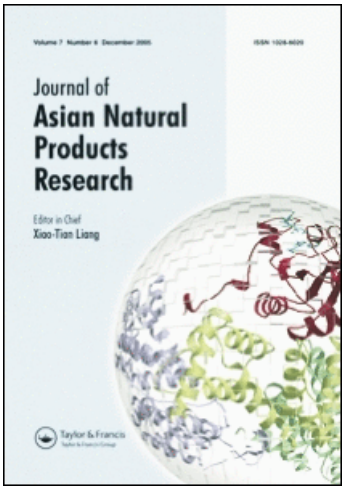

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New phthalide glycosides from *Helichrysum arenarium* (L.) Moench

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Two new prenylated phthalide glycosides **1** and **2** were isolated from the whole plant of *Helichrysum arenarium*, and their structures were elucidated on the basis of spectral data.

Keywords: *Helichrysum arenarium*; prenylated phthalide; arenophthalide

1. Introduction

Helichrysum arenarium, a well-known traditional Chinese medicine for the treatment of diabetes, is widely distributed in Xinjiang Uighur Autonomous Region, China [1]. The inflorescence of *H. arenarium* has been used as a traditional Chinese medicine for a long time based on its choleretic, hepatoprotective, and detoxifying activities. Previous studies on chemical constituents of *H. arenarium* showed the presence of flavonoids, coumarins, phthalides, terpenoids, and essential oils [2–6]. In our previous paper [7], we have reported nine flavonoids. The present paper deals with the isolation and structural elucidation of two new prenylated phthalide glycosides, named arenophthalide B (**1**) and arenophthalide C (**2**), which are *Z*/*E* isomeric compounds.

2. Results and discussion

Compound **1** (Figure 1) was obtained as plate crystals, and its molecular formula was established as $C_{19}H_{24}O_9$ on the basis of HR-FAB-MS at *m/z* 397.1491 $[M+H]^+$ (calcd for $C_{19}H_{25}O_9$, 397.1499). The UV absorption maxima at 226 and 260 nm indicated the presence of a benzene ring. The IR spectrum showed the presence of hydroxyl group (3394 cm^{-1}), carbonyl group (1703 cm^{-1}), and aromatic double bond group (1603 and 1545 cm^{-1}). The ^1H NMR spectrum coupled with HMQC experiment indicated the existence of one methoxyl at δ_H 3.87, one methyl at δ_H 1.79, three methylenes at δ_H 5.22, 4.35, 3.32, four methenyls at δ_H 4.24, 3.50, 3.30, 3.19, one alkenyl proton signal at δ_H 5.42, and one aromatic proton signal at δ_H 6.47. The *J*-modulated ^{13}C NMR spectrum displayed the signals of an ester carbonyl at δ_C 172.4, one methoxyl at δ_C 56.1, and a xylose moiety at δ_C 104.0 (C-1′), 75.0 (C-2′), 78.0 (C-3′), 71.3 (C-4′), 67.1 (C-5′). Six aromatic carbons at δ_C 114.5, 164.1, 99.5, 159.7, 105.0, 151.6, an ester carbonyl at δ_C 172.4, a methylene at δ_H 5.22, and the HMBC correlations between H-3 at δ_H 5.22 and C-1, C-5, C-9, C-4, C-8 have made it possible to assume that compound **1** had a

