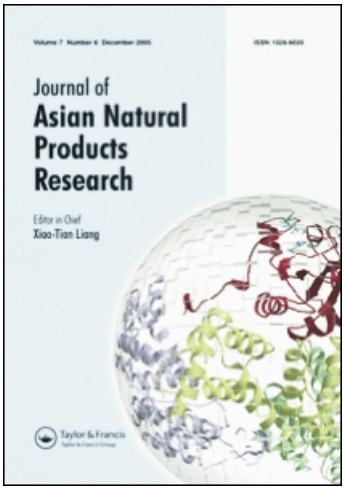

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Two new compounds from *Helichrysum arenarium* (L.)

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Two new compounds from *Helichrysum arenarium* (L.)

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Two new compounds were isolated from the whole plant of *Helichrysum arenarium* (L.) Moench. By means of spectroscopic data (IR, UV, 1D and 2D NMR, HR-MS, ESI-MS, and NOESY) and chemical evidence, the structures were established as 6,7-dimethoxy-4-hydroxy-1-naphthoic acid (**1**) and (*Z*)-5-hydroxy-7-methoxy-4-[3-methyl-4-(*O*-β-D-xylopyranosyl)but-2-enyl]isobenzofuran-1(3H)-one (**2**).

Keywords: *Helichrysum arenarium* (L.); Compositae; naphthoic acid; isobenzofuran

1. Introduction

Helichrysum arenarium (L.) Moench (Compositae) is distributed mainly in Xinjiang Uygur Autonomous Region of China, Mongolia, Europe, and Russia. It is a medicinal plant that has been long known in European traditional medicine as a cholagogue, choleretic, hepatoprotective, and detoxifying agents [1,2]. It also has activities of antioxidant, anti-bacteria on the basis of modern pharmacological research [3,4], and previous phytochemical study on this plant revealed the presence of flavonoids and phenolic acids [1]. In this paper, we report the isolation and structural elucidation of two new compounds from the titled whole herb.

2. Results and discussion

Compound **1** was obtained as white needles, mp 182–184°C. It showed positive reactions with $FeCl_3$ and bromocresol green reagent. The quasi-molecular ion at *m/z* 271.0578 $[M+Na]^+$ in the HR-ESI-MS spectrum indicated the molecular formula to be $C_{13}H_{12}O_5$. The ^1H NMR spectrum of **1** showed the presence of two active proton singlets at δ 12.46 (1H, br s), 9.13 (1H, br s), two aromatic proton singlets at δ 7.19 (1H, s), 7.42 (1H, s), two *ortho*-coupled proton signals at δ 6.84 (1H, d, $J = 8.4$ Hz), 7.43 (1H, d, $J = 8.4$ Hz), and two methoxyl groups at δ 3.79 (6H, s, $-OCH_3 \times 2$). The ^{13}C NMR spectrum of **1** had 13 carbon signals among which, except for one carboxyl carbon at δ 167.2 and two methoxyl carbons at δ 55.6, 56.1 mentioned above, 10 aromatic carbons were observed at δ 151.1, 147.5, 147.3, 140.3, 123.6, 121.7, 120.5, 115.1, 112.8, and 106.9, which were considered to be a naphthalene nucleus. By analysis of the ^{13}C NMR spectral data [5], the signals at δ 147.5 and 147.3 were two β carbon *ortho*-substituted by two methoxyl groups, which had correlations with two aromatic proton singlets at δ 7.19 (H-5) and 7.42 (H-8) in the NOESY spectrum of **1** (Figure 2). The signals at δ 151.1 and 140.3 were suggested to be two α-C (C-1 and C-4) connected the carboxyl group and the hydroxyl group, respectively, based on the ^1H NMR spectral data and the HMBC correlations (Table 1). The locations

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Table 1. ^{1}H and ^{13}C NMR spectral data of compounds **1** and **2** (300 MHz for ^{1}H and 75 MHz for ^{13}C in DMSO-d_6, δ values).

