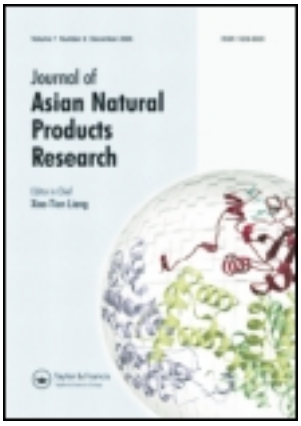

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Two new furan derivatives from bee-collected rape pollen

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Two new furan derivatives named pollenfurans A (**1**) and B (**2**) were isolated from the ethyl acetate extract of bee-collected rape pollen. Their structures were elucidated by spectroscopic analysis. The absolute configurations of the 6,7-diol moiety in both compounds **1** and **2** were confirmed by Snatzke's method, observing the induced circular dichroism after the addition of dimolybdenum tetraacetate in DMSO.

Keywords: bee-collected rape pollen; furan derivatives; pollenfuran A; pollenfuran B

1. Introduction

Bee-collected rape pollen, which is collected by the honey bee from *Brassica campestris* L., was considered as a wholesome nutritious food having wide nutritional properties. In the past 20 years, numerous researchers focus on the nutritional contents and extracts of the rape pollen. In addition, bee-collected rape pollen was also a traditional Chinese medicine. It has exhibited antioxidant [1], antitumor [2], hypolipidemic [3], and anti-inflammatory activities [4]. Up to date, bee-collected rape pollen is known as a rich source of protein, polysaccharide, fatty acid, flavonoids, some other phenolic compounds [5], and pyrrole ketohexoside derivatives [6]. In this study on chemical constituents of bee-collected rape pollen, two new furan derivatives, named pollenfurans A (**1**) and B (**2**), were isolated (Figure 1). Their structures were determined on the basis of various spectroscopic data. The cytotoxicity of compound **1** was evaluated against A549, Bel7420, BGC-823, HCT-8, and A2780 cell lines.

2. Results and discussion

Compound **1** was obtained as a brown yellow powder. The molecular formula of $C_{14}H_{18}O_7$ was determined from HR-ESI-MS at *m/z* 321.0950 $[M + Na]^+$, corresponding to six degrees of unsaturation. The ^{1}H NMR spectrum of compound **1** (see Table 1) showed two doublets at δ_H 6.52 (1H, d, $J = 3.5$ Hz) and δ_H 7.11 (1H, d, $J = 3.5$ Hz), which were characterized as H-4′ and H-3′ protons of a furan moiety. In combination with one oxymethylene proton signal at δ_H 4.63 (2H, s) and a doublet at δ_H 7.25 (1H, d, $J = 1.5$ Hz), the 5′-hydroxymethyl-furan-2-yl-methylene unit was established. The remaining signals of one oxymethine proton at δ_H 3.99 (1H, m) and one oxymethylene proton signal at δ_H 3.70 (2H, m) indicated the presence of a dihydroxyethyl moiety. In addition, an oxymethine signal at δ_H 5.62

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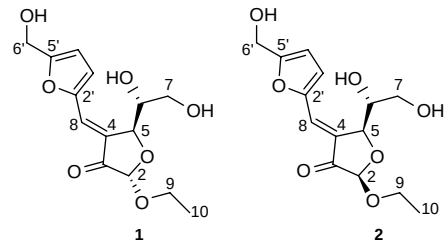

Figure 1. Structures of compounds **1** and **2**.

(1H, d, $J = 4.5$ Hz) and one ethoxyl group at δ_H 3.89 (2H, m) and δ_H 1.23 (3H, t, $J = 7.0$ Hz) were also observed in the ^{1}H NMR spectrum. The ^{13}C NMR spectrum of **1** (see Table 1) exhibited 14 carbon signals. Except for six carbon signals assigned for the 5′-hydroxymethyl-furan-2-yl-methylene group, two carbon signals for dihydroxyethyl moiety, and two carbon signals for ethoxyl group, the remaining four carbon signals were established to be dihydrofuran-3-one. In the HMBC spectrum, the correlations of H-8 at δ_H 7.25 (1H, d, $J = 1.5$ Hz) with C-3 at δ_C 197.2, C-4 at δ_C 127.7, and C-5 at δ_C 81.3 confirmed the presence of 4-(5′-hydroxymethyl-furan-2-yl-methylene)-dihydrofuran-3-one. The position of ethoxyl group and dihydroxyethyl moiety was determined at C-2 and C-5, respectively, by the HMBC correlations of H-7 at δ_H 3.70 (2H, m) with C-5 at δ_C 81.3 and H-9 at δ_H 3.89 with C-2 at δ_C 98.9 (Figure 2). Thus, the planar structure of **1** was characterized as 5-(6,7-dihydroxyethyl)-4-(5′-hydroxymethyl-furan-2-yl-methylene)-2-ethoxydihydrofuran-3-one.

