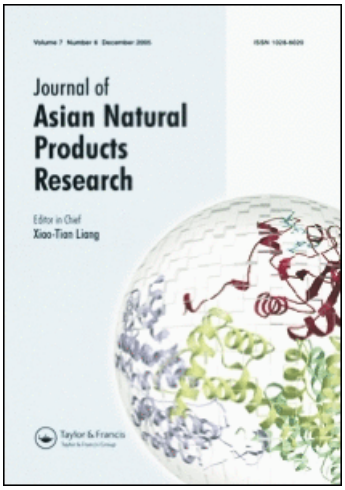


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# Two new secolignans from *Selaginella sinensis* (Desv.) Spring

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Two new secolignans, 3,4-*trans*-3-hydroxymethyl-4-[bis(4-hydroxyphenyl)methyl]-butyrolactone (**1**) and 2,3-*trans*-3,4-*trans*-2-methoxy-3-hydroxymethyl-4-[bis(4-hydroxyphenyl)methyl]tetrahydrofuran (**2**), together with six known compounds, were isolated from the whole grass of *Selaginella sinensis* (Desv.) Spring. Their structures were elucidated by NMR and MS experiments.

**Keywords:** *Selaginella sinensis*; secolignans; styraxlignolide D; neolloydosin



## 1. Introduction

*Selaginella* Beauv. consists of about 700 species in the world. There are 50 species distributed in China, and 20 of them are used as herbal medicines. *Selaginella sinensis* (Desv.) Spring is a special species of *Selaginella* Beauv. and widely distributed in the north and northeast of China, which has been used as a traditional medicine for its antibacterial, anti-inflammation, and hemostasis activities, especially for the treatment of chronic tracheitis. Some compounds, such as bisflavones, lignans, sesquilignans, glucosides, and pigments, have been isolated from this plant [1–5]. In the present paper, we describe the isolation and the structural elucidation of two new secolignan compounds, 3,4-*trans*-3-hydroxymethyl-4-[bis(4-hydroxyphenyl)-methyl]butyrolactone (**1**) and 2,3-*trans*-3,4-*trans*-2-methoxy-3-hydroxymethyl-4-[bis-(4-hydroxyphenyl)methyl]tetrahydrofuran (**2**), together with six known compounds, lariciresinol (**3**), lariciresinol-4-*O*-β-D-glucopyranoside (**4**), styraxlignolide D (**5**), matairesinol-4,4′-di-*O*-β-D-glucopyranoside (**6**), syringin (**7**), and neolloydosin (**8**). To our best knowledge, secolignans have only been found in *Piperomia* [6–10], *Justicia* [11], and *Urtica* species [12] until now, and this is the first report from the *Selaginella* family. All the known compounds are isolated for the first time from this plant.

## 2. Results and discussion

Compound **1** was obtained as a colorless solid. Its HR-ESI-MS showed $[M+Na]^+$ at *m/z* 337.1048, indicating the molecular formula of $C_{18}H_{18}O_5$. Meanwhile, the IR spectrum displayed the presence of hydroxyl (3334 $cm^{-1}$), γ-butyrolactone (1749 $cm^{-1}$), and aromatic ring (1612, 1512 $cm^{-1}$). The $^1H$ NMR spectrum of **1** showed eight aromatic protons at $\delta$ 7.18 (2H, d, $J = 8.5$ Hz), 6.73 (2H, d, $J = 8.5$ Hz) and 7.15 (2H, d, $J = 8.5$ Hz), 6.70 (2H, d, $J = 8.5$ Hz) as two AA′BB′ systems. Additionally, two oxygenated $CH_2$ groups at $\delta$ 4.28 (1H, t, $J = 8.6$ Hz),

