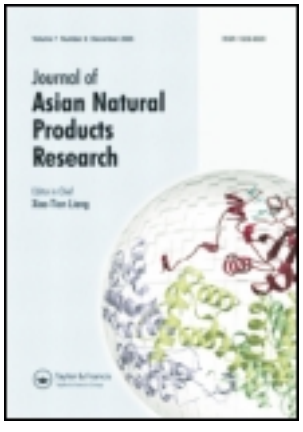

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Selaginellins I and J, two new alkynyl phenols, from *Selaginella tamariscina* (Beauv.) Spring

Kang-Ping Xu[a], Hui Zou[a], Qiang Tan[c], Fu-Shuang Li[a], Jian-Feng Liu[ac], Hong-Lin Xiang[a], Zhen-Xing Zou[a], Hong-Pin Long[a], Yuan-Jian Li[a] and Gui-Shan Tan[ab]*

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Selaginellins I (**1**) and J (**2**), two new compounds, were isolated from *Selaginella tamariscina* (Beauv.) Spring and were characterized as (*R*,*S*)-4-((2′,4′-dihydroxy-4-(hydroxymethyl)-3-((4-hydroxyphenyl)ethynyl)biphenyl-2-yl)(4-hydroxyphenyl)-methylene)cyclohexa-2,5-dienone (**1**) and (*R*,*S*)-4-((3-((3,4-dihydroxyphenyl)ethynyl)-4′-hydroxy-4-(hydroxymethyl)biphenyl-2-yl)(4-hydroxyphenyl)methylene)cyclohexa-2,5-dienone (**2**) on the basis of UV, IR, 1D and 2D NMR, and HR-ESI-MS spectroscopic analysis.

Keywords: Selaginella; *Selaginella tamariscina*; alkynyl phenols; selaginellin I; selaginellin J

1. Introduction

The genus *Selaginella* consists of about 700 species in the world and about 60 species are widely distributed in China [1]. *Selaginella tamariscina* (Beauv.) Spring has been used as traditional Chinese medicine for the effectiveness in promoting blood circulation for a long history. Recently, selaginellins A–H, new alkynyl phenols with unusual carbon skeleton, were isolated from *S. sinensis* [2], *S. tamariscina* [3], *and S. pulvinata* [4–6], respectively. In the course of our phytochemical study on the genus *Selaginella*, two new alkynyl phenols named as selaginellin I (**1**) and selaginellin J (**2**) were isolated from the whole herbs of *S. tamariscina* (Beauv.) Spring (Figure 1). Herein, the isolation and structural elucidation of these two compounds are discussed.

2. Results and discussion

Compounds **1** and **2** were isolated from 75% EtOH extract of *S. tamariscina* by repeated column chromatography (CC) and preparative HPLC.

Compound **1** was obtained as a red oil. ESI-MS gave the quasi-molecular ion peak at *m*/*z* 530.3 $[M + 2H]^+$, and HR-MS (*m*/*z* 527.1486 $[M - H]^-$) indicated a molecular formula of $C_{34}H_{24}O_6$. Its UV spectrum showed absorption maxima at 267, 299, and 430 nm, the characteristic values of a selaginellin chromophore [2–5]. The IR spectrum indicated the presence of OH groups (3399 cm^{-1}), C—H stretching vibrations (2920, 2853 cm^{-1}), unsaturated C=O (1651 cm^{-1}), C≡C (2198 cm^{-1}), and aromatic ring (1506 cm^{-1}). In the ^1H NMR spectrum, the extensive delocalization also took place in rings C and D as we

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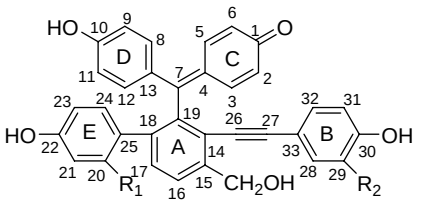

1 R_1 = OH, R_2 = H
2 R_1 = H, R_2 = OH

Figure 1. Structures of compounds **1** and **2**.

