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Two new rhamnopyranosides of neolignans from *Sanguisorba officinalis*

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Two new rhamnopyranosides of neolignans, (7*S*,8*R*)-4,9,5′,9′-tetrahydroxy-3,3′-dimethoxy-8-*O*-4′-neolignan-7-*O*-α-L-rhamnopyranoside (**1**) and (7*S*,8*R*)-4,9,9′-trihydroxy-3,3′,5′-trimethoxy-8-*O*-4′-neolignan-7-*O*-α-L-rhamnopyranoside (**2**), together with a known compound (7*S*,8*R*)-4,7,9,9′-tetrahydroxy-3,3′-dimethoxy-8-*O*-4′-neolignan (**3**), were isolated from the 80% EtOH extract of the roots of *Sanguisorba officinalis*. Their structures were characterized by spectroscopic analysis including 1D NMR, 2D NMR, and HR-ESI-MS, and chemical method.

Keywords: *Sanguisorba officinalis*; Rosaceae; neolignans

1. Introduction

Sanguisorba officinalis L. (Rosaceae), a perennial plant, distributes widely in the northern districts of China [1]. Its roots have traditionally valuable hemostatic, analgesic, and astringent properties [2]. In China, Korea, and Japan, this plant has been used for the treatment of inflammatory and metabolic disease such as diarrhea, chronic intestinal infections, duodenal ulcers, and bleeding [3]. Previous studies reported the isolation of triterpenoids, triterpenoid glycosides, and a series of hydrolysable tannins which were reported as characteristic constituents of *S. officinalis* and are considered to be partially responsible for the therapeutic effects of this herbal drug [4–6]. In our investigation on the components of this titled plant, two new rhamnopyranosides of neolignans, (7*S*,8*R*)-4,9,5′,9′-tetrahydroxy-3,3′-dimethoxy-8-*O*-4′-neolignan-7-*O*-α-L-rhamnopyranoside (**1**) and (7*S*,8*R*)-4,9,9′-trihydroxy-3,3′,5′-trimethoxy-8-*O*-4′-neolignan-7-*O*-α-L-rhamnopyranoside (**2**), together with a known compound (7*S*,8*R*)-4,7,9,9′-tetrahydroxy-3,3′-dimethoxy-8-*O*-4′-neolignan (**3**), have been obtained (Figure 1). This paper deals with the isolation and structural elucidation of the new compounds by spectroscopic analysis and chemical method.

2. Results and discussion

The $CHCl_3$-soluble fraction of the 80% EtOH extract of *S. officinalis* was purified by repeated column chromatography (CC) to afford compounds **1**–**3**.

Compound **1** was obtained as a white amorphous powder. Its molecular formula was determined as $C_{26}H_{36}O_{12}$ by HR-ESI-MS at *m/z* 539.2129 $[M - H]^-$, possessing nine degrees of unsaturation. The ^1H and ^{13}C NMR spectra of **1** showed characteristic resonances for a neolignan

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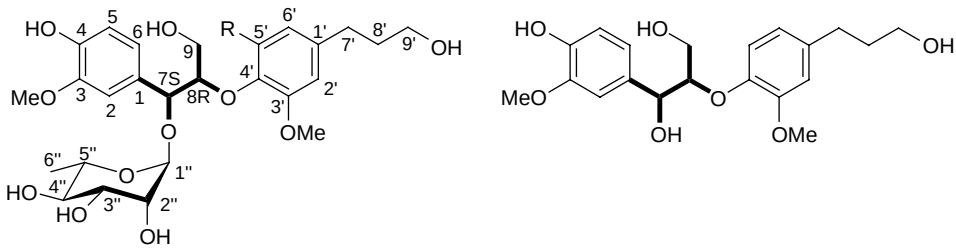

Figure 1. The structures of compounds **1**–**3**.

moiety and a hexose moiety (Table 1). Acidic hydrolysis of **1** with 2% HCl afforded L-rhamnose, which was identified by GC analysis of its trimethylsilyl imidazole derivative [7,8]. The ^{13}C NMR signals of C-3″ (δ_C 71.9) and C-5″ (δ_C 69.1) indicated the α-configurations of L-rhamnose unit (Table 1) [9].

