New Eudesmane and Cadalane Sesquiterpenes from *Parepigynum funingense*

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Z. Naturforsch. **2007**, *62b,* 272 – 274; received August 14, 2006

A new eudesmane sesquiterpene glycoside, named funingensin A (**1**), together with a novel cyclic ether based on the cadalane skeleton, named funingensin B (**2**), were isolated from the roots of *Parepigynum funingense*. Their structures were elucidated by spectroscopic methods, including one- and two-dimensional NMR (COSY, HMQC, HMBC and ROESY).

Key words: Parepigynum funingense, Eudesmane Sesquiterpene, Cadalane Sesquiterpene

Introduction

Parepigynum funingense Tsiang et P. T. Li (Apocynaceae), a member of a monotypic genus, is widely distributed in Yunnan Province, People's Republic of China [1]. Owing to the absence of any previous studies on the chemistry of this species, we examined an extract of the roots from *Parepigynum funingense*. In previous papers, we reported the structure elucidation of sixteen steroidal glycosides [2-4]. Our continuing phytochemical investigation on the constituents of this plant has resulted in the isolation of a new eudesmane sesquiterpene glycoside, named funingensin A (**1**), and a novel cadalane sesquiterpene, named funingensin B (**2**). Their structure elucidation is reported in this paper.

Results and Discussion

Compound **1** was obtained as a white powder. Its molecular formula was assigned to be $C_{21}H_{36}O_7$ based on negative-ion HRFABMS (m/z = 399.3468, calcd. 399.3452 for $C_{21}H_{35}O_7$, $[M\text{-}H]^-$). Careful comparison of the NMR data of **1** with those of 1α,6β-dihydroxy-5,10-bis-*epi*-eudesm-3-ene-6-*O*-β-D-glucopyranoside [5] showed that they had the same eudesmane sesquiterpene skeleton, both with an isopropyl group at C-7 and two oxygenated methine carbon atoms at C-1 and C-6. The most obvious difference between them was the position of the double bond. In the HMBC spectrum of **1**, long-range couplings were observed for H-5 (δ_H = 2.52) and H-3 (δ_H = 2.25) to C-15 (δ_C = 111.1), H-2 (δ_H = 2.03) and H-6 (δ_H = 4.93) to C-4 (δ_C = 145.1), requiring the double bond at C-4 and C-15. In the NOESY spectra, clear effects were observed between H-14 and H-6α, H-1 (δ_H = 3.69, dd, 1H, J = 11.3, 4.5 Hz) and H-5, as well as H-5, H-1 and H-11. These couplings indicated that **1** was a 5,10-bis-*epi*-eudesmane, and also determined the configurations at C-1, C-6 and C-7 as shown in Fig. 1. In the HMBC spectrum of **1**, long-range couplings were also observed between H-1′ of the glucosyl unit (δ_H = 5.11) and C-6 of the aglycon (δ_C = 72.5), suggesting that the sugar unit was connected to C-6. On the basis of the above evidence, compound **1** could be identified as 1α, 6β-dihydroxy-5,10-bis-*epi*-eudesm-4(15)-ene-6-*O*-β-D-glucopyranoside, and was named funingensin A. Closely related sesquiterpene glycosides with the skeleton of compound **1** have been isolated from *Dictamnus dasycarpus*, *Ainsliaea cordifolia* [6 – 9].

Compound **2** was obtained as white powder, and analyzed as $C_{15}H_{26}O$ by negative-ion HRFABMS (m/z = 221.3579, calcd. 221.3557 for $C_{15}H_{25}O$, $[M\text{–}H]^-$). Its ^{13}C NMR spectrum showed two down-field singlets (δ = 73.2, 81.0), and signals of 4 methines (δ = 26.0, 29.4, 48.2, 54.4), 5 methylenes (δ = 18.8, 19.4, 25.8, 38.2, 38.8), and 4 methyls (δ = 16.5, 26.3, 28.8, 32.8). The ^1H NMR spectrum displayed singlets at δ = 1.40 and 1.57, assignable to tertiary methyls attached to oxygen-bearing carbons. Other signals appeared at δ = 1.05 (d, J = 6.3 Hz, 3 H) and 1.08 (d, J = 6.3 Hz, 3 H), and were assigned to methyl protons of an isopropyl group, since both of them show