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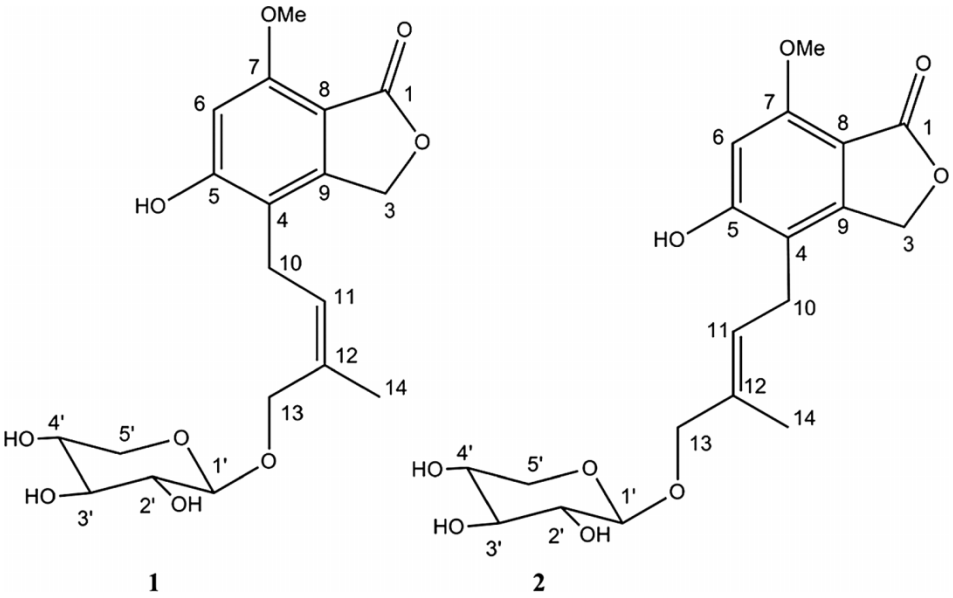

Figure 1. Structures of **1** and **2**.

phthalide skeleton. The other two methylenes at δ_H 4.35, 3.32, the alkenyl double bonds at δ_C 127.5, 133.7, and the methyl at δ_H 1.79 were indicated to be isoprene derivative because both of the HMBC correlations between the methyl at δ_H 1.79 and C-11, C-12, C-13 and between the methylene at δ_H 4.35 and C-11, C-12, C-14 were observed. The connectivity of the methylene at δ_H 3.32 to C-4 was explained by the HMBC correlations between H-10 and C-4, C-5, C-9. The location of xylose

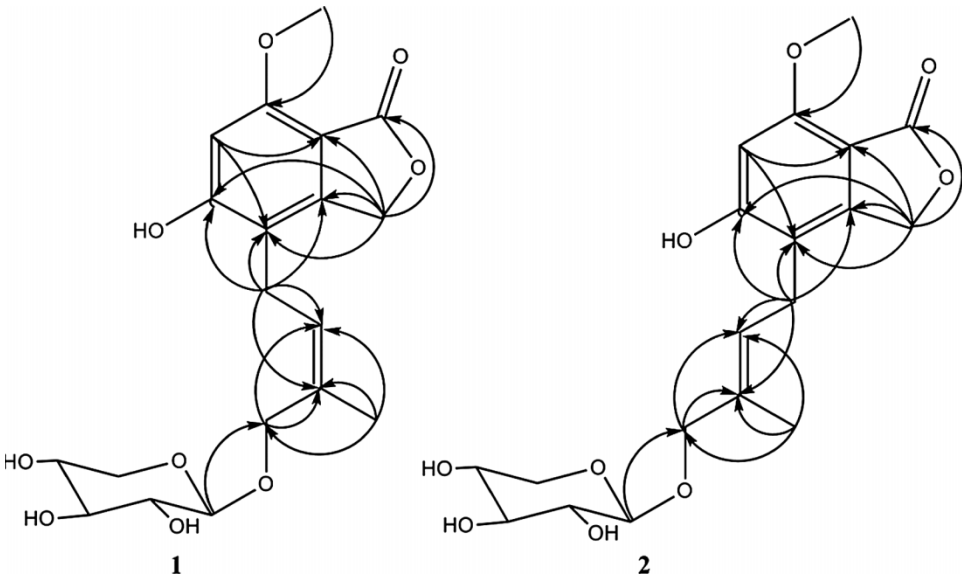

Figure 2. Key HMBC correlations of **1** and **2**.

