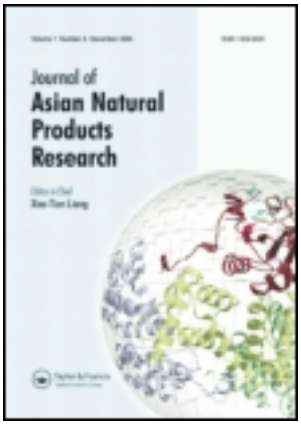

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Two new selaginellin derivatives from *Selaginella tamariscina* (Beauv.) Spring

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Two new selaginellin derivatives, selaginellins K (**1**) and L (**2**), were isolated from *Selaginella tamariscina* (Beauv.) Spring and characterized as 2-formyl-4,4′-dihydroxy-3-[(4-hydroxyphenyl)ethynyl]biphene and 4,4′-dihydroxy-2-methyl-3-[(4-hydroxyphenyl)ethynyl]biphene on the basis of their spectroscopic data including UV, IR, 1D, and 2D NMR as well as HR-ESI-MS spectroscopic analysis.

Keywords: selaginella; *Selaginella tamariscina*; selaginellin K; selaginellin L

1. Introduction

Selaginella tamariscina (Beauv.) Spring as a traditional Chinese medicine has been introduced in Chinese Pharmacopeia for the effectiveness in promoting blood circulation since the 1953rd edition. Pharmacological investigation of the genus *Selaginella* revealed its biological activities of antioxidant, antivirus, anti-inflammation, and effects on cardiovascular system protection [1–5]. Since a number of constituents such as flavones, phenylpropanoids, alkaloids, organic acids, anthraquinones, and steroids were reported, a selaginellin family consisting of selaginellin and selaginellins A–J was isolated from *S. sinensis* [6], *S. tamariscina* [7], and *S. pulvinata* [8–11], respectively, which belongs to the alkynyl phenols with a novel carbon skeleton. As a continuation of our work, herein, we report the isolation and structural elucidation of two new alkynyl phenols, named as selaginellins K (**1**) and L (**2**) from *S. tamariscina* (Figure 1). Compounds **1** and **2** belong to selaginellin derivatives, but their structures were different from the previously reported selaginellins. The fragment of rings C and D in selaginellins with typical delocalization was displaced by aldehyde group or methyl, and compound **1** showed a novel planar structure.

2. Results and discussion

The 75% EtOH extract of the whole plant of *S. tamariscina* was chromatographed over polyamide, HW-40C, and prep-HPLC to yield compounds **1** and **2**.

Compound **1** was obtained as an orange powder (freeze dried from water), and its molecular formula was determined as $C_{21}H_{14}O_4$ on the basis of ESI-MS at *m/z* 330.0 $[M]^+$ and HR-ESI-MS at *m/z* 331.0961 $[M + H]^+$, which indicated 15 degrees of unsaturation. Its UV spectrum showed absorption maxima at 261, 300, and 428 nm, the characteristic values of a selaginellin chromophore [6–8]. The IR spectrum showed absorption bands for hydroxyl (3435 cm^{-1}), aldehyde (2842,

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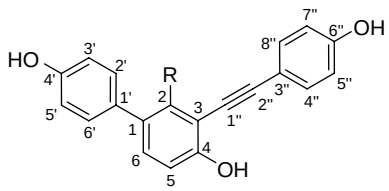

1 R = CHO
2 R = CH_3

Figure 1. The structures of compounds **1** and **2**.

2750 cm^{-1}), alkynyl (2196 cm^{-1}), carbonyl (1686 cm^{-1}), and aromatic groups (1620, 1513, 1480 cm^{-1}).

^1H NMR spectrum of **1** exhibited 14 proton signals, among which 3 were phenolic hydroxyl groups confirmed by adding heavy hydrogen reagent D_2O, and 1 was an aldehyde confirmed by the DEPT experiment that showed the methenyl signal at δc 191.3. The other 10 aromatic protons were involved in three spin systems on the basis of $^1H-^1H$ COSY analysis. Two doublets at δ_H 7.09 (2H, d, $J = 8.6$ Hz, H-4″, 8″) and δ_H 6.68 (2H, d, $J = 8.6$ Hz, H-5″, 7″) appearing as an AA′BB′ type suggested the presence of a *para*-substituted benzene ring, which was confirmed by HMBC correlations (Figure 2) between C-6″ (δ_C 158.7) and H-4″/8″ (δ_H 7.09), H-5″/7″ (δ_H 6.68). The HMBC correlations between the alkyne carbon at δ_C 100.8 (C-2″) and H-4″/H-8″ at δ_H 7.09 indicated the existence of a 4-alkynyl-phenol. Another *para*-substituted phenol was indicated by the two doublets at δ_H 6.87 (2H, d, $J = 8.5$ Hz, H-2′, 6′) and δ_H 6.60 (2H, d, $J = 8.5$ Hz, H-3′, 5′),