Compound **1**					Compound **2**				
No.	δ_C	δ_H	HMBC	NOESY	No.	δ_C	δ_H	HMBC	NOESY
1	140.3				1	168.2			
2	123.6	7.43 (1H, d, 8.4 Hz)	—COOH, 4-C	3-H	3	67.4	5.16 (2H, s)	1, 4, 7a-C	1′-H
3	115.1	6.84 (1H, d, 8.4 Hz)	4a-C	2-H	3a	149.9			
4	151.1				4	112.7			
4a	121.7[a]				5	162.0			
5	106.9	7.42 (1H, s)	4-C		6	98.9	6.50 (1H, s)	4, 7a-C	7-OCH_3
6	147.5[a]				7	157.5			
7	147.3[a]				7a	103.4			
8	112.8	7.19 (1H, s)	1-C		1′	23.5	3.20 (2H, d, 6.9 Hz)	3a, 5, 3′-C	3, 2′, 4′-H
8a	120.5[a]				2′	125.7	5.33 (1H, t, 6.9 Hz)	4, 4′, 5′-C	1′, 5′-H
C_1 —COOH	167.2	12.46 (br s)			3′	132.1			
C_4 —OH		9.13 (br s)			4′	66.4	4.23 (2H, s)	2′, 5′-C	1′, 5′-H
C_6 —OCH_3	56.1[a]	3.79 (3H, s)	6-C	5-H	5′	21.4	1.70 (3H, s)	2′, 4′-C	2′, 4′-H
C_7 —OCH_3	55.6[a]	3.79 (3H, s)	7-C	8-H	1″	102.6	4.12 (1H, d, 7.5 Hz)	4′-C	
					2″	73.3			
					3″	76.7			
					4″	69.7			
					5″	65.8			
					5-OH		10.62 (1H, br s)		
					7-OCH_3	55.5	3.80 (3H, s)	7-C	6-H

[a] Data may be exchangeable.

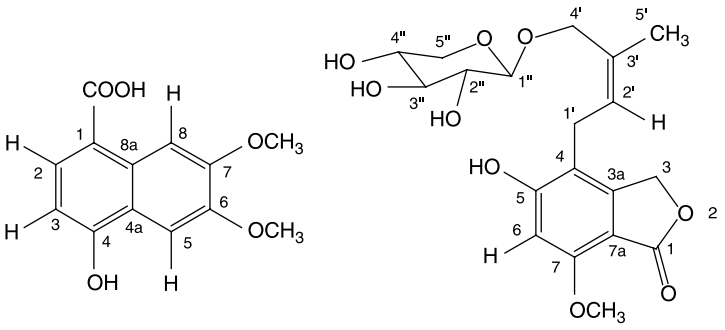

Figure 1. Structures of compounds **1** and **2**.

of 1-COOH and 4-OH were confirmed due to the signals at δ 7.43 (H-2) had long-range correlations with —COOH and C-4 in the HMBC experiment (Figure 2). The HMBC spectrum also showed the long-range correlations between H-3 and C-4_a, H-5 and C-4, and H-8 and C-1. With the above data, the structure of **1** was established as 6,7-dimethoxy-4-hydroxy-1-naphthoic acid (Figure 1).

Compound **2** was obtained as white needles, mp 175–177°C. It showed positive reactions with $FeCl_3$ and the Molish reagent. The sugar was identified as xylose by acid hydrolysis and co-TLC with an authentic sample. The molecular formula was analyzed as $C_{19}H_{24}O_9$ from its quasi-molecular ion at *m/z* 419.1315 $[M+Na]^+$ in the HR-ESI-MS spectrum and by ^1H and ^{13}C NMR spectral data. The IR spectrum of **2** indicated the presence of hydroxyl (3397 cm^{-1}), ester carbonyl (1702 cm^{-1}), and benzene ring (1602 and 1533 cm^{-1}). ^1H NMR spectrum of **2** showed an active proton at δ 10.62 (1H, br s), an aromatic proton at δ 6.50 (1H, s), a methoxyl group at δ 3.80 (3H, s), a methyl group at δ 1.70 (3H, s), two oxygen-bearing methylene singlets at δ 4.23 (2H, s), 5.16 (2H, s), and a coupled group of *ortho*-coupled proton signals at δ 5.33 (1H, t, $J = 6.9$ Hz), 3.20 (2H, d, $J = 6.9$ Hz). Additionally, the anomeric proton of xylose was observed at δ 4.12 (1H, d, $J = 7.5$), so the anomeric configuration of the xylose was β-orientation.

