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TWO NEW LINEAR FURANOCOUMARIN GLYCOSIDES FROM *Angelica dahurica*

Xiaodong Jia, Xu Feng, Xingzeng Zhao, Yunfa Dong, Youyi Zhao, and Hao Sun

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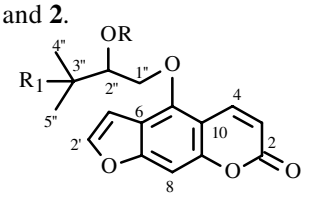
*Two new linear furanocoumarin glycosides, tert-*O-β-*D-apiofuranosyl-(1→6)-*O-β-*D-glucopyranosyl-oxypeucedanin hydrate (**1**) and sec-*O-β-*D-apiofuranosyl-(1→6)-*O-β-*D-glucopyranosyl-oxypeucedanin hydrate (**2**), were isolated from the fresh roots of* Angelica dahurica. *The structures of new compounds were elucidated on the basis of spectral analysis.*

Key words: *Angelica dahurica*, linear furanocoumarin glycosides, structure elucidate.

The roots of *Angelica dahurica* (Fisch. ex Hoffm.) Benth. et Hook. f. ex Franch. et Sav. cv. Hangbaizhi (Umbelliferae) are important Chinese traditional medicines. They have been widely used for the treatment of headache caused by cold, toothache, coryza, vitiligo, acne, freckle, etc. Previous phytochemical studies on this plant had only led to the isolation of about 20 coumarins and 3 coumarin glycosides [1-7]. Our research was focused on the water-soluble constituents from fresh materials of this plant and led to the isolation of 29 glycosides. We had already reported the isolation of a linear coumarin glycoside and a new neolignan glycoside from this plant in our previous articles. Herein, we describe the isolation and structure elucidation of two new linear furanocoumarin glycosides **1** and **2**.



1, 2

1: R = H, R_1 = Glc-Api

2: R = Glc-Api, R_1 = H

Compound **1** was obtained as a white amorphous powder, $[\alpha]_D^{20.8}$ –81.5° (*c* 0.0065, MeOH:H_2O=40:60). Its molecular formula $C_{27}H_{34}O_{15}$ was determined on the basis of its ESI-MS (621 $[M+Na]^+$) and confirmed by ^1H NMR and ^{13}C NMR data. Detailed analysis of its ^1H NMR, ^{13}C NMR, COSY, HSQC, and HMBC spectra indicated the presence of linear furanocoumarin glucoside and 2,3-dioxygenated isopentyloxy structural unit; see Table 1.

The ^1H NMR spectrum of **1** was measured in pyridine-d_5. In the aromatic proton region, there were a pair of doublets at δ 6.25 and 8.28 ppm (d, J = 9.5 Hz), which were identified as the signals of C-3-H and C-4-H of the α-pyrone ring system. A distinct singlet at δ 7.20 ppm was assigned to a single aromatic proton in the coumarin ring. A pair of doublets at δ 7.74 and 7.37 ppm (d, J = 2.4 Hz), which were identical with the signals of C-2′-H and C-3′-H, indicated that **1** was a linear furanocoumarin. Acid hydrolysis (view Experimental) of **1** together with two doublets at δ 5.13 ppm (d, J = 7.7 Hz) and 5.71 ppm (d, J = 2.3 Hz) in ^1H NMR spectra as well as signals in the ^{13}C NMR spectra indicated the presence of a β-D-glucose unit and a β-D-apiose unit.

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TABLE 1. ^{1}H NMR, ^{13}C NMR and HMBC Spectral Data for Compounds **1** and **2** in C_5D_5N [δ (ppm), 500 MHz for ^{1}H and 125 MHz for ^{13}C NMR