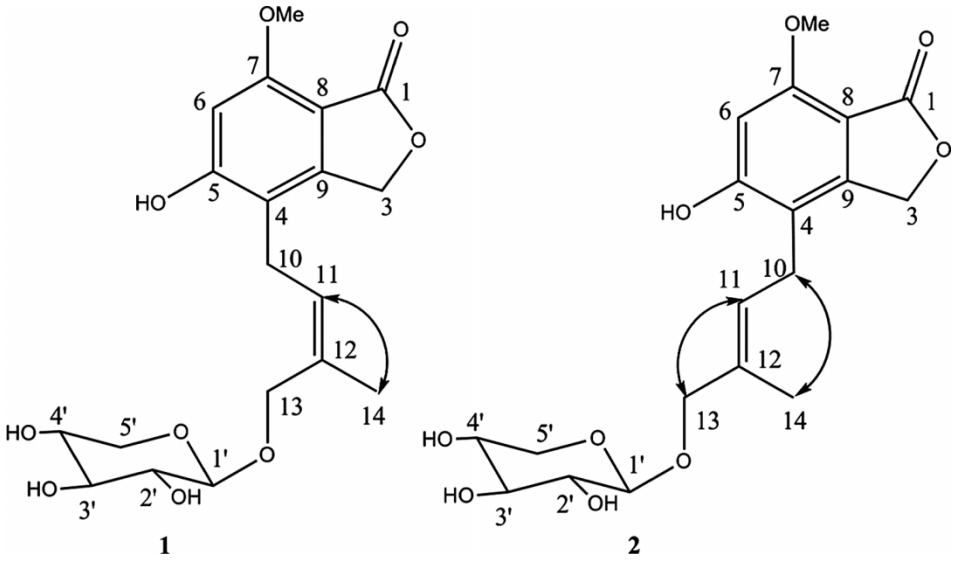

Figure 3. Key NOESY correlations of **1** and **2**.

moiety was assigned at C-13 from the HMBC correlation between H-1′ and C-13. Acid hydrolysis of compound **1** gave xylose as the sugar component, which was identified by comparison with authentic sample on TLC. The anomeric configuration of xylose was elucidated as β according to the coupling constant of H-1′

Table 1. ^{1}H and ^{13}C NMR spectral data for compounds **1** (400 MHz, in CD_3OD) and **2** (400 MHz, in DMSO-d_6).

	1		**2**	
Position	δ_C	δ_H	δ_C	δ_H
1	172.4		168.3	
3	69.9	5.22 (2H, s)	67.4	5.18 (2H, s)
4	114.5		112.4	
5	164.1		161.3	
6	99.5	6.47 (1H, s)	98.5	6.51 (1H, s)
7	159.7		157.4	
8	105.0		103.3	
9	151.6		149.9	
10	24.9	3.32 (2H, d, $J = 7.2$ Hz)	23.4	3.20 (2H, d, $J = 7.2$ Hz)
11	127.5	5.42 (1H, t, $J = 7.2$ Hz)	125.6	5.33 (1H, t, $J = 7.2$ Hz)
12	133.7		132.0	
13	68.1	4.38 (1H, d, $J = 11.2$ Hz), 4.32 (1H, d, $J = 11.2$ Hz)	66.0	4.23 (2H, s)
14	22.0	1.79 (3H, s)	21.3	1.70 (3H, s)
OMe	56.1	3.87 (3H, s)	55.3	3.80 (3H, s)
1′	104.0	4.24 (1H, d, $J = 7.6$ Hz)	102.4	4.11 (1H, d, $J = 7.6$ Hz)
2′	75.0	3.19 (1H, t, $J = 8.8$ Hz)	73.0	2.97 (1H, t, $J = 8.8$ Hz)
3′	78.0	3.30 (1H, t, $J = 8.8$ Hz)	76.3	3.10 (1H, t, $J = 8.8$ Hz)
4′	71.3	3.50 (1H, m)	69.3	3.29 (1H, m)
5′	67.1	3.88 (1H, dd, $J = 11.2$, 5.2 Hz), 3.19 (1H, t, $J = 10.8$ Hz)	65.5	3.72 (1H, dd, $J = 11.2$, 5.2 Hz), 3.03 (1H, t, $J = 10.8$ Hz)

(δ 4.24, 1H, d, $J = 7.6$ Hz). The hydroxyl was indicated to be connected to C-5 because both of the HMBC correlation between H-10 and C-5 and between H-6 and C-4, C-8 were observed. Furthermore, due to the long-range correlations between the methoxyl proton and C-7, the location of the methoxyl was assigned at C-7. In the NOESY spectrum, important correlations were observed between the methyl and H-11, and indicated the configuration of the double bonds is *cis*. Key HMBC correlations were shown in Figure 2 and key NOESY correlations were shown in Figure 3. On the basis of these spectral data, the structure of compound **1** was confirmed and named as arenophthalide B (Figure 1). Its NMR spectral data are shown in Table 1.

