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## Two new diterpenoids from *coleus forskohlii*

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Two new diterpenoids, forskolins I and J, have been isolated in our further investigation on *Coleus forskohlii* (Willd.) Briq. collected in Yunnan Province. Their structures have been determined as 1 $\alpha$ ,6 $\beta$ -diacetoxy-7 $\beta$ ,9 $\alpha$ -dihydroxy-8,13-epoxylabd-14-en-11-one (**1**) and 1 $\alpha$ ,9 $\alpha$ -dihydroxy-6 $\beta$ ,7 $\beta$ -diacetoxy-8,13-epoxylabd-14-en-11-one (**2**) by spectral methods (including 1D and 2D NMR techniques).

**Keywords:** *Coleus forskohlii*; Labiatae; Diterpenoid; Forskolin I; Forskolin J

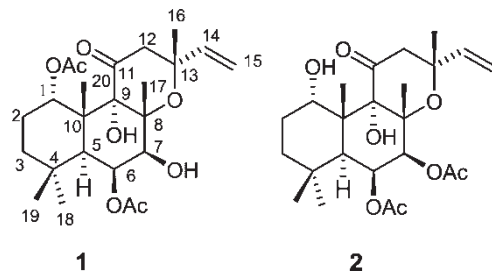
### 1. Introduction

*Coleus forskohlii* (Willd.) Briq. contains abundant labdane diterpenoids that possess significant bioactivity [1,2]. Previous studies on *C. forskohlii* have afforded eight labdane diterpenoids [3–6]. Further investigation on this plant has led to the isolation of two new labdane diterpenoids, named forskolins I and J (**1** and **2**, figure 1). We report here the isolation and structural elucidation of forskolins I and J.

### 2. Results and discussion

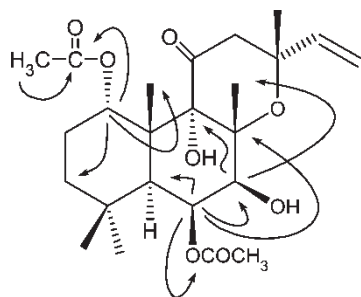
Compound **1** was obtained as colorless needles (acetone). EIMS  $m/z$  452  $[M]^+$ , together with  $^{13}C$  and DEPT NMR spectra, indicate the molecular formula as  $C_{24}H_{36}O_8$ , which was confirmed by HR-ESIMS analysis ( $[M + Na]^+$   $m/z$  475.2313). DEPT spectra show five tertiary methyl groups, four methylene groups, five methine groups, five quaternary carbons, two olefinic carbons, one ketonic carbon and two acetoxy signals. Comparison of the data of compound **1** with forskolin B [1,3] suggests that compound **1** has a typical 8,13-epoxylabd-14-en-11-one skeleton [1,3]. In its  $^1H$  NMR spectrum, the five methyl signals at  $\delta_H$  0.97, 1.06, 1.38, 1.46 and 1.59, and the signals of an AB coupling system at  $\delta_H$  3.07 (1H, d,  $J = 17.0$  Hz) and 2.49 (1H, d,  $J = 17.0$  Hz), and three olefinic proton signals

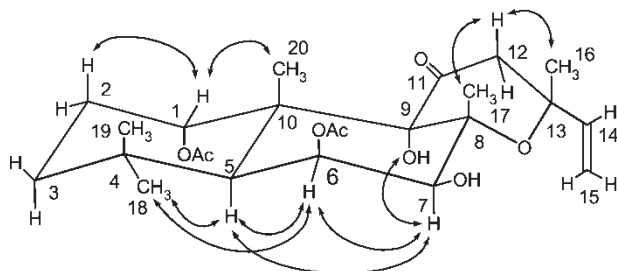
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Figure 1. Structures of compounds **1** and **2**.