reported previously in selaginellin C [4], which caused compound **1** to become racemic [2]. The delocalization of π-electrons makes rings C and D chemically equivalent [3,7], so the chemical shifts of C-1 and C-10 are both at δ 155.8 without the signal of C=O. Thus, the signals at δ 6.56 (4H, d, $J = 7.5$ Hz, H-2, 6, 9, 11) and 6.97 (4H, d, $J = 7.5$ Hz, H-3, 5, 8, 12) should be eight aromatic protons of ring C and ring D. Compound **1** contained an acetylene bond due to the carbon signals at δ 100.8 (C-27) and 84.0 (C-26). ^{1}H–^{1}H COSY spectrum indicated that the signals at δ 6.87 (2H, d, $J = 7.0$ Hz, H-28, 32) and 6.71 (2H, d, $J = 7.0$ Hz, H-29, 31) were aromatic protons of *para*-substituted benzene ring. In HMBC spectrum, the correlations between H-28, 32, H-29, 31, and C-27 showed that the C≡C bond was connected to ring B. Three aromatic protons at δ 7.63 (1H, d, $J = 7.0$ Hz, H-24), 6.72 (1H, d, $J = 7.0$ Hz, H-23), and 6.62 (1H, s, H-21) should belong to ring E based on ^{1}H–^{1}H COSY spectrum. In HMBC spectrum, correlations between H-24 and C-18 showed that ring E was connected to ring A at C-18. The other two *ortho*-aromatic protons [δ 7.49 (H-16, d, $J = 6.5$ Hz), 7.74 (H-17, d, $J = 6.5$ Hz)] in ring A were observed in ^{1}H–^{1}H COSY spectrum. The linkage position of hydroxymethyl [δ 4.63 (H-34, s) and δ 61.3 (C-34)] in ring A was established by HMBC cross-peaks of H-34/C-14 and H-34/C-16 (Figure 2). On the basis of the above evidence, compound **1** was determined as (*R*,*S*)-4-((2′,4′-dihydroxy-4-(hydroxymethyl)-3-((4-hydroxyphenyl)ethynyl)biphenyl-2-yl)(4-hydroxyphenyl)methylene)cyclohexa-2,5-dienone and named as selaginellin I.

Compound **2** was obtained as a red oil. ESI-MS showed the quasi-molecular ion peak at *m*/*z* 529.3 $[M + H]^+$, and HR-MS (*m*/*z* 527.1484 $[M - H]^-$) indicated a molecular formula of $C_{34}H_{24}O_6$. The UV spectrum showed absorption maxima characteristic of a selaginellin chromophore (265, 295, and 426 nm) as well. The IR spectrum indicated the presence of OH groups (3411 cm^{-1}), C—H stretching vibrations (2924 cm^{-1}), C≡C (2196 cm^{-1}), and aromatic ring (1512 cm^{-1}). Examination of the chemical shifts of compound **2** and comparing with the corresponding signals in compound **1** suggested that there are eight aromatic protons [δ 6.48 (4H, d, $J = 8.5$ Hz, H-2, 6, 9, 11) and 7.04 (4H, br, H-3, 5, 8, 12)] in ring C and ring D. The delocalization was also found in compound **2**, which leads to the identical chemical shifts of C-1 and C-10 (δ 156.9). Compound **2** showed an acetylene bond due to the carbon signals at δ 99.6 (C-27) and 83.6 (C-26). ^{1}H–^{1}H COSY spectrum indicated that the signals at δ 6.60 (H-31, d, $J = 8.0$ Hz), 6.45 (H-32, d, $J = 8.0$ Hz), and 6.56 (H-28, s) were aromatic protons of ring B with two *ortho*-substituted OH. The HMBC cross-peaks of H-28/C-27 and H-32/C-27 indicated that the C≡C bond was connected to ring B. Ring E was a *para*-substituted benzene ring according to the proton signals

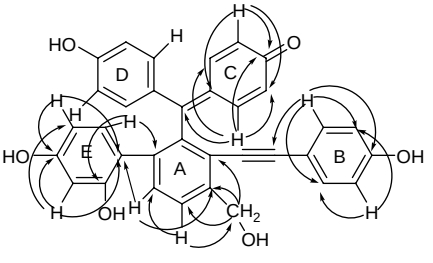

Figure 2. Key HMBC correlations of compound **1**.

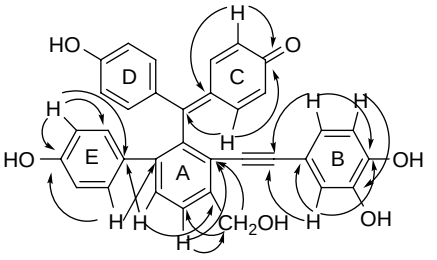

Figure 3. Key HMBC correlations of compound **2**.

at δ 6.55 (2H, d, $J = 8.5$ Hz) and 6.80 (2H, d, $J = 8.5$ Hz) and connected to ring A in position C-18 due to the HMBC cross-peaks H-24/C-18 and H-17/C-25 (Figure 3). Thus, the structure of compound **2** was determined as (*R*,*S*)-4-((3-((3,4-dihydroxyphenyl)ethynyl)-4′-hydroxy-4-(hydroxymethyl)biphenyl-2-yl) (4-hydroxyphenyl) methylene)cyclohexa-2,5-dienone and named as selaginellin J.

3. Experimental

3.1 General experimental procedures

UV spectra were determined with a Shimadzu UV-2450 instrument (Shimadzu Corporation, Tokyo, Japan). IR spectra were measured with Nicolet Avatar (Nicolet Instrument Corporation, Madison, WI, USA) 360 FT-IR instrument as a film on KBr disk. The ^{1}H and ^{13}C NMR spectra were obtained with Varian INOVA-500 spectrometers (Varian Inc. Corporate, Santa Clara, CA, USA) with TMS as internal standard. The MS was obtained with LCQ-Advantage (Thermo Electron Corporation, Hayward, CA, USA) mass spectrometer and Micromass ZabSpec (Micromass UK Ltd, Manchester, UK) HR-MS spectrometer.