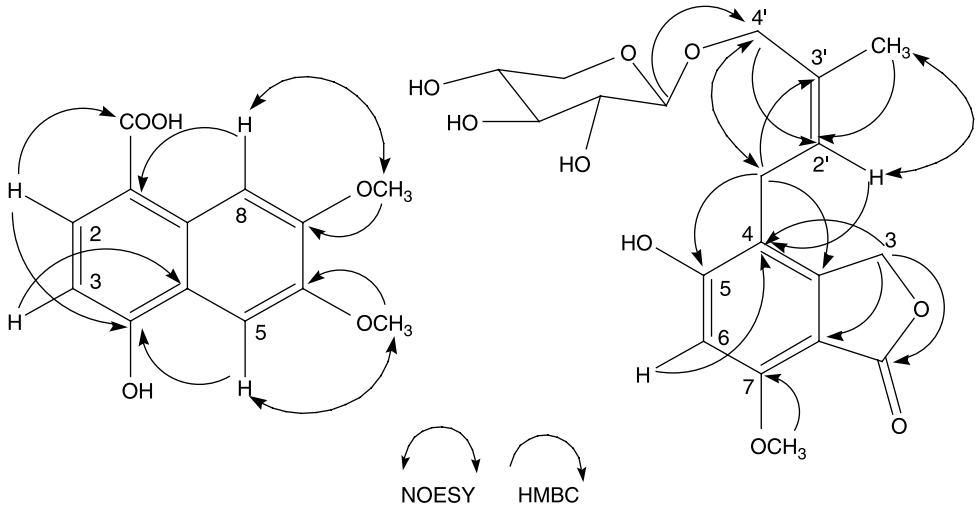

Figure 2. Key HMBC and NOESY correlations of compounds **1** and **2**.

In the ^{13}C NMR spectrum of **2** exhibited 19 carbon signals, including a methoxy group (δ 55.5), a ester carbonyl (δ 168.2), two oxygen-bearing methylene (δ 66.4, 67.4), a methylene (δ 23.5), six aromatic and two double bond carbons at δ 149.9, 112.7, 162.0, 98.9, 157.5, 103.4, 132.1, 125.7, and a methyl group (δ 21.4) except for a set of xylosyl group, their corresponding carbon signals were assigned due to the HMBC correlations (Table 1). In the HMBC experiment (Figure 2), the long-range correlations between the anomeric proton of xylose at δ 4.12 (H-1″) and C-4′, H-4′ and C-2′, H-5′ and C-2′, and H-1′ and C-3′ were observed. It displayed the presence of isopentenyl-connected xylose moiety in structure **2**. Furthermore, the configuration of the isopentenyl group was identified as *Z* due to the NOE correlations between H-5′ and H-2′, H-1′ and H-4′ in the NOESY spectrum (Figure 2).

The remaining aromatic carbon signals at δ 162.0 (C-5), 157.5 (C-7), 149.9 (C-3a), 112.7 (C-4), 103.4 (C-7a), and 98.9 (C-6) should be five-substituted benzene ring based on the ^{1}H NMR spectral data. The HMBC correlations between the proton signal at δ 3.80 ($-OCH_3$) and C-7, H-6 and C-4, and H-1′ and C-5 were observed (Figure 2). Remaining ester carbonyl (δ 168.2) and an oxygen-bearing methylene should form a five-numbered lactone, which connected C-3a and 7a of the benzene ring due to the long-range correlations of oxygen-bearing methylene signal at δ 5.16 (H-3) with C-4, C-7a, and C-1. Therefore, the structure of **2** was established as (*Z*)-5-hydroxy-7-methoxy-4-[3-methyl-4-(*O*-β-D-xylopyranosyl)but-2-enyl]isobenzofuran-1(3H)-one (Figure 1).

