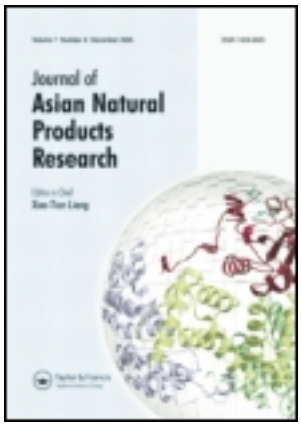

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Y. H. shen [a] & Y. L. Xu [a]
[a] State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, 650204, Yunnan, China

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Two new diterpenoids from *coleus forskohlii*

Y. H. SHEN and Y. L. XU*

State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204, Yunnan, China

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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 1α,6β-diacetoxy-7β,9α-dihydroxy-8,13-epoxylabd-14-en-11-one (**1**) and 1α,9α-dihydroxy-6β,7β-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 δ_H 0.97, 1.06, 1.38, 1.46 and 1.59, and the signals of an AB coupling system at δ_H 3.07 (1H, d, $J = 17.0$ Hz) and 2.49 (1H, d, $J = 17.0$ Hz), and three olefinic proton signals

*Corresponding author. Tel.: +86-871-5223324. Fax: +86-871-5150227. E-mail: xuyl@mail.kib.ac.cn

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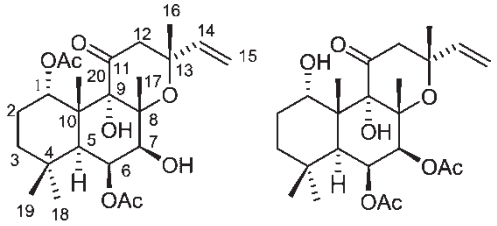

1 2

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

at δ_H 6.06, 4.95 and 5.13, confirm this assumption. The HMBC spectrum shows cross-peaks of δ_H 5.58 (1H, brs, 1β-H) with δ_C 37.07 (C-3), 43.16 (C-5), 43.58 (C-10) and 167.98 (OAc), δ_H 5.84 (1H, dd, $J = 2.7, 4.6$ Hz, 6α-H) with δ_C 43.16 (C-5), 73.56 (C-7), 81.47 (C-8), 43.58 (C-10) and 170.70 (OAc), δ_H 4.28 (1H, d, $J = 4.6$ Hz, 7α-H) with δ_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 $^1H—^1H$ COSY spectrum. Additionally, the relative configurations of 1-OAc, 6-OAc and 7-OH have been determined as, respectively, α, β and β orientation from ROESY correlations of 1-H with 2β-H and 20β-Me; 6-H with 5α-H and 18α-Me; 7-H with 5α-H, 6α-H and 9α-OH respectively (figure 3). Thus, compound **1** was determined as 1α,6β-diacetoxy-7β,9α-dihydroxy-8,13-epoxylabd-14-en-11-one, and named forskolin I.

Compound **2**, colorless prisms (pyridine), was assigned the molecular formula $C_{24}H_{36}O_8$ by EIMS *m/z* 452 $[M]^+$, ^1H and ^{13}C NMR spectra, which was verified by HR-ESIMS ($[M + Na]^+$ *m/z* 475.2316). The NMR data of compound **2** are very similar to those of **1**. Further comparison of ^{13}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 δ_H 5.00 (1H, d, $J = 1.4$ Hz, 1β-H) with δ_C 36.40 (C-3), 42.20 (C-5) and 19.58 (C-20); δ_H 6.17 (1H, dd, $J = 3.3, 5.2$ Hz, 6α-H) with δ_C 42.20 (C-5), 75.08 (C-7), 80.88 (C-8), 42.90 (C-10); δ_H 2.13 (3H, s, 6-OAc) with δ_C 69.72 (C-6); δ_H 6.13 (1H, $J = 5.2$ Hz, 7α-H) with δ_C 69.72 (C-6), 80.88 (C-8); and δ_H 1.98 (3H, s, 7-OAc) with δ_C 75.08 (C-7) indicate 1-OH, 6-OAc and 7-OAc substitution at 1α, 6β and 7β, respectively, in **2** (figure 4), which were confirmed by ROESY correlations of 1-H with 20β-Me; 6-H with 5α-H, 18α-Me and 9α-OH; and 7-H with 5α-H and 6α-H (figure 5). Therefore,

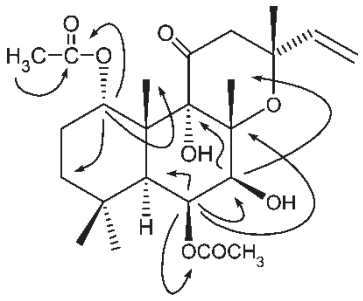

Figure 2. Selected HMBC correlations of **1**.

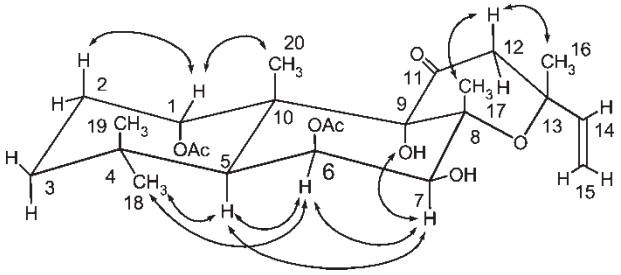

Figure 3. Key ROESY correlations of **1**.

compound **2** was deduced to be 1α,9α-dihydroxy-6β,7β-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}H, ^{13}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 ×) of 95% ethanol at room temperature and filtered. The filtrate was then concentrated *in vacuo* and partitioned

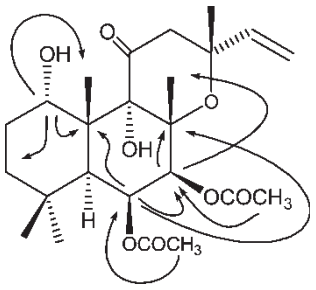

Figure 4. Selected HMBC correlations of **2**.