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3.86 (1H, t, $J = 8.6$ Hz) and 3.70 (1H, dd, $J = 2.7$, 10.8 Hz), 2.92 (1H, dd, $J = 2.7$, 10.8 Hz) and three CH groups at $\delta$ 3.77 (1H, d, $J = 11.6$ Hz), 3.49 (1H, m), and 2.43 (1H, m) were observed. The $^{13}$C NMR and HSQC spectra showed the presence of a lactone C=O at $\delta$ 180.8 (C-2), two oxygen-bearing $CH_2$ at $\delta$ 60.7 (C-7) and 72.7 (C-5), and three CH groups at $\delta$ 41.4 (C-4), 49.7 (C-3), and 55.9 (C-6), as well as carbon signals of two aromatic rings ($\delta$ 116.4–157.2). In addition, its molecular formula indicated 10 degrees of unsaturation, among which eight were attributed to two phenyl moieties and one was caused by the carbonyl group, which confirmed the presence of a lactone ring. The $^1$H–$^1$H COSY correlations provided the correlations of H-3 and H-7, H-4 and H-3, H-4 and H-5, and H-6 and H-4. In fact, in the HMBC spectrum, C-2 showed correlations with H-4, H-5, and H-7; C-3 showed correlation with H-5. These evidences further confirmed the presence of a γ-butyrolactone group. Besides, the signals of C-6 correlated with H-2′, H-2″, H-6′, H-6″, H-3, and H-5, which indicated that C-6 was substituted by two aromatic rings and a lactone ring. A 3,4-*trans* orientation was established from the NOE cross-peaks between H-3 and H-6, H-4 and H-7a. The positions of the two aromatic rings were deduced by the NOESY spectrum, which gave clear correlations of H-2′ with H-3 and H-6″ with H-5a. Thus, compound **1** is 3,4-*trans*-3-hydroxymethyl-4-[bis(4-hydroxyphenyl)methyl]butyrolactone (Figure 1).

Compound **2** was obtained as a colorless solid. Its HR-ESI-MS showed $[M+Na]^+$ at *m/z* 353.1364, indicating the molecular formula of $C_{19}H_{22}O_5$. Meanwhile, the IR spectrum indicated the presence of the hydroxyl group (3335 cm$^{-1}$) and aromatic ring (1612, 1512 cm$^{-1}$). Comparison of NMR spectral data of **2** with those of **1** revealed that both the compounds shared the same skeleton, and the significant difference was the absence of the carbonyl carbon in the $^{13}$C NMR spectrum and the presence of a proton at $\delta$ 5.00 (1H, s, H-2) and a methoxyl group at $\delta$ 3.33 (3H, s) in the $^1$H NMR spectrum and two carbons at $\delta$ 109.3 (C-2) and 54.8 (C—OMe) of the hemiacetal group in the $^{13}$C NMR spectrum of **2**, respectively. Moreover, H-2 correlated with C-4, C-5, C-7 and the methoxyl group in the HMBC spectrum, indicating that this compound was a tetrahydrofuran derivative and the location of the methoxyl group was assigned to C-2. The singlet of H-2 suggested that the dihedral angle $H_2$—$C_2$—$C_3$—$H_3$ was nearly 90°, which indicated a *trans* orientation of H-2 and H-3 [8]. The overlapping $^1$H NMR signals for H-5, H-6, and H-7a, notwithstanding, and a strong NOE cross-peak from H-4 to H-7b

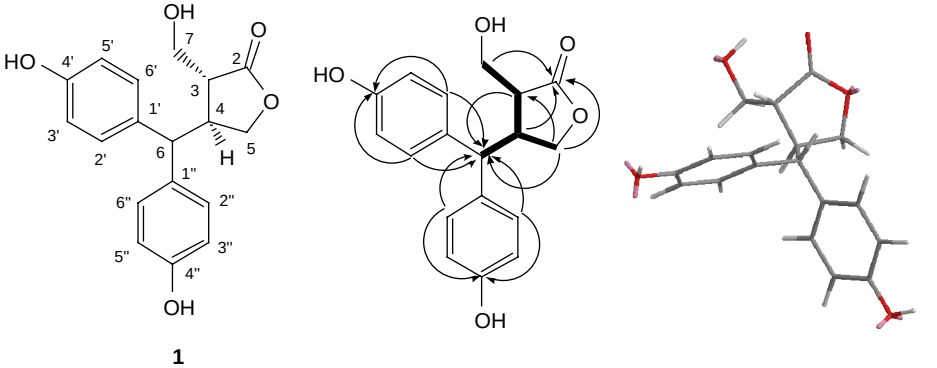


Figure 1. Structure, key HMBC (⌒), $^1$H–$^1$H COSY (▬) correlations, and energy-minimized 3D model of **1**.