Comparison of its ^{1}H and ^{13}C NMR spectral data of the aglycone of **1** with those of the known compound **3**, obtained from the same source, revealed that **1** and **3**

Table 1. ^{1}H and ^{13}C NMR spectral data of compounds **1** and **2** (^{1}H: 600 MHz; ^{13}C: 125 MHz, in CD_3OD).

	δ_H (*J* in Hz)		δ_C	
Position	**1**	**2**	**1**	**2**
1	–	–	134.2, s	134.4, s
2	7.06 (d, 1.8)	7.07 (d, 1.8)	111.3, d	111.6, d
3	–	–	147.9, s	147.7, s
4	–	–	146.5, s	146.8, s
5	6.72 (d, 8.0)	6.75 (d, 8.0)	115.2, d	115.5, d
6	6.80 (dd, 1.8, 8.0)	6.83 (dd, 1.8, 8.0)	120.5, d	120.6, d
7	4.82 (d, 5.1)	4.85 (d, 5.1)	73.9, t	73.9, t
8	4.18 (m)	4.20 (m)	87.0, t	87.1, t
9	3.30 (t, 4.8)	3.33 (t, 4.8)	61.7, t	61.9, t
1′	–	–	138.0, s	137.4, s
2′	6.24 (d, 1.8)	6.31 (d, 1.8)	115.0, d	104.6, d
3′	–	–	152.5, s	151.9, s
4′	–	–	138.6, s	136.8, s
5′	–	–	145.5, d	149.2, s
6′	6.12 (d, 1.8)	6.20 (d, 1.8)	107.6, d	106.1, d
7′	2.55 (t, 4.8)	2.59 (t, 4.8)	32.0, t	32.2, t
8′	1.80 (m)	1.82 (m)	32.6, t	32.7, t
9′	3.59 (t, 4.8)	3.61(t, 4.8)	67.0, t	66.7, t
1″	4.83 (d, 1.3)	4.80 (d, 1.3)	90.8, d	91.3, d
2″	3.67 (m)	3.65 (m)	72.5, d	72.7, d
3″	3.30 (m)	3.27 (m)	71.9, d	72.0, d
4″	3.30 (m)	3.32 (m)	73.7, d	73.9, d
5″	3.75 (m)	3.73 (m)	69.1, d	69.3, d
6″	1.18 (d, 6.0)	1.22 (d, 6.0)	18.5, d	18.8, d
OCH_3	3.82 (s)	3.83 (s)	56.1, q	56.3, q
OCH_3	3.78 (s)	3.80 (s)	56.2, q	56.5, q
OCH_3	–	3.73 (s)		54.9, q

possessed a similar skeleton [10]. The difference between them laid in the downfield shift of C-7 by 7.2 ppm and of C-5′ by 25.7 ppm, suggesting that the rhamnose unit and a hydroxy group were substituted at C-7 and C-5′, respectively. The structural feature was further confirmed by the HMBC correlation between the anomeric proton (δ_H 4.83, d, $J = 1.3$ Hz) of the hexose unit and C-7 (δ_C 73.9) of the aglycone (Figure 2). The small coupling constant ($J_{7,8} = 5.1$ Hz) in the ^{1}H NMR spectrum indicated a *erythro* configuration between H-7 and H-8. The negative Cotton effect at 240 nm ($\Delta\varepsilon$ −2.54), together with the clear NOESY correlations between H-8/H-2 and H-8/H-6 indicated the 7*S*,8*R*-configuration in **1** [11]. Thus, the structure of **1** is defined as (7*S*,8*R*)-4,9,5′,9′-tetrahydroxy-3,3′-dimethoxy-8-*O*-4′-neolignan-7-*O*-α-L-rhamnopyranoside.