at  $\delta_{\text{H}}$  6.06, 4.95 and 5.13, confirm this assumption. The HMBC spectrum shows cross-peaks of  $\delta_{\text{H}}$  5.58 (1H, brs, 1 $\beta$ -H) with  $\delta_{\text{C}}$  37.07 (C-3), 43.16 (C-5), 43.58 (C-10) and 167.98 (OAc),  $\delta_{\text{H}}$  5.84 (1H, dd,  $J = 2.7, 4.6$  Hz, 6 $\alpha$ -H) with  $\delta_{\text{C}}$  43.16 (C-5), 73.56 (C-7), 81.47 (C-8), 43.58 (C-10) and 170.70 (OAc),  $\delta_{\text{H}}$  4.28 (1H, d,  $J = 4.6$  Hz, 7 $\alpha$ -H) with  $\delta_{\text{C}}$  70.82 (C-6), 81.47 (C-8) and 82.29 (C-9), which reveal the locations of 1-OAc, 6-OAc, and 7-OH (figure 2). The above inferences are also supported by the  $^1\text{H}$ - $^1\text{H}$  COSY spectrum. Additionally, the relative configurations of 1-OAc, 6-OAc and 7-OH have been determined as, respectively,  $\alpha$ ,  $\beta$  and  $\beta$  orientation from ROESY correlations of 1-H with 2 $\beta$ -H and 20 $\beta$ -Me; 6-H with 5 $\alpha$ -H and 18 $\alpha$ -Me; 7-H with 5 $\alpha$ -H, 6 $\alpha$ -H and 9 $\alpha$ -OH respectively (figure 3). Thus, compound **1** was determined as 1 $\alpha$ ,6 $\beta$ -diacetoxy-7 $\beta$ ,9 $\alpha$ -dihydroxy-8,13-epoxylabd-14-en-11-one, and named forskolin I.

Compound **2**, colorless prisms (pyridine), was assigned the molecular formula  $\text{C}_{24}\text{H}_{36}\text{O}_8$  by EIMS  $m/z$  452  $[\text{M}]^+$ ,  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra, which was verified by HR-ESIMS ( $[\text{M} + \text{Na}]^+ m/z$  475.2316). The NMR data of compound **2** are very similar to those of **1**. Further comparison of  $^{13}\text{C}$  NMR of **2** with that of **1** showed that **2** has the same 8,13-epoxylabd-14-en-11-one skeleton [1,3]. Moreover, the HMBC correlations of  $\delta_{\text{H}}$  5.00 (1H, d,  $J = 1.4$  Hz, 1 $\beta$ -H) with  $\delta_{\text{C}}$  36.40 (C-3), 42.20 (C-5) and 19.58 (C-20);  $\delta_{\text{H}}$  6.17 (1H, dd,  $J = 3.3, 5.2$  Hz, 6 $\alpha$ -H) with  $\delta_{\text{C}}$  42.20 (C-5), 75.08 (C-7), 80.88 (C-8), 42.90 (C-10);  $\delta_{\text{H}}$  2.13 (3H, s, 6-OAc) with  $\delta_{\text{C}}$  69.72 (C-6);  $\delta_{\text{H}}$  6.13 (1H,  $J = 5.2$  Hz, 7 $\alpha$ -H) with  $\delta_{\text{C}}$  69.72 (C-6), 80.88 (C-8); and  $\delta_{\text{H}}$  1.98 (3H, s, 7-OAc) with  $\delta_{\text{C}}$  75.08 (C-7) indicate 1-OH, 6-OAc and 7-OAc substitution at 1 $\alpha$ , 6 $\beta$  and 7 $\beta$ , respectively, in **2** (figure 4), which were confirmed by ROESY correlations of 1-H with 20 $\beta$ -Me; 6-H with 5 $\alpha$ -H, 18 $\alpha$ -Me and 9 $\alpha$ -OH; and 7-H with 5 $\alpha$ -H and 6 $\alpha$ -H (figure 5). Therefore,

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

Figure 3. Key ROESY correlations of **1**.

compound **2** was deduced to be  $1\alpha,9\alpha$ -dihydroxy- $6\beta,7\beta$ -diacetoxy- $8,13$ -epoxylabd- $14$ -en- $11$ -one, and named forskolin J.

### 3. Experimental

#### 3.1 General experimental procedures

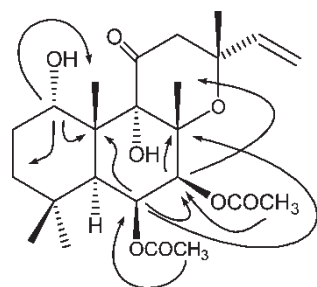
Melting points were measured on an XRC-1 micromelting apparatus and are uncorrected. IR spectra were obtained on a Bio-Rad FTS-135 infrared spectrometer with KBr pellets. Optical rotations were taken on a SEPA-300 polarimeter. The MS spectra were taken on a VG Autospec-3000 spectrometer (70 eV).  $^1\text{H}$ ,  $^{13}\text{C}$  and 2D NMR were recorded on Bruker AM-400 and DRX-500 spectrometers with TMS as internal standard. Silica gel for TLC and column chromatography was obtained from Qingdao Marine Chemical Inc., China.

