLa	KB
1[c]	9.7 ± 1.0	4.7 ± 0.4	**4**[c]	> 100	> 100
2[c]	32.2 ± 3.0	> 100	**5**[c]	99.6 ± 8.3	> 100
3[c]	> 100	> 100	Etoposide[b]	4.0 ± 0.3	10.0 ± 0.9

[a] IC_{50} is defined as the concentration of drug required to inhibit cell growth by 50% compared with untreated control. It is expressed as mean ± SD of at least three determinations.
[b] Reference control (> 98%). [c] The purity (%) of tested compound exceeded 90%

group, values of C-1 and C-1′ at δ_C 135.3 and 132.5 in compound **4** accounted for the appearances of equatorial and axial guaiacyl groups. The NOESY cross-peak was observed between H-7 (δ_H 4.79) and H-8′ (δ_H 2.84). Thus, the relative configuration could be proposed as 7,8-*cis*-8,8′-*cis*-7′,8′-*trans*. The CD spectrum of compound **4** was identical with episesartemin which has the absolute configuration 7*R*,8*R*,8′*R*,7′*S* [21]. Therefore, the aglycone of compound **4** was (+) epipinoresinol. On acid hydrolysis, **4** afforded D-glucose. The anomeric protons of glucoses at δ_H 4.88 (1H, *d*, *J* = 7.1 Hz) and 4.87 (1H, *d*, *J* = 7.0 Hz), respectively, showed HMBC correlations with the aromatic C-atoms at C-4 (δ_C 145.5) and C-4′ (δ_C 146.0). Accordingly, compound **4** was established as epipinoresinol-4, 4′-di-*O*-*β*-*D*-glucopyranoside.

All isolated compounds were evaluated for cytotoxic activities against human uterine cervical adenocarcinoma (HeLa) and human oral squamous carcinoma (KB) cell lines (**Table 3**). Compounds **1** and **2** showed cytotoxicity and compounds **3, 4**, and **5** displayed no cytotoxicity against the HeLa cell line. Compound **1** displayed cytotoxicity against the KB cell line and was more cytotoxic than etoposide. Compound **2** is the stereoisomer of **1**, and the variation of cytotoxicity between them indicated a critical stereochemistry requirement. Compound **1**, which is the first reported example of 8.8′-*trans*,7.O.9′ monotetrafuran lignan exhibiting cytotoxicity in the KB cell line, represents a novel analogue as an antitumor lead compound for SAR and lead optimization studies.

Materials and Methods

The plant material, purchased from Yuntian Medicinal Material Corporation, was cultivated in Deqin, Yunnan province, People's Republic of China, in September 2008, and was identified as the roots and rhizomes of *Sinopodophyllum emodi* (Wall.) Ying by Professor Qishi Sun of the Shenyang Pharmaceutical University, according to the Chinese Traditional Medicine Dictionary [22]. A voucher specimen (SE 20081009) was deposited in the Department of Natural Products Chemistry, Shenyang Pharmaceutical University, Shenyang, People's Republic of China.

(−)-*Tanegool-7′-methyl ether* (**1**): Sticky oil; $[\alpha]_D^{25}$ −19.4 (*c* 0.14, $CHCl_3$); CD (*c* = 1.2 g/L, MeOH) Δ *ε* (nm) 228 (+54.9), 258 (−7.6), 284 (+18.5); UV (MeOH): λ_{max} (log *ε*) = 208 (2.73), 230 (1.82), 280 (0.81) nm; IR (KBr): ν_{max} = 3420, 2935, 1604, 1516, 1273, 1158, 1123, 1057, 1034 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6) data, see **Table 1**; ^{13}C-NMR (75 MHz, DMSO-d_6) data, see **Table 2**; (+) ESI-MS: *m*/*z* 413 $[M + Na]^+$, 429 $[M + K]^+$; (−) ESI-MS: *m*/*z* 389 $[M - H]^-$, 425 $[M + Cl]^-$; HR-ESI-MS: *m*/*z* 413.1574 $[M + Na]^+$ (calcd. for $C_{21}H_{26}O_7Na^+$, 413.1576).

(+)-*7′-Methoxylariciresinol* (**2**): Sticky oil; $[\alpha]_D^{25}$ +9.0 (*c* 0.07, $CHCl_3$); CD (*c* = 1.3 g/L, MeOH) Δ *ε* (nm) 228 (+73.3), 258 (−4.0), 284 (+27.0); UV (MeOH): λ_{max} (log *ε*) = 208 (2.54), 230 (1.34), 280 (0.65) nm; IR (KBr): ν_{max} = 3419, 2936, 1607, 1517, 1274, 1157, 1121, 1083, 1032 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6) data, see **Table 1**; ^{13}C-NMR (75 MHz, DMSO-d_6) data, see **Table 2**; (+) ESI-MS: *m*/*z* 413 $[M + Na]^+$, 429 $[M + K]^+$; (−) ESI-MS: *m*/*z* 389 $[M - H]^-$, 425 $[M + Cl]^-$; HR-ESI-MS: *m*/*z* 413.1562 $[M + Na]^+$ (calcd. for $C_{21}H_{26}O_7Na^+$, 413.1576).

Sinolignan C (**3**): Amorphous powder; $[\alpha]_D^{25}$ −10.0 (*c* 0.3, MeOH); CD (*c* = 1.6 g/L, MeOH) Δ *ε* (nm) no Cotton effect; UV (MeOH): λ_{max} (log *ε*) = 208 (1.82), 228 (0.50), 278 (0.16) nm; IR (KBr): ν_{max} = 3410, 2928, 1619, 1520, 1271, 1221, 1095, 1043 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6) data, see **Table 1**; ^{13}C-NMR (75 MHz, DMSO-d_6) data, see **Table 2**; (+) ESI-MS: *m*/*z* 561 $[M + Na]^+$, 577 $[M + K]^+$; (−) ESI-MS: *m*/*z* 537 $[M - H]^-$, 573 $[M + Cl]^-$; HR-ESI-MS: *m*/*z* 561.1945 $[M + Na]^+$ (calcd. for $C_{26}H_{34}O_{12}Na^+$, 561.1948).

Epipinoresinol-4,4′-di-O-β-D-glucopyranoside (**4**): Amorphous powder; $[\alpha]_D^{25}$ −25.0 (*c* 0.3, MeOH); CD (*c* = 1.8 g/L, MeOH) Δ *ε* (nm) 230 (+1.1), 238 (+0.8), 254 (−1.0), 286 (+0.5); UV (MeOH): λ_{max} (log *ε*) = 208 (2.46), 228 (1.10), 278 (0.36) nm; IR (KBr): ν_{max} = 3420, 2928, 1631, 1514, 1273, 1223, 1160, 1077, 1045 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6) data, see **Table 1**; ^{13}C-NMR (75 MHz, DMSO-d_6) data, see **Table 2**; (+) ESI-MS: *m*/*z* 705 $[M + Na]^+$; (−) ESI-MS: *m*/*z* 681 $[M - H]^-$, 717 $[M + Cl]^-$, 727 $[M + HCOO]^-$; HR-ESI-MS: *m*/*z* 705.2370 $[M + Na]^+$ (calcd. for $C_{32}H_{42}O_{16}Na^+$, 705.2371).

Supporting information

General experimental procedures, detailed extraction/isolation of compounds, NMR and CD spectra of new compounds, as well as protocols for cell culture and cytotoxicity assays, along with the determination of the absolute configurations of the sugar moieties are available as Supporting Information.

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Conflict of Interest

There are no conflicts of interest among all authors.

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