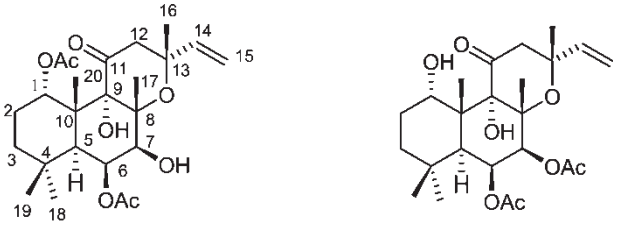

Figure 5. Key ROESY correlations of **2**.

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 $CHCl_3$–MeOH and $CHCl_3$—acetone to give **1**.

Compound 1. Colorless needles (acetone), $[\alpha]_D^{15.8}$ + 9.81 (*c* 0.484, $CHCl_3$); mp 174–180°C; IR (KBr) (cm^{-1}): 3486, 2949, 2932, 2869, 1729, 1635, 1395, 1366, 1233, 1207, 1175, 1103, 1042, 992, 943; ^{13}C and ^1H NMR data see tables 1 and 2, respectively; EIMS: (rel %) *m/z*: 452 [26, M^+], 434 [58, $M^+ - H_2O$], 419 [1, $M^+ - H_2O - CH_3$], 392 [18, M^+ − HOAc], 377 [4, M^+ − HOAc − CH_3], 359 (8), 342 (28), 332 [12, M^+ − 2HOAc], 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: $[M + Na]^+$ *m/z* 475.2313, calcd for $C_{24}H_{36}O_8 + Na^+$ 475.2307.

Compound 2. Colorless prisms (pyridine), $[\alpha]_D^{18.1}$ 0 (*c* 0.105, $CHCl_3$), mp. 277–280°C; IR (KBr) (cm^{-1}): 3395, 2950, 1740, 1370, 1098, 1057, 973, 922, 897, 867, 808, 789, 752, 718, 691, 664, 646, 628; ^{13}C and ^1H NMR data see tables 1 and 2, respectively; EIMS (rel %) *m/z*: 452 (43, M^+), 434 [5, $M^+ - H_2O$], 419 [12, $M^+ - H_2O - CH_3$], 392 [25, M^+ − HOAc],

Table 1. ^{13}C NMR data of **1** and **2** (**1** in $CDCl_3$, **2** in C_5D_5N).

Carbon	*1*	*2*	*Carbon*	*1*	*2*
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. ^{1}H NMR and COSY data of **1** and **2** (**1** in $CDCl_3$, **2** in C_5D_5N, *J* in Hz).

1			***2***		
Hydrogen	δ_H	*COSY*	*Hydrogen*	δ_H	*COSY*
1β-H	5.58 (brs)	2-H_2	1β-H	5.00 (d, 1.4)	2β-H, 1-OH
2β-H	2.03 (m)	1β-H, 2α-H, 3-H_2	2β-H	2.14 (m)	1β-H, 2α-H, 3-H_2
2α-H	1.64 (m)	1β-H, 2β-H, 3-H_2	2α-H	1.53 (m)	2β-H, 3-H_2
3α-H	1.51 (m)	2-H_2, 3β-H	3α-H	2.02 (m)	2-H_2, 3β-H
3β-H	1.14 (m)	2-H_2, 3α-H	3β-H	1.01 (m)	2-H_2, 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_2	14-H	6.26 (dd, 17.2, 10.8)	15-H_2
15-H_{cis}	4.95 (d, 10.7)	14-H	15-H_{cis}	4.90 (d, 10.8)	14-H
15-H_{trans}	5.13 (d, 17.4)	14-H	15-H_{trans}	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, $M^+ - HOAc\text{-}OH$], 355 (10), 342 (16), 332 [5, $M^+ - 2HOAc$], 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: $[M + Na]^+$ *m/z* 475.2316, calcd. for $C_{24}H_{36}O_8 + Na^+$ 475.2307.

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References

[1] S.B. Katti, P.K. Jauhari, J.S. Tandon. *Indian J. Chem.*, **17B**, 321 (1979).
[2] Sujata, V. Bhat, Alihussein, N. Dohadwalla, Balbir, S. Bajwa, Nandkumar, K. Dadkar, Horst Dornauer, N.J. de Souza. *J. Med. Chem.*, **26**, 486 (1983).
[3] Q.D. Jin, B.H. He. *Acta Bot. Yunnan*, **20**, 469 (1998).
[4] Q.D. Jin, X.H. Xie, Q.Z. Mu. *Nat. Prod. R&D*, **2**, 6 (1990).
[5] C.S. Yao, Y.L. Xu. *Chin. Chem. Lett.*, **12**, 339 (2001).
[6] Y.H. Shen, C.S. Yao, Y.L. Xu. *Chin. Chem. Lett.*, **13**, 740 (2002).