3. Experimental

3.1 General experimental procedures

Melting points were determined on Yanaco MP-S3 melting point apparatus and are uncorrected. The optical rotation was measured on Perkin-Elmer 241 polarimeter. The UV spectra were recorded on a Shimadzu UV-260 UV–VIS instrument. IR spectra were recorded on a Bruker IFS-55 instrument as KBr pellets. NMR spectra were recorded with a Bruker ARX-300 or Bruker ARX-600. ESI-MS was performed on Finnigan LCQ mass spectrometer. HR-ESI-MS data were performed on QSTARLCQ mass spectrometer.

3.2 Plant material

The plant material of *H. arenarium* (L.) Moench was collected in August 2006, in Xinjiang Province, China, and identified by Prof. Qishi Sun (Drug Inspection Institute). A voucher specimen (No. 20060820) is deposited in Research Department of Natural Medicine, Shenyang Pharmaceutical University.

3.3 Extraction and isolation

Dried whole plant (6.5 kg) of *H. arenarium* was extracted with 70% ethanol. The extract was concentrated *in vacuo*, then partitioned with petroleum ether, $CHCl_3$, EtOAc, and *n*-BuOH successively. The EtOAc extract (28 g) was subjected to column chromatography on silica gel gradiently eluted with $CHCl_3$–MeOH to give fraction 3 (100:1) and fraction 13 (100:6). Fraction 3 was rechromatographed on silica gel gradiently eluted with $CHCl_3$–EtOAc to give subfraction 4 (100:7). Subfractions 4 and 13 were purified on Sephadex LH-20 with $CHCl_3$–MeOH (1:1) to yield **1** (31.0 mg) and **2** (42.0 mg), respectively.

3.3.1 Compound **1**

White needles (MeOH); mp 182–184°C; UV (CH_3OH) λ_{max} (log ε): 250 (2.40), 295 (3.22) nm; IR (KBr) ν_{max} (cm^{-1}): 3428, 2940, 1680, 1597, 1524, 1432, 1283, 1206, 1117, 763; ^{1}H and ^{13}C NMR spectral data, see Table 1; HR-ESI-MS: *m/z* 271.0578 (calcd for $C_{13}H_{12}O_5Na$, 271.0582); ESI-MS *m/z* 271 $[M+Na]^+$.

3.3.2 Compound **2**

White needles ($CHCl_3$–MeOH); mp 175–177°C; $[\alpha]_D^{20}$ − 5.777 ($c = 0.1$, CH_3CH_2OH); UV (CH_3CH_2OH) λ_{max} (log ε): 226 (2.00), 260 (0.78), 296 (0.40) nm; IR (KBr) ν_{max} (cm^{-1}): 3397, 2917, 1738, 1702, 1602, 1533, 1448, 1356, 1226, 1060, 839; ^1H and ^{13}C NMR spectral data, see Table 1; HR-ESI-MS: *m/z* 419.1315 (calcd for $C_{19}H_{24}O_9Na$, 419.1318); ESI-MS *m/z* 419 $[M+Na]^+$, 815 $[2M+Na]^+$, 395 $[M-H]^-$, 791 $[2M-H]^-$.

3.4 Acid hydrolysis of compound **2**

Compound **2** (5 mg) was refluxed in a mixture of concentrated HCl–H_2O–EtOH (2:1:2) (10 ml) on a water bath for 2 h. The hydrolysate was partitioned between EtOAc and H_2O, and the aqueous layer was compared with authentic samples on TLC with silica gel [$CHCl_3$–CH_3OH–H_2O (9:6:1), lower phase], which showed the sugar was xylose.

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