	δ (C) (DEPT)	δ (H)	HMBC (seleceted)	ROESY (seleceted)
1	78.9 (CH)	3.69 (dd, J = 11.3, 4.5)	H-14	H-5
2	33.3 (CH_2)*	1.87 (m), 2.03 (m)		
3	36.5 (CH_2)	2.25 (m), 2.34 (m)		
4	145.1 (C)		H-2, H-6	
5	48.6 (CH)	2.52 (d, J = 11.0)	H-14, H-15	H-1, H-11
6	72.5 (CH)	4.93 (dd, J = 11.8, 4.7)	H-1′, H-4, H-11	H-14
7	39.5 (CH)	2.17 (br s)	H-12, H-13	
8	22.2 (CH_2)*	1.62 (m), 1.75 (m)		
9	33.0 (CH_2)*	1.59 (m), 1.98 (m)		
10	43.0 (C)			
11	25.4 (CH)	2.49 (m)		H-5
12	22.8 (CH_3)	0.94 (d, J = 6.6)	H-7, H-13	
13	24.2 (CH_3)	1.29 (d, J = 6.7)	H-7, H-12	
14	12.8 (CH_3)	1.05 (s)		H-6
15	111.1 (CH_2)	5.77 (br s), 5.16 (br s)	H-3, H-5	
Glc-1′	99.9 (CH)	5.11 (d, J = 7.7)	H-6, H-3′, H-5′	
2′	75.7 (CH)*	4.02 (m)		
3′	78.5 (CH)*	4.21 (m)		
4′	72.4 (CH)*	4.19 (m)		
5′	78.6 (CH)*	3.95 (m)		
6′	63.2 (CH)	4.59 (dd, J = 11.8, 2.0)		
		4.39 (dd, J = 11.8, 5.0)		

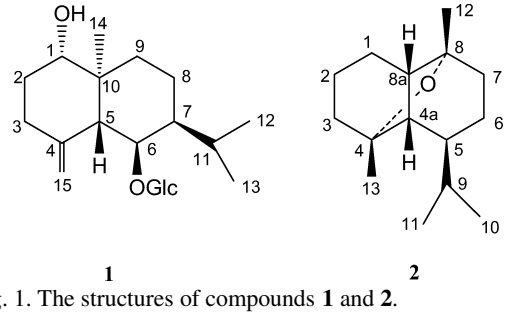
Table 1. ^{1}H and ^{13}C NMR spectral data of **1** (δ in ppm, J in Hz, [D_5]pyridine).

* Overlap with other signals.

	δ (C) (DEPT)	δ (H)	HMBC (seleceted)	ROESY (seleceted)
1	25.8 (CH_2)*	1.74 (m), 1.85 (m)		
2	19.4 (CH_2)*	1.76 (m), 1.96 (m)		
3	38.2 (CH_2)*	2.03 (m), 1.98 (m)	H-13	
4	81.0 (C)		H-13	
4a	48.2 (CH)	2.31 (dd, J = 9.5, 3.9)	H-9, H-13	H-8a, H-9, H-13
5	26.0 (CH)	0.17 (m)	H-11, H-10	
6	18.8 (CH_2)	1.52 (m), 1.64 (m)	H-9	
7	38.8 (CH_2)*	1.82 (m), 1.94 (m)	H-12	
8	73.2 (C)		H-12	
8a	54.4 (CH)	3.33 (m)	H-12	H-4a, H-9, H-12
9	29.4 (CH)	0.69 (m)		H-4a, H-8a
10	16.5 (CH_3)	1.05 (d, J = 6.3)	H-11	
11	28.8 (CH_3)	1.09 (d, J = 6.3)	H-10	
12	32.8 (CH_3)	1.40 (s)		H-8a
13	26.3 (CH_3)	1.57 (s)		H-4a

Table 2. ^{1}H and ^{13}C NMR spectral data of **2** (δ in ppm, J in Hz, [D_5]pyridine).