There are three chiral carbons C-2, C-5, and C-8 in **1**, and the relative stereochemistry of **1** was determined by the NOESY experiment. In the NOESY spectrum, H-6 at δ_H 3.99 (1H, m) exhibited the NOESY correlation with H-3′ at δ_H 7.11 (1H, d, $J = 3.5$ Hz), but H-8 at δ_H 7.25 (1H, d, $J = 1.5$ Hz) did not exhibit correlation with H-5 at δ_H 5.62 (1H, d, $J = 4.5$ Hz) and H-6 at δ_H 3.99 (1H, m), implying the *E*-configuration of the double bond (Figure 3). The β-configuration of dihydroxyethyl group at C-5 and the α-configuration of the ethoxy at C-2 were elucidated by the NOESY correlation of H-2 at δ_H 4.98 (1H, s) with H-7 at δ_H 3.70 (2H, m).

The absolute configuration of the 6,7-diol moiety in compound **1** was determined using induced circular dichroism

Table 1. ^{1}H and ^{13}C NMR spectral data of compounds **1** and **2** (CD_3COCD_3).

	1		**2**	
	^{1}H	^{13}C	^{1}H	^{13}C
2	4.98 (1H, s)	98.9	5.15 (1H, s)	99.3
3		197.2		198.8
4		127.7		128.2
5	5.62 (1H, d, $J = 4.5$)	81.3	5.64 (1H, br s)	81.6
6	3.99 (1H, m)	75.9	4.14 (1H, m)	76.0
7	3.70 (2H, m)	63.2	3.55 (2H, m)	63.2
8	7.25 (1H, d, $J = 1.5$)	121.9	7.16 (1H, d, $J = 1.5$)	121.3
9	3.89 (2H, m)	65.1	3.65 (2H, m)	63.6
10	1.23 (3H, t, $J = 7.0$)	15.1	1.18 (3H, t, $J = 7.0$)	15.1
2′		150.7		150.9
3′	7.11 (1H, d, $J = 3.5$)	121.5	7.04 (1H, d, $J = 3.5$)	120.4
4′	6.52 (1H, d, $J = 3.5$)	110.6	6.54 (1H, d, $J = 3.5$)	110.8
5′		160.5		160.9
6′	4.63 (2H, s)	57.1	4.65 (2H, s)	57.4

Notes: ^{1}H NMR data (δ) were measured at 500 MHz, ^{13}C NMR data (δ) were measured at 125 MHz. Chemical shifts (δ) are in ppm and J in Hz.

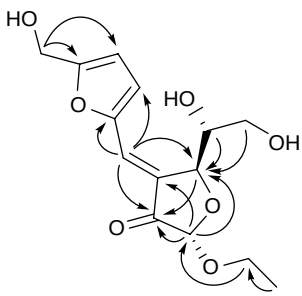

Figure 2. Selected HMBC correlations of compound **1**.

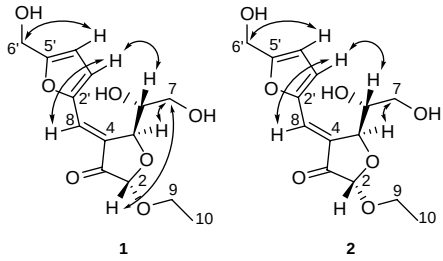

Figure 3. Key NOESY correlations of compounds **1** and **2**.

spectra by Snatzke's method [7–9], which involved the *in situ* complexation of a 1,2-diol with $[Mo_2(OAc)_4]$. The sign of the positive Cotton effect around 310 nm observed in the spectrum allowed us to assign the *R*-configuration to C-6 in compound **1**. Therefore, the structure of compound **1** was characterized as (6*R*)-5β-(6,7-dihydroxyethyl)-4-(5′-hydroxymethyl-furan-2-yl-methylene)-2α-ethoxy-dihydrofuran-3-one, named pollenfuran A.

