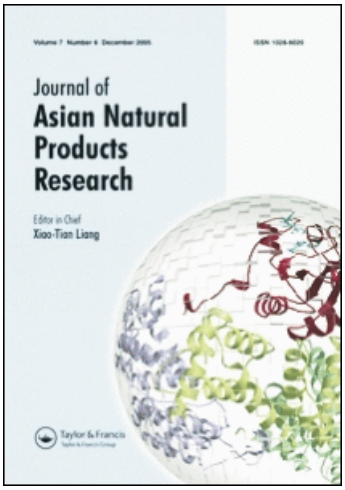

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A new dicoumarinoid glycoside from *Daphne giraldii*

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Note

A new dicoumarinoid glycoside from *Daphne giraldii*

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A new dicoumarinoid glycoside, named giraldoid A (**1**), has been isolated from *Daphne giraldii* Nitsche. The structure of **1** was determined as 7-*O*-β-glucosyl-8-(7-hydroxy-2*H*-1-benzopyran-2-one-8-)yl-2*H*-1-benzopyran-2-one on the basis of chemical reactions and spectroscopic methods.

Keywords: *Daphne giraldii* Nitsche; Thymelaeaceae; Giraldoid A; 7-*O*-β-Glucoside-8-(7-hydroxy-2*H*-1-benzopyran-2-one-8-)yl-2*H*-1-benzopyran-2-one

1. Introduction

The bark of rhizome of *Daphne giraldii* Nitsche (Thymelaeaceae), commonly called "Zu Shima", is native to Shanxi, Gansu, Sichuan and Qinghai Provinces of China [1]. It has been used in Chinese folk medicines to treat aches and rheumatism, especially for toothache, waistache, rheumatoid arthritis, quadriplegia, *etc.* [2–5]. According to our pharmacological investigation, the fraction (ZSM-B), which was washed with 30% alcohol from a macroporous resin column of the water extract, exhibited painkilling and anti-inflammatory activities. From this active part a new dicoumarinoid has been isolated and named as giraldoid A. This paper deals with the isolation and structural elucidation of the new compound.

2. Results and discussion

From the n-butanol-soluble part of ZSM-B, compound **1** (figure 1) was isolated by repeated chromatography on a silica gel column.

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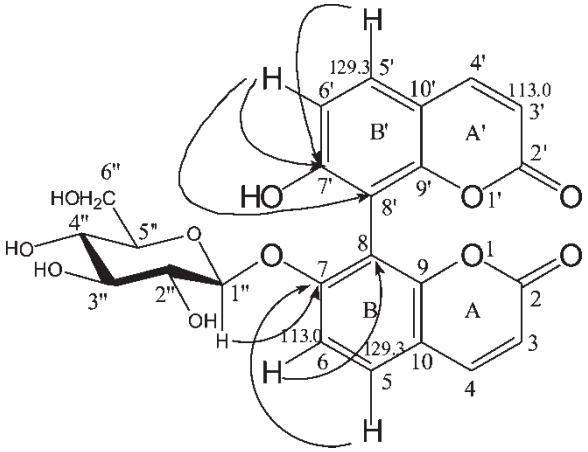

Figure 1. Structure and key HMBC correlations of giraldoid A (**1**).

Compound **1** was obtained as a white amorphous powder (MeOH), mp 212–214°C. It gave a positive Molish test and showed a blue spot with $FeCl_3$–$K_3[Fe(CN)_6]$. Acid hydrolysis carried out on TLC yielded only glucose. The IR spectrum indicates hydroxyl groups (3397 cm^{-1}), conjugated carbonyl groups (1715 cm^{-1}), phenyl groups (1602 and 1492 cm^{-1}) and a carbon–oxygen group (1283 cm^{-1}). The HR-FABMS (negative) spectrum showed an $[M-1]^-$ peak at *m/z* 483.0927, corresponding to a molecular formula of $C_{24}H_{20}O_{11}$. The ^{13}C NMR spectrum (Table I) suggested that compound **1** had a sugar unit for the existence of carbon signals at δ 100.5, 77.2, 76.5, 73.3, 69.5, 60.6. In addition to the sugar

Table 1. 1D and 2D NMR spectral data of compound **1** (DMSO-d_6).

