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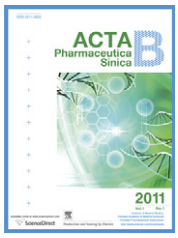

ORIGINAL ARTICLE

A new sesquiterpene lactone and a new aromatic glycoside from *Illicium difengpi*

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Abstract A new sesquiterpene lactone (**1**) and a new aromatic glycoside (**2**), together with three known compounds (**3**–**5**) were isolated from the stem bark of *Illicium difengpi* K. I. B et K. I. M. Their structures were determined by spectroscopic methods, including 1D and 2D NMR, HRESIMS, and chemical methods. The absolute configuration of the secondary alcohol in **1** was confirmed by Mosher's method. Compound **2** exhibited significant anti-inflammatory activity with IC_{50} value of 6.72 μmol/L.

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1. Introduction

The genus *Illicium* is known to be characterized by prezizaane sesquiterpene lactones, prenylated C_6–C_3 compounds, aromatic glycosides and neolignans[1–12]. Prezizaane sesquiterpene lactones are considered to be characteristic constituents of the genus *Illicium*, some of which are found to exhibit diverse biological activities including neurotoxic and neurotrophic effects[13,14]. *Illicium difengpi* K. I. B et K. I. M. (Illiciaceae) is a toxic shrub indigenous to China and grows in the mountainous areas of Guangxi Province. The stem bark has been applied as a traditional Chinese medicine for the treatment of rheumatic arthritis, and is listed in *Pharmacopeia of the People' Republic of China*. Our previous investigation on the chemical constituents of this plant has led to the isolation of nine new neolignans and two new aromatic glycosides[15]. In continuation, a new sesquiterpene lactone, difengpilactone (**1**), a new aromatic glycoside, 4-*O*-(glycer-2-yl)-dihydroconiferylalcohol-1′-*O*-*β*-D-mannopyranoside (**2**), together with three known compounds, anislactone A (**3**), oligandrumin D (**4**), and 11-*O*-debenzoyl-11α-*O*-2-methyl-cyclopent-1-enecarboxyltashironin (**5**) were obtained from the stem bark of the plant. In this paper, the isolation and structural elucidation of two new and three known compounds, and their anti-inflammatory activities are presented.

2. Results and discussion

Compound **1** was obtained as a white amorphous powder with $[\alpha]_D^{20}$+85.0 (*c* 0.10, MeOH). The UV spectrum showed a maximum absorption band at 245 nm. Its molecular formula $C_{16}H_{22}O_6$ was determined by HRESIMS (*m*/*z* 311.1495 $[M+H]^+$, calcd for 311.1489), with requiring six degrees of unsaturation. The IR spectrum exhibited the presence of hydroxyl (3420 cm^{-1}) and carbonyl functions, including ester carbonyl (1773 cm^{-1}), ketone carbonyl (1735 cm^{-1}), and α, *β*-conjugated carbonyl (1710 cm^{-1}) groups. The ^{1}H NMR spectrum (Table 1) showed the signals of three methyl [δ_H 1.39 (3H, s, H_3-9), 1.30 (3H, s, H_3-10) and 1.25 (3H, d, *J*=6.5 Hz, H_3-15)], four methylene [δ_H 3.30 (2H, s, H_2-4), 2.68 (1H, dt, *J*=4.5, 11.5 Hz, H-12a), 2.50 (1H, dt, *J*=4.5, 11.5 Hz, H-12b), 1.71 (1H, m, H-13a), 1.57 (1H, m, H-13b), 4.47 (1H, d, *J*=10.0 Hz, H-8a), 4.04 (1H, d, *J*=10.0 Hz, H-8b)], one oxygenated methine [δ_H 3.86 (1H, m, H-14)], and one methoxyl [δ_H 3.68 (3H, s)] groups. The ^{13}C NMR and DEPT spectra (Table 1) exhibited 16 resonances including four methyl, four methylene, one methane and seven quaternary carbons. The resonances at δ_C 199.0, 176.6, and 173.6 indicated the presence of three carbonyl groups. The presence of one olefinic functionality was also indicated by the resonances at δ_C 133.0 and 170.0. Based on the above data, compound **1** was determined as a sesquiterpene lactone with two rings.

Detailed analyses of the 1D and 2D NMR spectra indicated the structure of **1** (Fig. 1) and allowed assignment of all proton and carbon signals. HMBC correlations from H_2-8 to C-1 and C-2, from H_3-10 to C-2 and C-8, and from H_3-9 to C-1 and C-7 are indicative of a five-member lactone ring with two methyl groups located at C-2 and C-7. The HMBC correlations from H_2-4 to C-2, C-5 and C-6, from H_3-9 to C-3 and C-7, as well as from H_3-10 to C-2 and C-6, indicated a cyclohexane-1,4-dione moiety, which was deduced to be fused at C-2 and C-7. This conclusion was further confirmed by the key long-range correlations of H_2-8/C-6 and H_3-9/C-3. The unit of olefinic functionality was placed at C-5 according to the HMBC correlations from H_2-12 to C-5 and from H_2-4 to C-11. Correlations in the ^{1}H–^{1}H COSY and HSQC spectra of **1** indicated the presence of CH_2(12)–CH_2(13)–CH(14)–CH_3(15) unit (Fig. 2), and the location of which was confirmed to be at C-11 by HMBC

Table 1 ^{1}H and ^{13}C NMR data of compounds **1** and **2**.[a]

No.	**1** (Chloroform-d_3)		No.	**2** (Methanol-d_4)	
	δ_H (*J* in Hz)	δ_C		δ_H (*J* in Hz)	δ_C
1		173.6	1		138.7
2		58.0	2	6.79 (s)	114.4
3		199.0	3		152.2
4	3.30 (s)	29.0	4		146.8
5		133.0	5	6.96 (dd, *J*=8.0, 3.0)	119.8
6		176.6	6	6.67 (d, *J*=8.0)	122.1
7		53.7	7	2.57 (t, *J*=7.5)	33.0
8	4.47 (d, *J*=10.0)	72.8	8	1.76 (m)	35.9
	4.04 (d, *J*=10.0)		9	3.50 (t, *J*=6.0)	62.5
9	1.39 (s)	14.0	1′	3.71–3.82 (overlapped)	63.0
10	1.30 (s)	18.7	2′	4.27 (m)	81.6
11		170.0	3′	3.71–3.82 (overlapped)	62.5
12	2.68 (dt, *J*=11.5, 4.5)	24.1	1″	4.25 (d, *J*=7.0)	105.0
	2.50 (dt, *J*=11.5, 4.5)		2″	3.20–3.31 (overlapped)	71.9
13	1.71 (m)	37.5	3″	3.14 (m)	75.4
	1.57 (m)	67.5	4″	4.02 (m)	69.2
14	3.86 (m)		5″	3.20–3.31 (overlapped)	78.2
15	1.25 (d, *J*=6.5)	23.8	6″	3.71–3.82 (overlapped)	62.4
OCH_3	3.68 (s)	52.3	OCH_3	3.78 (s)	56.7

[a]NMR data were measured in chloroform-d_3 and methanol-d_4 at 500 MHz for proton and 125 MHz for carbon.