C atom	**1**			C atom	**2**		
	δ_H	δ_C	HMBC		δ_H	δ_C	HMBC
2	6.25 (d, 9.5)	160.86		2		161.10	2,10
3	8.28 (d, 9.5)	112.65	2,10	3	6.23 (d, 9.5)	112.83	2,5,8,9
4		139.95	2,5,8,9	4	8.31 (d, 9.5)	140.98	
5		149.70		5		149.69	
6		114.38		6		113.38	
7	7.20 (s)	158.55		7		158.51	
8		93.89	6,7,9,3′	8	7.19 (s)	93.60	6,7,9,3′
9		153.24		9		153.30	
10	7.74 (d, 2.4)	107.50		10		107.25	
2′	7.37 (d, 2.4)	145.55	6,7,3′	2′	7.72 (d, 2.3)	145.40	6,7,3′
3′	5.23 (dd, 2.1, 9.6)	106.12	6,7,2′	3′	7.34 (d, 2.3)	106.56	6,7,2′
1_a″	4.76 (dd, 5.0, 9.6)	75.77	5,3″	1_a″	5.00 (dd, 3.1, 9.8)	73.60	5,3″
1_b″	4.71 (dd, 2.1, 5.0)		5,2″,3″	1_b″	4.80 (dd, 6.5, 9.8)		5,2″,3″
2″		77.91	4″,5″	2″	4.40 (dd, 3.1, 6.5)	87.40	4″,5″, g-1
3″	1.69 (s)	79.60		3″		72.01	
4″	1.68 (s)	24.65	2″,3″	4″	1.64 (s)	26.40	2″,3″
5″	5.13 (d, 7.7)	22.48	2″,3″	5″	1.58 (s)	26.30	2″,3″
G-1	3.95 (m)	98.71	3″ ,g-2	G-1	5.19 (d, 7.7)	105.58	2″ ,g-2
2	4.18 (m)	75.26	g-1,g-3	2	3.94 (m)	75.30	g-1,g-3
3	3.94 (m)	78.76	g-4, g-5	3	4.20 (m)	78.76	g-4, g-5
4	4.08 (m)	72.08	g-3, g-5	4	3.99 (m)	72.08	g-3, g-5
5	4.68 (dd, 2.2, 11.5)	76.80	g-4, g-6	5	4.08 (m)	76.80	g-4, g-6
6_a	4.08 (dd, 5.2, 11.5)	69.19	g-5	6_a	4.70 (dd, 2.2, 11.5)	69.19	g-5
6_b	5.71 (d, 2.3)		g-5	6_b	4.09 (dd, 5.1, 11.5)		g-5
A-1	4.37 (m)	111.21	a-2, g-6	A-1	5.72 (d, 2.3)	111.21	a-2, g-6
2		76.46	a-1, a-3	2	4.37 (m)	76.46	a-1, a-3
3	4.32 (m)	80.41		3		80.41	
4_a	4.55 (m)	75.13	a-3	4_a	4.32 (m)	75.13	a-3
4_b	4.18 (m)			4_b	4.57 (m)		
5		65.78	a-3	5	4.20 (m)	65.78	a-3

In the aromatic proton region of the ^{13}C NMR spectrum, the signal at δ 160.86 can be easily assigned to C-2. We can also see the following structural segments: 6 signals of a glucoside, 5 signals of an apioside, and 5 signals of the 2,3-dioxygenated isopentyloxy structural unit.

All chemical shifts of the carbons that were connected with the hydrogen proton were ascertained through HSQC, including C-3, C-4, C-2′, C-3′, singlet proton, carbons in the 2,3-dioxygenated isopentyloxy structural unit, and C-1 and C-6 in the sugar skeleton.

By analysis of the above spectra the chemical shifts of C-2, 3, 4 in the α-pyrone ring system were ascertained. During our investigation of HMBC, such relations were assured: δ 107.50 ppm was assigned to C-10 from the correlations of C-3-H to C-2 and δ 107.50 ppm; the position of the glucosyl unit was ascribed to C-3″ from the correlation between the glucoside-1-H and C-3″ signal. The apiosyl unit was assigned to glucosyl-6-C from the chemical downshift of glucosyl-6-C and the observed correlation between the apiosyl anomeric proton signal and the glucosyl-6-C in the HMBC spectrum. The 2,3-dioxygenated isopentyloxy structural unit was assigned to C-5 from the weak correlation between C-5 and H-1″.

Therefore, compound **1** was characterized as a new compound, tert-*O*-β-D-apiofuranosyl-(1→6)-*O*-β-D-glucopyranosyl-oxypeucedanin hydrate.

Compound **2** was obtained as a white amorphous powder, mp 162-163°C, $[\alpha]_D^{21.2}$ −1.59° (*c* 0.085, MeOH : H_2O 40 : 60). Its molecular formula $C_{27}H_{34}O_{15}$ was determined on the basis of its ESI-MS (621 [M+Na]+) and confirmed by ^{1}H NMR and ^{13}C NMR data. Detailed analysis of its ^{1}H NMR, ^{13}C NMR, COSY, HSQC, and HMBC spectra indicated that compound **2** has a structure similar to **1**; see Table 1.