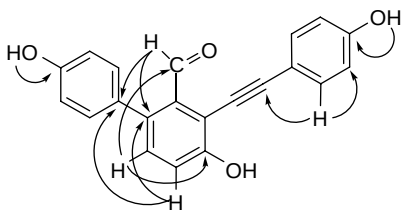

Figure 2. Key HMBC correlations of **1**.

which was confirmed by the HMBC experiment. The signals at δ_H 7.51 (1H, d, $J = 8.0$ Hz, H-5) and δ_H 7.99 (1H, d, $J = 8.0$ Hz, H-6) suggested an *ortho*-substituted benzene ring. The HMQC spectrum indicated the linkage between H-5 (δ_H 7.51)/C-5 (δ_C 130.3) and H-6 (δ_H 7.99)/C-6 (δ_C 127.9) and the HMBC spectrum showed the correlations of H-6 (δ_H 7.99)/C-2 (δ_C 147.5), C-3 (δ_C 127.1), C-4 (δ_C 157.1), 2-CHO (δ_C 191.3) and H-5 (δ_H 7.51)/C-1 (δ_C 141.5), C-1′ (δ_C 133.4), which confirmed that the basic structure of **1** was an aromatic system with 1,2,3,4-tetrasubstituted benzene. The chemical shifts for H-5 (δ_H 7.51) and H-6 (δ_H 7.99) confirmed that the hydroxyl should be connected with C-4 (δ_C 157.1), and the correlations of 2-CHO (δ_H 10.58)/C-1 (δ_C 141.5), C-1′ (δ_C 133.4), C-4 (δ_C 141.5), and H-6 (δ_H 7.99)/C-2 (δ_C 147.5), 2-CHO (δ_C 191.3), C-1′ (δ_C 133.4) indicated that the aldehyde group should be located at C-2 and the *para*-substituted phenol should be located at C-1. The long-range correlation of H-6/C-4 confirmed the allocation of H-5 and H-6. The complete structure was revealed with the aid of DEPT, HMQC, and HMBC spectra. Accordingly, the structure of **1** was characterized as 2-formyl-4,4′-dihydroxy-3-[(4-hydroxyphenyl)ethynyl]biphene on the basis of the reasonable combination of above substructures, and the important HMBC correlations are illustrated in Figure 2.

Compound **2** was obtained as an orange powder (freeze dried from water), and its molecular formula was determined as $C_{21}H_{16}O_3$ on the basis of ESI-MS at *m/z* 316.0 $[M]^+$ and HR-ESI-MS at *m/z* 339.0985 $[M + Na]^+$, which indicated 14 degrees of unsaturation. Its UV spectrum showed absorption maxima at 265, 300, and 433 nm. The IR spectrum showed absorption bands for hydroxyl (3429 cm^{-1}), methyl (2924 cm^{-1}), alkynyl (2198 cm^{-1}), and aromatic groups (1618, 1508, 1483 cm^{-1}). The ^1H NMR spectrum of **2** indicated the similar structural

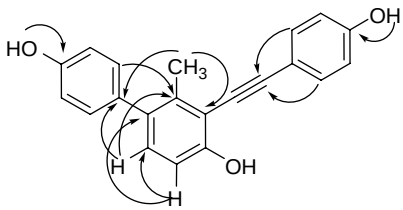

Figure 3. Key HMBC correlations of **2**.

fragments to **1** as follows, two *para*-substituted phenols, an 1,2,3,4-tetrasubstituted benzene ring, except for an aromatic methyl connected with C-2 (δ_C 139.6) instead of the aldehyde group in **1**. The ^{13}C NMR spectral data of **2** showed characteristic signals similar to those of **1**, except for one signal at δ_C 40.9, indicating the presence of an aromatic methyl, which was confirmed by the HMQC correlation between the carbon at δ_C 40.9 and the proton at δ_H 2.55 (3H). Comparison of the spectroscopic data of **2** with those of **1** suggested that **2** was the homolog of **1** and its structure was established as 4,4′-dihydroxy-2-methyl-3-[(4-hydroxyphenyl)ethynyl]biphene on the basis of ^1H, ^{13}C, 2D NMR analysis, and the important HMBC correlations are illustrated in Figure 3.