Compound **2** was isolated as a white amorphous powder. Its molecular formula was determined as $C_{27}H_{38}O_{12}$ by HR-ESI-MS at *m/z* 553.2283 $[M - H]^-$. Inspection of its NMR spectral data revealed that **2** possessed a neolignan moiety and a hexose moiety (Table 1). Comparison of the ^{13}C NMR spectrum of **2** with that of **1** (Table 1) indicated the presence of one more methoxyl in compound **2**, which was linked to C-5′ by the HMBC correlation between OCH_3 (δ_H 3.73, s) and C-5′ (δ_C 149.2; Figure 2). Similarly, a small coupling constant ($J_{7,8} = 5.1$ Hz) in the ^{1}H NMR spectrum and clear NOE correlations between H-8/H-2 and H-8/H-6 were observed. The CD spectrum of **2** also showed a negative Cotton effect at 240 nm ($\Delta\varepsilon$ −2.36). On the basis of the above evidence, the absolute configuration was determined to be 7*S*,8*R* [11]. Thus, the structure of **2** was established and named as (7*S*,8*R*)-4,9,9′-trihydroxy-3,3′,5′-trimethoxy-8-*O*-4′-neolignan-7-*O*-α-L-rhamnopyranoside.

3. Experimental

3.1 General experimental procedures

Melting points were determined on a XT-4 microscopic thermometer without correction. Optical rotations were measured on a Perkin-Elmer 341 polarimeter. IR spectra were recorded on a Nicolet Magna FT-IR 750 spectrophotometer using KBr disks. NMR spectra were recorded on Bruker AM-300, Bruker AM-400, and Varian Inova NMR spectrometers. The chemical shift (δ) values are given in ppm with TMS as internal standard, and coupling constants (J) are in Hz. FAB-MS and HR-ESI-MS spectra were recorded on a VG AutoSpec-3000 mass spectrometer. Column chromatographic separations were carried out using silica gel (200–300 mesh and H60, Qingdao Haiyang Chemical Group Corporation, Qingdao, China), MCI gel CHP20P (75–150 μm, Mitsubishi Chemical Industries, Tokyo, Japan), and Sephadex LH-20 (Pharmacia Biotech AB, Uppsala, Sweden) as packing material. TLC was carried out on

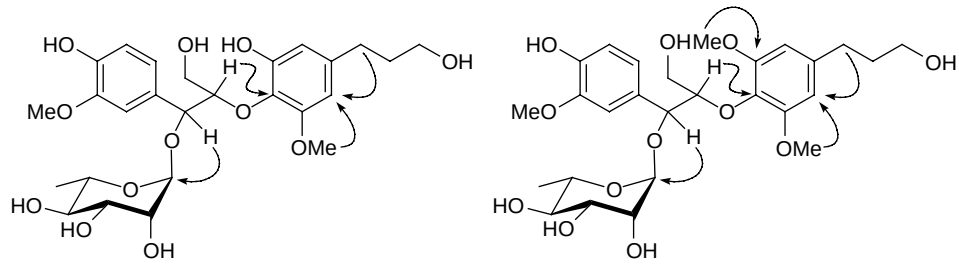

Figure 2. Key HMBC (↷) correlations of compounds **1** and **2**.

precoated silica gel GF254 plates (Yantai Chemical Industries, Yantai, China), and the TLC spots were viewed at 254 nm and visualized using 5% sulfuric acid in alcohol containing 10 mg/ml of vanillin. Analytical HPLC was carried out on a Waters 2690 instrument with a 996 photodiode array detector (PAD) coupled with an Alltech ELSD 2000 detector. Semipreparative and preparative HPLC were carry out on a Varian SD1 instrument with a 320 single-wave detector. Their chromatographic separations were carried out on C-18 columns (250 × 10 mm, 5 μm, Waters; 220 × 25 mm, 10 μm, respectively, Merck, Darmstadt, Germany), using a gradient solvent system comprising H_2O and MeCN, with a flow rate of 3.0 and 15.0 ml/min, respectively.

3.2 Plant material

The dried roots of *S. officinalis* were collected in the suburb of Qujing, Yunnan Province of China, in October 2010 and identified by one of the authors (J.G. Chen). A voucher specimen (20101001) has been deposited in the Herbarium of the College of Biological Resources and Environment Science, Qujing Normal University, Qujing, Yunnan Province, China.