* Overlap with other signals.



1 **2**

Fig. 1. The structures of compounds **1** and **2**.

COSY correlations with H-9. In the HMBC spectrum, long range correlations could be observed for H-9 to C-4a and C-6, H-12 to C-8a and C-7, H-13 to C-4a and C-3, indicating that the isopropyl group was attached at C-5, and the two tertiary methyls were situated at C-4 and C-8. From the above data it was established that **2** possessed the cadalane skeleton [10] bearing an ether bridge connecting positions 4 and 8. In the ROESY spectra, clear couplings were observed between H-4a, H-8a and Me-13, H-8a, Me-12 and H-9, requiring *cis* relationships between H-4a, H-8a, Me-12, Me-13 and the isopropyl group. On the basis of the above evidence, compound **2** could be identified as 5β-isopropyl-4β, 8β-dimethyl-4α, 8α-epoxy-1, 2, 3, 4, 4a, 5, 6, 7, 8, 8a-decahydronaphthalene, and was named funingensin B. Cyclic ether compounds based on the cadalane skeleton are not common, but have been isolated from the brown alga *Dilophus fasciola* [10 – 11].

Experimental Section

General

Optical rotations: Horiba SEAP-300 spectropolarimeter. NMR Spectra: 1D, Bruker AM-400 spectrometer; 2D, Bruker DRX-500 spectrometer; δ in ppm, rel. to $SiMe_4$, *J* in Hz. MS: VG Autospec-3000 spectrometer.

Plant material

The roots of *Parepigynum funingense* were collected from Jinchang, Malipo County, Yunnan Province, People's Republic of China, in April 2000. The plant was identified by Prof. Xun Gong at Kunming Insitiute of Botany, the Chinese Academy of Sciences, where a voucher specimen (No. 0774313) is deposited.

Extraction and isolation

The dried roots (15 kg) of *P. funingense* were extracted three times with 75 % EtOH under reflux. After removal of the solvent *in vacuo*, the aqueous solution was passed through a HPD-100 column and the absorbed materials were eluted with 65 % aqueous methanol and methanol, successively. The 65 % methanol eluate was concentrated *in vacuo* to give a residue (138 g), which was chromatographed on a silica gel (200 – 300 mesh) column and eluted with gradient mixtures of chloroform/methanol from 9 : 1 (v/v) to 2 : 1 (v/v) to afford eight fractions. Fraction 2 was further subjected to repeated silica gel column chromatography using $CHCl_3$-MeOH (15 : 1, v/v) as eluent, and passed over RP-18 eluted with methanol/water (4 : 6, v/v) to afford compound **1** (12 mg). Fraction 1 was further subjected to silica gel (200 – 300 mesh) column chromatography using a mixture of petroleum ether/acetone (3 : 1, v/v) as eluent to yield pure **2** (9 mg).

Funingensin A (1α, 6β-dihydroxy-5,10-bis-*epi*-eudesm-4(15)-ene-6-*O*-β-D-glucopyranoside, **1**), white powder. – $[\alpha]_D^{23} = -52.4°$ (*c* = 0.39, MeOH). – HR-FAB-MS (neg.): *m/z* = 399.3468 (calcd. 399.3452 for $C_{21}H_{35}O_7$, $[M–H]^-$). – FAB-MS (neg.): *m/z* (%) = 399 (100), 237 (8). – ^1H, ^{13}C NMR: see Table 1.

Funingensin B (5β-isopropyl-4β, 8β-dimethyl-4α, 8α-epoxy-1, 2, 3, 4, 4a, 5, 6, 7, 8, 8a-decahydronaphthalene, **2**), white powder. – $[\alpha]_D^{23} = -58.7°$ (*c* = 0.35, MeOH). – HR-FAB-MS (neg.): *m/z* = 221.3579 (calcd. 221.3557 for $C_{15}H_{25}O$, $[M–H]^-$). – FAB-MS (neg.): *m/z* (%) = 221 (100). – ^1H, ^{13}C NMR: see Table 2.

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