Differences were observed in the chemical shifts of C-2″, C-3″, and glucoside-C-1 of **2** with respect to **1**, suggesting

that the position of the sugar moieties substituted in the 2,3-dioxygenated isopentyloxy structural unit was the point of difference between the two compounds. The position of the sugar moieties was ascribed to C-2″ instead of C-3″ by analysis of the HMBC spectrum. The structure was determined in the same way as for compound **1**.

Therefore, compound **2** was assigned to the new compound sec-*O*-*β*-D-apiofuranosyl-(1→6)-*O*-*β*-D-glucopyranosyl-oxypeucedanin hydrate.

EXPERIMENTAL

General Methods. ^{1}H NMR, ^{13}C NMR and 2D NMR spectra: Bruker ALF 500 spectrometers operating at 500 MHz; ESI-MS: Agilent 1100 LC/MSD SL; JASCO P-1020 Optical Rotation Apparatus.

Plant Material. Fresh roots, collected from Jiangsu province of PR China in 2004, were taxonomically identified by Prof. Chang-Qi Yuan. A voucher specimen was deposited in Nanjing Botanical Garden Mem. Sun Yat-Sen, Nanjing, Jiangsu, China.

Extraction and Purification. The fresh roots (38.0 kg) were extracted with ethanol at room temperature. After removal of ethanol, the water suspension was re-extracted with petroleum ether, EtOAc. The obtained aqueous portion was subjected to HP-20 (H_2O→MeOH). The methanol elute (70.0 g) was chromatographed on silica gel [$CHCl_3$: MeOH:H_2O (10:1:0.0→17:3:0.2→4:1:0.1→7:3:0.5)] to furnish four fractions (fractions 1 to 4). Fraction 3 was subjected to ODS column and then Sephadex LH-20 to afford compound **1** (13.0 mg) and **2** (14.0 mg).

Acid Hydrolysis of Compounds. Samples (5 mg each) were refluxed with 2 N H_2SO_4 (5 mL) at 80°C for 4 h. After neutralization with $Ba(OH)_2$ and extraction with $CHCl_3$, the aqueous supernatant separated from the $CHCl_3$-layer was dried and dissolved in DMSO (2 mL) and then extracted with *n*-hexane (2 mL). Reactions of the solution with a hexamethyldisilazane : trimethylchlorosilane (2 : 1) mixture with shaking for 15 min yielded the corresponding derivatives. After deposition for 1 h, the upper solution was detected by GC, and compared with authentic sample derivatives under the same conditions.

Shimadzu GC-2010 with ZB-WAX (30 mm × 0.25 mm × 0.25 mm); SPL temperature: 225°C; column temperature: 0-2 min 160°C, then raised to 190°C with 2.5°C per min; Split ratio (1 : 50); total flow: 50.0 mL/min; FID temperature: 250°C.

Compound 1, tert-*O*-*β*-D-apiofuranosyl-(1→6)-*O*-*β*-D-glucopyranosyl-oxypeucedanin hydrate, white amorphous powder, $[\alpha]_D^{20.8}$ −81.5° (*c* 0.0065, MeOH:H_2O 40:60).

ESI-MS *m/z*: 621 $[M+Na]^+$ indicates that the molecular weight is 598; combined with the data of ^{1}H NMR and ^{13}C NMR, the molecular formula can be deduced to $C_{27}H_{34}O_{15}$.

Compound 2, sec-*O*-*β*-D-apiofuranosyl-(1→6)-*O*-*β*-D-glucopyranosyl-oxypeucedanin hydrate, white amorphous powder, mp 162-163°C, $[\alpha]_D^{21.2}$ −1.59° (*c* 0.085, MeOH : H_2O 40:60); ESI-MS *m/z*: 621 $[M+Na]^+$ indicate the molecular weight is 598; combined with the data of ^{1}H NMR and ^{13}C NMR, the molecular formula can be deduced to $C_{27}H_{34}O_{15}$.

For ^{1}H NMR and ^{13}C NMR as well as HMBC spectral data; see Table 1.

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