3.2 Plant material

Herbs of *S. tamariscina* were collected in Jiangxi Province, China, in July 2006 and identified by Prof. Zhen-Ji Li (Xiamen University, Xiamen, China). A voucher specimen is deposited in School of Pharmaceutical Sciences, Central South University (No. JB-003).

3.3 Extraction and isolation

The whole herbs of *S. tamariscina* (14.0 kg) were soaked in 75% EtOH for two times (130 liters, 100 liters, 15 days each time). After removal of the solvent under reduced pressure, the extract (1450 g) was chromatographed over macroporous absorption resin column with EtOH–H_2O gradient elution (30, 60, and 95%). The 60% EtOH portion was subjected to CC on silica gel eluting with $CHCl_3$–MeOH (in gradient) to obtain fractions 140–152. Fractions 140–152 were further purified through Sephadex LH-20 (MeOH–H_2O in gradient) and preparative HPLC [YMC-Pack ODS-A (250 × 10 mm), 0.2% HAc–MeOH (40:60)] to yield compounds **1** (15.7 mg) and **2** (12.5 mg).

3.3.1 Selaginellin I (=(R,S)-4-((2′,4′-dihydroxy-4-(hydroxymethyl)-3-((4-hydroxyphenyl)ethynyl)biphenyl-2-yl)(4-hydroxyphenyl)methylene)cyclohexa-2,5-dienone (**1**)

Red oil. UV (MeOH) λ_{max} (nm): 267, 299, 430. IR (KBr) ν_{max} (cm^{-1}): 3399, 3152, 2920, 2853, 2198, 1651, 1556, 1536, 1506, 1399. ^{1}H and ^{13}C NMR spectral data, see Table 1. HR-ESI-MS *m/z*: 527.1486 $[M - H]^-$ (calcd for $C_{34}H_{23}O_6$, 527.1495).

3.3.2 Selaginellin J (=(R,S)-4-((3-((3,4-dihydroxyphenyl)ethynyl)-4′-hydroxy-4-(hydroxymethyl)biphenyl-2-yl)(4-hydroxyphenyl)methylene)cyclohexa-2,5-dienone (**2**)

Red oil. UV (MeOH) λ_{max} (nm): 265, 295, 426. IR (KBr) ν_{max} (cm^{-1}): 3411, 2924, 2196, 1594, 1576, 1512. ^{1}H and ^{13}C NMR spectral data, see Table 1. HR-ESI-MS *m/z*: 527.1484 $[M - H]^-$ (calcd for $C_{34}H_{23}O_6$, 527.1495).

Table 1. ^{1}H (500 MHz) and ^{13}C NMR (125 MHz) spectral data of compounds **1** and **2** in DMSO-d_6[a] (δ in ppm, J in Hz).

	1		**2**	
Position	δ(H)	δ(C)	δ(H)	δ(C)
1	–	155.8	–	156.9
2/6	6.56 (2H, d, $J = 7.5$)	114.2	6.48 (2H, d, $J = 8.5$ Hz)	123.7
3/5	6.97 (2H, d, $J = 7.5$)	129.7	7.04 (2H, br)	136.6
4	–	132.8	–	130.0
7	–	131.7	–	129.8
8/12	6.97 (2H, d, $J = 7.5$)	129.7	7.04 (2H, br)	136.6
9/11	6.56 (2H, d, $J = 7.5$)	114.2	6.48 (2H, d, $J = 8.5$ Hz)	123.7
10	–	155.8	–	156.9
13	–	132.8	–	130.0
14	–	117.9	–	121.5
15	–	141.7	–	142.8
16	7.49 (1H, d, $J = 6.5$)	125.6	7.68 (1H, d, $J = 8.0$ Hz)	127.4
17	7.74 (1H, d, $J = 6.5$)	118.5	7.35 (1H, d, $J = 8.0$ Hz)	130.0
18	–	139.1	–	140.6
19	–	151.3	–	140.8
20	–	155.8	6.80 (1H, d, $J = 8.5$ Hz)	130.0
21	6.62 (1H, s)	111.9	6.55 (1H, d, $J = 8.5$ Hz)	115.2
22	–	157.8	–	157.0
23	6.72 (1H, d, $J = 7.0$)	114.6	6.55 (1H, d, $J = 8.5$ Hz)	115.2
24	7.63 (1H, d, $J = 7.0$)	120.7	6.80 (1H, d, $J = 8.5$ Hz)	130.0
25	–	129.7	–	131.1
26	–	84.0	–	83.6
27	–	100.8	–	99.6
28	6.87 (1H, d, $J = 7.0$)	132.2	6.56 (1H, s)	118.6
29	6.71 (1H, d, $J = 7.0$)	115.7	–	145.8
30	–	158.0	–	147.6
31	6.71 (1H, d, $J = 7.0$)	115.7	6.60 (1H, d, $J = 8.0$ Hz)	116.2
32	6.87 (1H, d, $J = 7.0$)	132.2	6.45 (1H, d, $J = 8.0$ Hz)	123.7
33	–	112.9	–	115.2
34	4.63 (2H, s)	61.3	4.78 (2H, s)	61.7

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

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