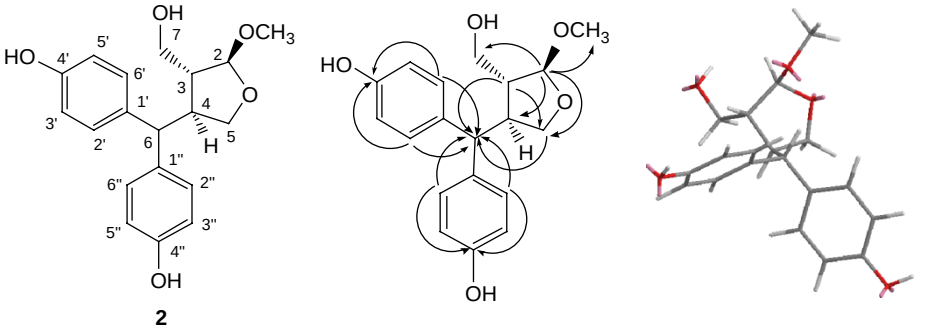


Figure 2. Structure, key HMBC correlations, and energy-minimized 3D model of **2**.

indicated the *trans* orientation of H-3 and H-4. The positions of the two aromatic rings were deduced by the NOESY spectrum, which gave correlations of H-2′ with H-3; H-6″ with H-5a. Thus, compound **2** is 2,3-*trans*-3,4-*trans*-2-methoxy-3-hydroxymethyl-4-[bis(4-hydroxyphenyl)-methyl]tetrahydrofuran (Figure 2).

The known compounds lariciresinol (**3**) [13], lariciresinol-4-*O*-β-D-glucopyranoside (**4**) [14], styraxlignolide D (**5**) [15], matairesinol-4,4′-di-*O*-β-D-glucopyranoside (**6**) [14], syringin (**7**) [16], and neolloydosin (**8**) [17] were identified by comparison of their $^{1}$H and $^{13}$C NMR, MS, and physical data with those reported in the literature.

## 3. Experimental

### 3.1 General experimental procedures

Optical rotations were obtained using a Perkin-Elmer 341 polarimeter. UV spectra were measured with a Shimadzu UV–VIS 2201 spectrophotometer. IR spectra were measured with a Shimadzu FTIR-8201 PC spectrometer. The $^{1}$H and $^{13}$C NMR spectra were obtained on a Bruker DPX-400 spectrometer (400 MHz for $^{1}$H NMR and 100 MHz for $^{13}$C NMR) with TMS as an internal reference. HR-ESI-MS were recorded on an APEX II spectrometer. Preparative HPLC was performed on a Shimadzu-8A instrument, using an RP-$C_{18}$ column (20 × 250 mm) at a flow rate of 2.5 ml/min (UV detection at 273 nm). Column chromatography was performed on Diaion HP-20 (Mitsubishi Chemical Corporation, Tokyo, Japan), silica gel (160–200 mesh; Qingdao Marine Chemical Industry, Qingdao, China), Toyopearl HW-40 and Sephadex LH-20 (TOSOH Corporation, Tokyo, Japan). TLC was conducted on self-made silica gel G (Qingdao Marine Chemical Industry) plates. The chemical reagents were purchased from Beijing Chemical Plant (Beijing, China) and Tianjin No. 3 Reagent Plant (Tianjin, China).

### 3.2 Plant material

The fresh plants of *S. sinensis* were collected from Xixia County, Henan Province of China, in May 2006, and identified by Prof. Cheng-Ming Dong of the Henan University of Traditional Chinese Medicine. Its voucher specimen (JB20060510) is deposited in our laboratory.

### 3.3 Extraction and isolation

The fresh whole plants of *S. sinensis* (7.5 kg) were extracted with 70% aq. $Me_2CO$ twice at room temperature to afford a residue (800 g), which was suspended in water, and extracted with

Table 1. $^{1}H$ and $^{13}C$ NMR spectral data of **1** and **2**.