Compound **2** (Figure 1) was obtained as needle crystals. The spectral data of **2** were almost identical to those of arenophthalide B (**1**), except for the difference from the isoprenyl moiety. The configuration of the double bonds is *trans*, because important NOESY correlations between H-11 and H-13 and between H-10 and H-14 were observed. Thus, the structure of compound **2** was confirmed and named as arenophthalide C (Figure 1). Its NMR spectral data are shown in Table 1.

3. Experimental

3.1 General experimental procedures

Melting points were measured on a BUCHI Melting Point B-540 apparatus. The UV spectra were measured on a UV-2550 (Shimadzu, Kyoto, Japan). IR spectra were recorded on a Bio-Rad FTS-165 instrument (Bio-Rad, Hercules, CA, USA) as KBr discs. FAB-MS data were obtained on a VQ Quattro mass spectrometer. ^{1}H, ^{13}C, and 2D NMR spectra were performed on an INOVA-400 spectrometer (Varian, Palo Alto, CA, USA) using TMS as the internal standard for measurement. Macroporous resin AB-8, silica gel (200–300 mesh), and D-xylose were purchased from Nankai University Chemtech Co. (Tianjin, China), Qingdao Ocean Chemtech Co. (Qingdao, China), and Lanjitech Co. (Shanghai, China), respectively.

3.2 Plant material

The whole plants of *H. arenarium* were collected from Buerjing country of Xinjiang, PRC and identified by professor Guanmian Sheng, Xinjiang Institute of Ecology and Geography, Chinese Academy of Science. A voucher specimen of the sample (No. HA031018) is kept in the Xinjiang Key Laboratory of Plant Resources and Natural Products Chemistry, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, China.

3.3 Extraction and isolation

The dried whole plant of *H. arenarium* (5.0 kg) was crushed to powder and extracted with 70% ethanol by heating. The crude alcoholic extract was concentrated under reduced pressure. The water solution of part of the crude extract (150.0 g) was subjected to macroporous resin AB-8 and eluted by water, 30, 50, 70% ethanol, respectively, to yield four fractions: 1 (11.9 g), 2 (81.3 g), 3 (27.5 g), and 4 (9.6 g). Fraction 2 (10 g) was separated by column chromatography on silica gel and eluted with EtOAc–EtOH mixture to yield six fractions. Fraction 2.4 was subjected to PTLC with EtOAc–EtOH–H_2O (50:10:1) to afford compound **1** (11 mg). Fraction 2.5 was separated by a flash chromatography (silica gel, $CHCl_3$–CH_3OH–H_2O, 90:10:0.5) to yield compound **2** (6 mg).

3.3.1 Arenophthalide B (*1*)

Plate crystals; mp 185–186°C. IR (KBr) ν_{max}: 1545, 1603, 1703, 1738, 2922, 3394 cm^{-1}; UV λ_{max}^{MeOH} (log ε): 226 (4.21),

260 (4.02), and 296 (3.74) nm; ^{1}H and ^{13}C NMR (CD_3OD) spectral data, see Table 1. HR-FAB-MS: *m/z* 397.1491 $[M+H]^+$ (calcd for $C_{19}H_{25}O_9$, 397.1499).

*3.3.2 Arenophthalide C (**2**)*

Needle crystals; mp 177–178°C. IR (KBr) ν_{max}: 1545, 1651, 1701, 2926, 3390 cm^{-1}; UV λ_{max}^{MeOH} (log ε): 226 (4.20), 260 (4.02), and 296 (3.75) nm; ^{1}H and ^{13}C NMR (DMSO-d_6) spectral data, see Table 1. HR-FAB-MS: *m/z* 397.1485 $[M+H]^+$ (calcd for $C_{19}H_{25}O_9$, 397.1499).

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