Compound **2** was also obtained as a brown yellow powder. The molecular formula was determined to be $C_{14}H_{18}O_7$ on the basis of positive HR-ESI-MS (*m/z* 321.0994 $[M + Na]^+$), corresponding to six unsaturation degrees, just as compound **1**. A comparison of the 1D and 2D NMR and the MS data of **2** with those of **1** suggested that they shared the same planar structure. The NOESY spectrum showed the correlation of H-6 at δ_H 4.14 (1H, m) with H-3′ at δ_H 7.04 (1H, d, $J = 3.5$ Hz), but H-8 at δ_H 7.16 (1H, d, $J = 1.5$ Hz) was not correlated with H-5 at δ_H 5.64 (1H, br s) and H-6 at δ_H 4.14 (1H, m), which indicated the same *E*-configuration of the double bond as **1**. Moreover, the NOESY spectrum did not show correlation between H-2 at δ_H 5.15 (1H, s) and H-7 at δ_H 3.55 (2H, m), which determined the β-configurations of the dihydroxyethyl group at C-5 and the ethoxy at C-2 [10]. The absolute configuration of **2** was determined to be 6*R* by the same method as that of **1**. Therefore, the structure of compound **2** was elucidated as (6*R*)-5β-(6,7-dihydroxyethyl)-4-(5′-hydroxymethyl-furan-2-yl-methylene)-2β-ethoxy-dihydrofuran-3-one, named pollenfuran B.

Bioassay experiments using the 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide method [11] revealed that compound **1** exhibited no cytotoxicity against A549, Bel7420, BGC-823, HCT-8, and A2780 cell lines at 10 μg/ml.

3. Experimental

3.1 General experimental procedures

The optical rotations were measured on a PerkinElmer 241 digital polarimeter in CH_3OH. IR spectra were recorded on an IMPACT 400 (KBr) spectrometer. UV spectra were scanned by a JASCO V-650 spectrophotometer. CD spectra were measured on a JASCO J-815 spectropolarimeter. ^1H NMR (500 MHz), ^{13}C NMR (125 MHz), HSQC, and HMBC spectra were obtained on an INOVA-500 with TMS as an internal standard and values were given in parts per million (δ). HR-mass spectra were performed on a VG-Autospec-300 mass spectrometer. Silica gel (160–200, 200–300 mesh, Qingdao Marine Chemical, Inc., Qingdao, China) was utilized for column chromatography, and silica gel plates (Qingdao Marine Chemical, Inc.) were used for preparative TLC. Sephadex LH-20 (Pharmacia Fine Chemicals, Uppsala, Sweden) was used for compound purification.

3.2 Plant material

Bee-collected rape pollen was collected in Zhao Country, Hebei Province of China, in September 2007 and identified by Dr Zhi-Wu Zhang from College of Food Science and Engineering, Inner Mongolia Agricultural University. A voucher specimen (ID-S-2364) was deposited at the Institute of Materia Medica, Chinese Academy of Medical Sciences, Beijing 100050, China.

3.3 Extraction and isolation

Bee-collected rape pollen (15 kg) was extracted under reflux conditions with 95% EtOH (8 liters × 3 × 2 h each). The combined ethanolic extracts were evaporated to near dryness under vacuum and the resulting mixture (8.48 kg) was suspended in H_2O and partitioned successively with petroleum ether (1.5 liters × 3), EtOAc (1.5 liters × 3), and *n*-BuOH (1.5 liters × 3). The EtOAc fraction (180 g) was chromatographed on a silica gel column, eluting with petroleum ether–acetone (100:1, 50:1, 30:1, 20:1, 10:1, 5:1, 3:1, 1:1, 1:2, 1:3) and acetone to yield fractions 1–6. Fraction 4 (36 g) was rechromatographed over silica gel column, eluted with petroleum ether–EtOAc, to afford six subfractions 4a–4f. Subfraction 4d (2 g) was chromatographed on Sephadex LH-20 to afford compound **1** (40 mg). Subfraction 4e (1.8 g) was chromatographed on Sephadex LH-20 to afford compound **2** (8 mg).

3.3.1 Pollenfuran A (*1*)

Brownish yellow powder; $[\alpha]_D^{25} + 19.3$ ($c = 0.05$, MeOH); UV λ_{max}: 360 nm; IR (KBr) ν_{max}: 3397, 2930, 1618, 1427, 1319, 1161, 1118, 1059 cm^{-1}; ^1H and ^{13}C NMR spectral data, see Table 1; HR-ESI-MS *m/z*: 321.0951 $[M + Na]^+$ (calcd for $C_{14}H_{18}O_7Na$, 321.0950).

3.3.2 Pollenfuran B (*2*)

Brownish yellow powder; $[\alpha]_D^{25} + 10.6$ ($c = 0.03$, MeOH); UV λ_{max}: 360 nm; IR (KBr) ν_{max}: 3390, 2932, 1626, 1390, 1319, 1172, 1101, 1051 cm^{-1}; ^1H and ^{13}C NMR spectral data, see Table 1; HR-ESI-MS *m/z*: 321.0994 $[M + Na]^+$ (calcd for $C_{14}H_{18}O_7Na$, 321.0950).

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