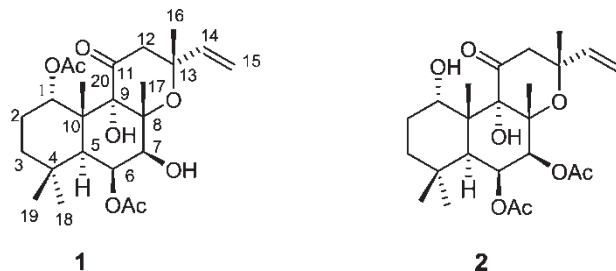
#### 3.2 Plant material

Roots of *Coleus forskohlii* (Willd.) Briq. were collected in Yunnan Province, China, in September 1999, and were identified by Professor H.W. Li, Kunming Institute of Botany. A voucher specimen has been deposited in the Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences.

#### 3.3 Extraction and isolation

Dried roots of *Coleus forskohlii* (5 kg) were extracted with 25 L ( $3 \times$ ) of 95% ethanol at room temperature and filtered. The filtrate was then concentrated *in vacuo* and partitioned

Figure 4. Selected HMBC correlations of **2**.

Figure 5. Key ROESY correlations of **2**.

with light petroleum, chloroform and n-butanol. The chloroform extract was evaporated to afford 50 g of residue. The residues were subsequently subjected to column chromatography on silica gel, eluted with light petroleum–acetone (from light petroleum to light petroleum–acetone 1:1). The fractions were combined by monitoring with TLC to obtain fractions 1–6. Fraction 2 was then recrystallized with pyridine to afford **2**. Fraction 5 was chromatographed repeatedly on silica gel eluted with  $\text{CHCl}_3$ –MeOH and  $\text{CHCl}_3$ –acetone to give **1**.

**Compound 1.** Colorless needles (acetone),  $[\alpha]_D^{15.8} + 9.81$  (*c* 0.484,  $\text{CHCl}_3$ ); mp 174–180°C; IR (KBr) ( $\text{cm}^{-1}$ ): 3486, 2949, 2932, 2869, 1729, 1635, 1395, 1366, 1233, 1207, 1175, 1103, 1042, 992, 943;  $^{13}\text{C}$  and  $^1\text{H}$  NMR data see tables 1 and 2, respectively; EIMS: (rel %) *m/z*: 452 [26,  $\text{M}^+$ ], 434 [58,  $\text{M}^+ - \text{H}_2\text{O}$ ], 419 [1,  $\text{M}^+ - \text{H}_2\text{O} - \text{CH}_3$ ], 392 [18,  $\text{M}^+ - \text{HOAc}$ ], 377 [4,  $\text{M}^+ - \text{HOAc} - \text{CH}_3$ ], 359 (8), 342 (28), 332 [12,  $\text{M}^+ - 2\text{HOAc}$ ], 324 (28), 313 (9), 282 (24), 259 (32), 239 (28), 219 (30), 209 (33), 193 (66), 180 (38), 165 (84), 152 (61), 135 (51), 123 (86), 109 (64), 99 (66), 95 (94), 85 (71), 69 (81), 55 (100); HR-ESIMS:  $[\text{M} + \text{Na}]^+$  *m/z* 475.2313, calcd for  $\text{C}_{24}\text{H}_{36}\text{O}_8 + \text{Na}^+$  475.2307.

**Compound 2.** Colorless prisms (pyridine),  $[\alpha]_D^{18.1} 0$  (*c* 0.105,  $\text{CHCl}_3$ ), mp. 277–280°C; IR (KBr) ( $\text{cm}^{-1}$ ): 3395, 2950, 1740, 1370, 1098, 1057, 973, 922, 897, 867, 808, 789, 752, 718, 691, 664, 646, 628;  $^{13}\text{C}$  and  $^1\text{H}$  NMR data see tables 1 and 2, respectively; EIMS (rel %) *m/z*: 452 (43,  $\text{M}^+$ ), 434 [5,  $\text{M}^+ - \text{H}_2\text{O}$ ], 419 [12,  $\text{M}^+ - \text{H}_2\text{O} - \text{CH}_3$ ], 392 [25,  $\text{M}^+ - \text{HOAc}$ ],

Table 1.  $^{13}\text{C}$  NMR data of **1** and **2** (**1** in  $\text{CDCl}_3$ , **2** in  $\text{C}_5\text{D}_5\text{N}$ ).