		Correlated proton	
No.	δ_C	*One bond*	*Long-range*
2	160.5		H-3, H-4
3	111.2	δ 6.20 (1H, d, J = 9.4 Hz)	
4	145.0	δ 8.02 (1H, d, J = 9.4 Hz)	H-5
5	129.3	δ 7.62 (1H, d, J = 8.6 Hz)	H-4
6	113.0	δ 6.99 (1H, d, J = 8.6 Hz)	
7	159.1		H-5, H-1″
8	106.6		H-6
9	153.3		H-4
10	114.0		H-3, H-4, H-6
2′	160.1		H-3′, H-4′
3′	113.0	δ 6.33 (1H, d, J = 9.5 Hz)	
4′	144.7	δ 8.09 (1H, d, J = 9.5 Hz)	H-5′
5′	129.3	δ 7.78 (1H, d, J = 8.8 Hz)	H-4′
6′	111.9	δ 7.31 (1H, d, J = 8.8 Hz)	
7′	158.2		H-5′, H-6′
8′	109.7		H-6′
9′	152.5		H-4′
10′	113.5		H-3′, H-4′, H-6′
1″	100.5	5.04 (d, J = 8.0 Hz)	H-2″
2″	73.3	2.96 (t, J = 8.0 Hz)	H-3″
3″	77.2	3.35 (m)	H-2″, H-4″
4″	69.5	3.10 (m)	H-6″
5″	76.5	3.24 (m)	H-6″
6″	60.6	3.45 (m), 3.66 (m)	H-4″, H-5″

unit, the aglycone moiety exhibits 18 signals of sp^2 hybridized carbons. Among them, δ 160.5 and 160.1 are two conjugated carbonyl signals, and δ 129.3 and 113.0 were identified as two overlapped signals as the height of each is twice that of the other signals. The ^{1}H NMR (in DMSO-d_6, Table I) spectrum of **1** revealed eight aromatic proton signals at δ 8.09 (1H, d, $J = 9.5$ Hz), 8.02 (1H, d, $J = 9.4$ Hz), 7.78 (1H, d, $J = 8.8$ Hz), 7.62 (1H, d, $J = 8.6$ Hz), 7.31 (1H, d, $J = 8.8$ Hz), 6.99 (1H, d, $J = 8.6$ Hz), 6.33 (1H, d, $J = 9.5$ Hz) and 6.20 (1H, d,$J = 9.4$ Hz). Among them are four protons whose coupling-constants at 9.5 and 9.4 Hz indicate two coumarin frameworks, while another four protons have coupling-constants at 8.8 and 8.6 Hz, indicating that they are connected on ring B at *ortho*-positions. Except for the two coumarin frameworks and a sugar unit, there is only an hydroxyl group and a oxygen atom in the structure.