| | **1** | | **2** | |
|---|---|---|---|---|
| Position | $\delta_C$ | $\delta_H$ ($J$, Hz) | $\delta_C$ | $\delta_H$ ($J$, Hz) |
| 2 | 180.8 | | 109.3 | 5.00 (s) |
| 3 | 49.7 | 2.43 (m) | 50.0 | 2.15 (m) |
| 4 | 41.4 | 3.49 (m) | 44.0 | 3.53 (m) |
| 5a | 72.7 | 4.28 (t, $J = 8.6$) | 72.9 | 3.61 (m) |
| 5b | | 3.86 (t, $J = 8.6$) | | 3.55 (m) |
| 6 | 55.9 | 3.77 (d, $J = 11.6$) | 50.1 | 3.60 (m) |
| 7a | 60.7 | 3.70 (dd, $J = 2.7$, 10.8) | 59.1 | 3.62 (m) |
| 7b | | 2.92 (dd, $J = 2.7$, 10.8) | | 3.40 (m) |
| 1′ | 135.1 | | 136.4 | |
| 2′, 6′ | 129.7 | 7.18 (d, $J = 8.5$) | 129.4 | 7.23 (d, $J = 8.5$) |
| 3′, 5′ | 116.4 | 6.73 (d, $J = 8.5$) | 116.3 | 6.72 (d, $J = 8.5$) |
| 4′ | 157.2 | | 156.8 | |
| 1″ | 135.6 | | 137.3 | |
| 2″, 6″ | 129.9 | 7.15 (d, $J = 8.5$) | 129.1 | 7.07 (d, $J = 8.5$) |
| 3″, 5″ | 116.5 | 6.70 (d, $J = 8.5$) | 116.2 | 6.64 (d, $J = 8.5$) |
| 4″ | 157.2 | | 156.8 | |
| 2-OMe | | | 54.8 | 3.33 (s) |

At 400 and 100 MHz, respectively, in $CD_3OD$.



ethyl ether, ethyl acetate, and *n*-butanol, successively. The ethyl ether layer (10 g) was chromatographed on a silica gel column using a gradient system of petroleum ether–EtOAc and $CHCl_3$–MeOH, yielding **3** (27 mg). The ethyl acetate layer (65 g) was chromatographed on silica gel, eluting with a gradient system of $CHCl_3$–MeOH (50:1 → 1:1) to afford fractions A–D. Fraction C (11.2 g) was subjected to silica gel (EtOAc–EtOH–$H_2O$, 30:2:1) to give four fractions. Fraction 1 (1.7 g) was subjected to Sephadex LH-20 (MeOH) and preparative HPLC (MeOH–$H_2O$, 3:7), to give compounds **1** (6 mg) and **2** (8 mg). A part of fraction 2 (3.5 g) was chromatographed on Sephadex LH-20 (MeOH) to yield **4** (31 mg) and **5** (27 mg). The *n*-butanol layer (120 g) was chromatographed on Diaion HP-20, eluting with a gradient system of MeOH–$H_2O$ (10 → 50%). The 30% MeOH part (17.2 g) was then successfully subjected to Sephadex LH-20 (MeOH) to yield **6** (11 mg) and **7** (12 mg). The 50% MeOH part (5.7 g) was chromatographed on silica gel (EtOAc–EtOH–$H_2O$, 25:2:1) to afford **8** (5 mg).

### *3.3.1 3,4-Trans-3-hydroxymethyl-4-[bis(4-hydroxyphenyl)methyl]butyrolactone* (**1**)

A colorless solid; $[\alpha]_D^{20}$ +49 ($c = 0.23$, MeOH); IR (KBr) $\nu_{max}$: 3334, 2923, 1749, 1612, 1512, 1444, 1367, 1228, 1174, 1026, 833, 582 $cm^{-1}$; UV (MeOH) $\lambda_{max}$: 205, 233, 281 nm. $^{1}H$ and $^{13}C$ NMR spectral data are shown in Table 1. HR-ESI-MS: *m/z* 337.1047 $[M+Na]^+$ (calcd for $C_{18}H_{18}O_5Na$, 337.1052).

### *3.3.2 2,3-Trans-3,4-trans-2-methoxy-3-hydroxymethyl-4-[bis(4-hydroxyphenyl)-methyl]tetrahydrofuran* (**2**)

A colorless solid; $[\alpha]_D^{20}$ −91 ($c = 0.12$, MeOH); IR (KBr) $\nu_{max}$: 3355, 2947, 2893, 1612, 1512, 1450, 1373, 1234, 1033, 833, 578 $cm^{-1}$; UV (MeOH) $\lambda_{max}$: 204, 237, 277 nm. $^{1}H$ and $^{13}C$ NMR spectral data are shown in Table 1. HR-ESI-MS: *m/z* 353.1364 $[M+Na]^+$ (calcd for $C_{19}H_{22}O_5Na$, 353.1365).

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