Carbon	<b>1</b>	<b>2</b>	Carbon	<b>1</b>	<b>2</b>
1	77.59	73.16	12	48.55	49.25
2	22.88	26.58	13	75.47	75.36
3	37.07	36.40	14	146.13	147.14
4	33.74	33.77	15	110.37	109.58
5	43.16	42.20	16	30.62	30.44
6	70.82	69.72	17	23.13	23.21
7	73.56	75.08	18	32.74	32.30
8	81.47	80.88	19	22.93	23.08
9	82.29	82.31	20	19.82	19.58
10	43.58	42.90	OAc	170.70, 21.70	169.93, 20.80
11	204.91	206.21	OAc	167.98, 21.61	169.72, 20.42

Table 2. <sup>1</sup>H NMR and COSY data of **1** and **2** (**1** in CDCl<sub>3</sub>, **2** in C<sub>5</sub>D<sub>5</sub>N, *J* in Hz).

<b>1</b>			<b>2</b>		
Hydrogen	δ <sub>H</sub>	COSY	Hydrogen	δ <sub>H</sub>	COSY
1β-H	5.58 (brs)	2-H <sub>2</sub>	1β-H	5.00 (d, 1.4)	2β-H, 1-OH
2β-H	2.03 (m)	1β-H, 2α-H, 3-H <sub>2</sub>	2β-H	2.14 (m)	1β-H, 2α-H, 3-H <sub>2</sub>
2α-H	1.64 (m)	1β-H, 2β-H, 3-H <sub>2</sub>	2α-H	1.53 (m)	2β-H, 3-H <sub>2</sub>
3α-H	1.51 (m)	2-H <sub>2</sub> , 3β-H	3α-H	2.02 (m)	2-H <sub>2</sub> , 3β-H
3β-H	1.14 (m)	2-H <sub>2</sub> , 3α-H	3β-H	1.01 (m)	2-H <sub>2</sub> , 3α-H
5α-H	2.30 (d, 2.7)	6α-H	5α-H	2.70 (d, 3.3)	6α-H
6α-H	5.84 (dd, 2.7, 4.6)	5α-H, 7α-H	6α-H	6.17 (dd, 3.3, 5.2)	5α-H, 7α-H
7α-H	4.28 (1H, d, 4.6)	6α-H	7α-H	6.13 (d, 5.2)	
12α-H	3.07 (d, 17.0)	12β-H	12α-H	3.46 (d, 16.5)	12β-H
12β-H	2.49 (d, 17.0)	12α-H	12β-H	2.69 (d, 16.5)	12α-H
14-H	6.06 (dd, 17.4, 10.7)	15-H <sub>2</sub>	14-H	6.26 (dd, 17.2, 10.8)	15-H <sub>2</sub>
15-H <sub>cis</sub>	4.95 (d, 10.7)	14-H	15-H <sub>cis</sub>	4.90 (d, 10.8)	14-H
15-H <sub>trans</sub>	5.13 (d, 17.4)	14-H	15-H <sub>trans</sub>	5.33 (d, 17.2)	14-H
16-Me	1.38 (s)		16-Me	1.41 (s)	
17-Me	1.59 (s)		17-Me	1.83 (s)	
18-Me	1.06 (s)	19-Me	18-Me	0.95 (s)	19-Me
19-Me	0.97 (s)	18-Me	19-Me	0.98 (s)	18-Me
20-Me	1.46 (s)		20-Me	1.65 (s)	
OAc	2.08 (s)		OAc	2.13 (s)	
OAc	2.01 (s)		OAc	1.98 (s)	

375 [14, M<sup>+</sup> – HOAc-OH], 355 (10), 342 (16), 332 [5, M<sup>+</sup> – 2HOAc], 282 (15), 233 (29), 219 (27), 207 (71), 191 (51), 175 (38), 165 (72), 152 (47), 137 (38), 123 (66), 109 (62), 99 (66), 95 (76), 81 (77), 69 (74), 55 (100); HR-ESIMS: [M + Na]<sup>+</sup> *m/z* 475.2316, calcd. for C<sub>24</sub>H<sub>36</sub>O<sub>8</sub> + Na<sup>+</sup> 475.2307.

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