In ^{1}H NMR spectrum, δ 8.02 (1H, d, $J = 9.4$ Hz) and 6.20 (1H, d, $J = 9.4$ Hz) are typical 4-H and 3-H signals of coumarin and they show correlations with carbon signals at δ 145.0 and 111.2 respectively (HMQC, see table 1); thus, the two carbon signals are assigned to C-4 and C-3, respectively. In the HMBC spectrum, the signal at δ 6.20 (H-3) has a long-range correlation with δ 114.0, and thus this signal is assigned to C-10; δ 8.02 (H-4) has long-range correlations with δ 160.5 (C-2), 153.3, 129.3 and 114.0 (C-10), therefore δ 153.3 and 129.3 are assigned to C-9 and C-5 respectively. The proton signal at δ 7.62 is linked to C-5, as shown by the cross peak with δ 129.3 in the HMQC spectrum. By the same coupling constant, the proton signal at δ 6.99 is assigned to H-6. On the basis of the information from the HMQC and HMBC spectra, carbon signals at δ 113.0, 159.1, 106.6 are assigned to C-6, C-7 and C-8 respectively (Table I). The glycosidic linkage was determined to be at C-7 position based on the cross peak due to a long-range coupling between the anomeric proton (δ 5.04, H-1″) and C-7 (δ 159.1) in the HMBC spectrum, and the anomeric configuration of the sugar moiety was determined to be a β on the basis of the coupling constant for H-1″ ($J = 8.0$ Hz). In the same way, the hydroxy group was determined to be linked to C-7′ of another coumarin framework, and the other aromatic proton and carbon signals have been assigned by analysis of their 1D and 2D-NMR data. In HMBC, the signal at δ 7.31 (H-6′) has a long-range cross peak with δ 109.7, suggesting that the carbon is C-8′. Thus the two coumarin frameworks are connected at C-8 and C-8′. On the basis of the above evidences, compound **1** was elucidated as 7-*O*-β-glucosyl-8-(7-hydroxy-2*H*-1-benzopyran-2-one-8-)yl-2*H*-1-benzopyran-2-one finally. Further determination was carried out by HMQC and HMBC (Table 1).

3. Experimental

3.1 General experimental procedures

Melting points were determined on a Yanaco micromelting point apparatus and are uncorrected. The UV spectrum was recorded on Shimadzu UV-2201. The IR spectrum was recorded on a Bruker IFS-55. ^{1}H and ^{13}C NMR, along with 2D-NMR spectra, were obtained on a Bruker ARX-300 (300 MHz for ^{1}H, 75 MHz for ^{13}C) NMR spectrometer, using TMS as an internal standard. HR-FABMS was measured with a Bruker AREX II mass spectrometer. Separation and purification were performed by column chromatography on silica gel (Qingdao Haiyang Chemical Co., Ltd.). TLC was performed on silica gel GF_{254} (10–40 μm).

3.2 Plant material

The bark of rhizome of *Daphne giraldii* Nitsche was provided by the Shanhaiguan Pharmaceutical Factory and identified by Professor Zhong-kai Yan at the Research Institute of Changchun Traditional Chinese Medicine.

3.3 Extraction and isolation

The air-dried bark of rhizomes of *Daphne giraldii* Nitsche (4 kg) was extracted with boiling water three times. The extracts were collected together and concentrated, and then mixed with EtOH (3 × original volume) to produce a precipitate. The supernatant was then evaporated under reduced pressure to obtain the crude extract (540 g). Subsequently, the crude extract was suspended in water and subjected to a Macroporous Resin AB-8 column eluted with distilled water, 30% and 80% ethanol respectively, which yielded three fractions (ZSM-A, ZSM-B and ZSM-C). ZSM-B (70 g) was then extracted with EtOAC and n-BuOH successively. The n-BuOH extract (20 g) was subjected to column chromatography on silica gel (200–300 mesh) eluted with $CHCl_3$–MeOH (from 99:1 to 1:1) to give ten fractions. Fraction 6, eluted with $CHCl_3$–MeOH (85:15), was further purified by column chromatography on silica gel (10–40 μm) and gave compound **1** (21 mg).

Giraldoid A (1). White powder, mp 212–214°C; UV (MeOH) λ_{max} (nm) (log ε): 205 (4.79); IR ν_{max} (KBr) (cm^{-1}): 3397, 1715, 1602, 1492, 1401, 1283, 1062, 906, 833, 767, 620. Negative HR-FABMS *m/z* 483.0927 $[M - 1]^-$ (calcd for $C_{24}H_{19}O_{11}$, 483.0933). ^1H, ^{13}C NMR, HMQC and HMBC (DMSO-d_6) data are given in table 1.

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