3.3 Extraction and isolation

The roots (5 kg) of *S. officinalis* were cut into small pieces and ground, and then extracted with 80% EtOH (10 liters × 3). After removal of EtOH under reduced pressure, the aqueous brownish syrup (2 liters) was partitioned successively with petroleum ether, $CHCl_3$, and EtOAc. Concentration of the solvent afforded petroleum ether extract (51 g), $CHCl_3$ extract (81 g), and EtOAc extract (143 g). The $CHCl_3$ extract (81 g) was chromatographed over silica gel column, eluting with a $CHCl_3$–MeOH gradient to afford 80 fractions (F1–F80). Fractions F17–F25 (A) (5.3 g) were permeated through Sephadex LH-20 using a MeOH–CH_3Cl (1:1) system to give 30 subfractions A1–A30. Fractions A10–A15 (214 mg) were further purified with silica gel chromatography eluted with CH_3Cl–MeOH (95:5 → 1:1) to afford **3** (33 mg). Fractions F41–F55 (3.2 g) were further purified by repeated CC over Sephadex LH-20 ($CHCl_3$–MeOH, 1:1, and MeOH), silica gel chromatography eluted with $CHCl_3$–MeOH (8:2) and then preparative HPLC (MeOH–H_2O, from 50% to 75%), to obtain **1** (22 mg; 23.35 min) and **2** (29 mg; 24.60 min).

3.3.1 (7S,8R)-4,9,5′,9′-Tetrahydroxy-3,3′-dimethoxy-8-O-4′-neolignan-7-O-α-L-rhamnopyranoside (1)

A white amorphous powder; $C_{26}H_{36}O_{12}$; m.p. 188–190°C; $[\alpha]_D^{22}$ −66.48 (*c* 0.26, MeOH); UV (MeOH) λ_{max} (log ε) 204 (4.05), 279 (3.66) nm; CD (MeOH): $\Delta\varepsilon_{240\,nm}$ −2.54; IR (KBr) ν_{max} 3420, 1605, 1515 cm^{-1}; ^1H and ^{13}C NMR spectral data: see Table 1; FAB-MS (neg.): *m/z* 539 $[M - H]^-$; HR-ESI-MS (neg.): *m/z* 539.2126 $[M - H]^-$ (calculated for $C_{26}H_{35}O_{12}$, 539.2129).

3.3.2 (7S,8R)-4,9,9′-Trihydroxy-3,3′,5′-trimethoxy-8-O-4′-neolignan-7-O-α-L-rhamnopyranoside (2)

A white amorphous powder; $C_{27}H_{38}O_{12}$; m.p. 197–199°C; $[\alpha]_D^{22}$ −73.55 (*c* 0.41, MeOH); UV (MeOH) λ_{max} (log ε) 205 (5.01), 280 (4.23) nm; CD (MeOH): $\Delta\varepsilon$ 240 nm −2.36; IR (KBr) ν_{max} 3418, 1595, 1511 cm^{-1}; ^1H and ^{13}C NMR spectral data: see Table 1; FAB-MS (neg.): *m/z* 553 $[M - H]^-$; HR-ESI-MS (neg.): *m/z* 553.2283 $[M - H]^-$ (calculated for $C_{27}H_{37}O_{12}$, 553.2285).

3.4 Sugar analysis of compounds 1 and 2

The solutions of those sugar parts obtained as described above in pyridine (2 ml) were

added to L-cysteine methyl ester hydrochloride (1.5 mg) and were kept at 60°C for 1 h each. Then, trimethylsilyl imidazole (1.5 ml) was added to the reaction mixture and kept at 60°C for 30 min. The supernatant was subjected to GC analysis under the following conditions: column temperature: 180/280°C, programed increase: 3°C/min, carrier gas: N_2 (1 ml/min), injector and detector temperature: 250°C, injection volume: 4 μL, split ratio: 1/50. Configuration identification of L-rhamnose was carried out by comparing with its derivative's retention time [7,8]. Retention times in GC of standard L/D-rhamnose derivatives were 15.849/16.312 min. By comparing with the retention time of the authentic sugars in the form of derivatives under the same condition, the sugar moieties of compounds **1** and **2** were determined to be L-rhamnose. All chemical reagents and standard sugars were purchased from Sigma-Aldrich Corporation (St Louis, MI, USA).

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