3. Experimental

3.1 General experimental procedures

UV spectra were obtained on a UV Probe-2450 spectrometer. IR spectra were obtained using KBr disks on an AVATAR 360FT-IR spectrophotometer (Nicolet Instrument Corporation, Madison, WI, USA). ESI-MS spectra were registered on a LCQ-Advantage mass spectrometer. HR-ESI-MS spectra were recorded on a Micromass Zabspec (Micromass UK Ltd, Manchester, UK) HR-MS spectrometer and JMS-T100 CS. NMR spectra, including COSY, NOESY, HMBC, and HMQC experiments, were recorded on a Varian Unity INOBA-400 MHz spectrometer with tetramethylsilane (TMS) as an internal standard. Polyamide (30–60 mesh; China National Medicine Corporation Ltd, Shanghai, China), Sephadex LH-20, and HW-40C (TOYOPEARL TOSOH, Tokyo, Japan) were used for column chromatography (CC), and silica gel GF-254 (Qingdao Marine Chemical Factory, Qingdao, China) was used for TLC. Pre-HPLC experiments were carried out on a preparative YMC-Pack ODS-A column (15 μm, 250 × 20 mm, YMC, Kyoto, Japan).

3.2 Plant material

The herbs of *S. tamariscina* were purchased from the BaiJia Chinese Herbal Medicine Co. Ltd (Changsha, China), and identified by Associate Professor Jin-Ping Li (Central South University, Changsha, China). A voucher specimen has been deposited in the School of Pharmaceutical Sciences, Central South University (No. 0906010).

3.3 Extraction and isolation

The whole herbs of *S. tamariscina* (10.0 kg) were extracted with 75% EtOH for three times, and after removing the solvent, the dried extract was obtained and dissolved with MeOH by treating in a refrigerator for 24 h, and then filtered. The filtrate was passed over polyamide resin CC eluted with a gradient of aqueous EtOH (30, 45, 70, 95%, V/V) to yield five portions. A part of the 70% portion was subjected to HW-40C column with 60% MeOH–H_2O isocratic elution to obtain Fractions 7–9 (810 mg). Fractions 7–9 were further purified by Sephadex LH-20 (MeOH–H_2O in gradient) and preparative HPLC [YMC-Pack ODS-A (250 × 20 mm), H_2O–MeOH (30:70)] to give compounds **1** (32.0 mg) and **2** (44.0 mg).

3.3.1 2-Formyl-4,4′-dihydroxy-3-[(4-hydroxyphenyl)ethynyl]biphene (**1**)

Orange powder. UV(MeOH) λ_{max} (nm): 261, 300, 428. IR(KBr) ν_{max} (cm^{-1}): 3435,

Table 1. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectral data of compounds **1** and **2** in DMSO-d_6 (δ in ppm, J in Hz).

	1		**2**	
Atom	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C
1		141.5		140.4
2		147.5		139.6
3		127.1		123.6
4		157.1		159.4
5	7.51 d (8.0)	130.3	7.25 d (8.0)	128.9
6	7.99 d (8.0)	127.9	7.48 d (8.0)	130.2
1′		133.4		130.5
2′	6.87 d (8.5)	129.5	6.80 d (8.5)	129.3
3′	6.60 d (8.5)	114.9	6.55 d (8.5)	114.6
4′		157.3		157.3
5′	6.60 d (8.5)	114.9	6.55 d (8.5)	114.6
6′	6.87 d (8.5)	129.5	6.80 d (8.5)	129.3
1″		82.4		85.1
2″		100.8		97.9
3″		129.6		137.9
4″	7.09 d (8.6)	133.2	6.97 d (8.7)	132.7
5″	6.68 d (8.6)	115.7	6.68 d (8.7)	115.5
6″		158.7		158.0
7″	6.68 d (8.6)	115.7	6.68 d (8.7)	115.5
8″	7.09 d (8.6)	133.2	6.97 d (8.7)	132.7
2-CHO	10.58 s	191.3		
2-Me			2.55 s	40.9

Note: The assignments were based on DEPT, ^{1}H–^{1}H COSY, HMQC, and HMBC experiments.

2842, 2750, 2196, 1686, 1620, 1513, 1480. For ^{1}H and ^{13}C NMR spectral data, see Table 1. ESI-MS *m/z*: 330.0 $[M]^+$. HR-ESI-MS *m/z*: 331.0961 $[M + H]^+$ (calcd for $C_{21}H_{15}O_4$, 331.0970).

*3.3.2 4,4′-Dihydroxy-2-methyl-3-[(4-hydroxyphenyl)ethynyl]biphene (**2**)*

Orange powder. UV(MeOH) λ_{max} (nm): 265, 300, 433. IR(KBr) ν_{max} (cm^{-1}): 3429, 2924, 2198, 1618, 1508, 1483. For ^{1}H and ^{13}C NMR spectral data, see Table 1. ESI-MS: *m/z* 316.0 $[M]^+$. HR-ESI-MS: *m/z* 339.0985 $[M + Na]^+$ (calcd for $C_{21}H_{16}O_3Na$, 339.0997).

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