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The Diterpenoid Quinones from *Coleus forskohlii*

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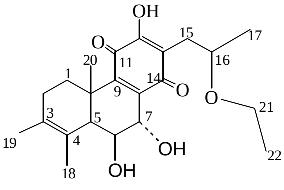
Abstract: Two new diterpenoid quinones, coleon S and T were isolated from the chloroform extract of the leaves of *Coleus forskohlii,* and based on spectroscopic data, their structures were identified as 1,4-phenathrenedione-4b,5,6,8a,9,10-hexahydro-3,9β,10α-trihydroxy-4b,7,8-rimethyl -2-(2-ethoxypropyl)(**1**) and 1,4-phenathrenedione-2,3,4b,5,6, 8a,9,10-octahydro-3,9β,10α-tri-hydroxy-4b,7,8-trimethyl-2-propylene(**2**), respectively.

Keywords: *Coleus forskohlii,* diterpenoid quinones, Coleon S, Coleon T.

Coleus forskohlii is only distributed in Yunnan and the southern regions of Asia. The decoction of the plant is used in local folk medicine against asthma, cough and bronchitis. Meanwhile, the plant was developed into a new drug for the treatment of asthma, cough, acute and chronic bronchitis several years ago by our group[1]. It appears that the Coleus is rich source of diterpenoids with different oxygenation patterns[2], and six diterpenoids have been isolated from its whole plant distributed in Yunnan[3]. But the constituent of its leaves has not been reported as yet. Our investigation on this plant led to the isolating two new diterpenoid quinones. Diterpenoid quinones were isolated from this plant for the first time. The present paper reported the isolation and identification of these two new compounds.



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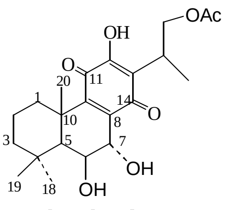
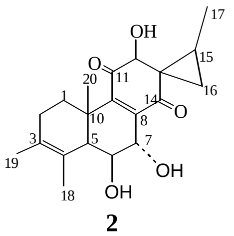


Lophanthoidin E



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Compound **1** was obtained as yellow needles. The molecular ion peak at *m*/*z* 390 in its MS, together with the ^{13}C NMR and DEPT spectra data indicated the molecular formula of $C_{22}H_{30}O_6$. The strong absorption at 3367, 1657, 1639, 1607 cm^{-1} in IR, along with the signals at δ_C 188.68s, 184.40s, 154.55s, 147.27s, 141.85s, 117.90s in the ^{13}C NMR revealed the presence of a diterpenoid quinone skeleton. Comparing the ^{13}C NMR data of compound **1** with those of lophanthoidin E[4] showed that they possessed similar structures in B-ring and C-ring except for A-ring. The signals of δ_C 126.81s, 126.02s combined with the absence of olefinic proton in ^{1}H NMR displayed the presence of two tetrasubstituted olefinic carbons in A-ring. In addition, the HMBC showed the cross peaks between δ_H 1.82(3H, s, 18-Me) to δ_C 126.81s(C-3), 126.02s(C-4) and 45.04d(C-5), and δ_H 1.65(3H, s, 19-Me) to δ_C 30.75t(C-2), 126.81s(C-3), 126.02s(C-4), indicating that the double bond should be at C-3 and C-4. On the other hand, the presence of three methylenes (35.07t, 30.75t, 30.44t), an oxygenated methine and a methyl attached to a methine suggested that a propyl occurred at C-13, which was oxygenated at C-2. The assumption was supported by the correlation of δ_H 2.74(1H, dd, J = 5.40, 13.8, 15-Ha), 2.46(1H, dd, J = 7.53, 13.8, 15-Hb) to δ_C 154.55s(C-12), 117.90s(C-13), 188.68s(C-14), 74.69d(C-16), 20.37q(C-17) in HMBC. The signals of δ_C 64.11t, 15.93q in ^{13}C NMR exhibited the presence of oxygenated ethyl. The correlation between δ_H 3.51(2H, q, J = 7.00, H-21) to δ_C 74.69d(C-16) and 15.93q(C-22) exhibited that the oxygenated ethyl was attached to C-16. The signals of δ_H 3.86(1H, d, J = 3.60), 4.18(1H, d, J = 4.50) in ^1H NMR showed correlation to C-5, C-6, C-7 and C-6, C-7, C-8 in HMBC respectively, but no correlation to any carbon was observed in HMQC. Hence, they were attributed to the proton signals of 6β-OH and 7α-OH. HMBC, HMQC and ^1H-^1H COSY spectra data were identical to this assumption. Accordingly, compound **1** was identified as1,4-phenanthrenedione-4b,5,6,8a,9,10-hexahydro-3,9β,10α-trihydroxy-4b,7,8-trimethyl-2-(2-ethoxypropyl), and named as Coleon S.

Compound **2** was obtained as white needles (acetone-petroleum ether). The molecular ion peak at *m*/*z* 346 in its MS, together with ^{13}C NMR and DEPT spectra data suggested the molecular formula of $C_{20}H_{26}O_5$. The absorption peaks at 3521, 1699, 1673, 1609 cm^{-1} in the IR exhibited that compound **2** possessed a diterpenoid quinone skeleton. Comparing the ^{13}C NMR data of compound **2** with those of compound **1** showed that they possessed the similar skeleton expect for C-12 and C-13. The signals of δ_C 154.55s (C-12), 117.90s (C-13) in compound **1** were replaced by δ_C 77.24d, 36.37s in compound **2**, indicating that a single bond should be at C-12 and C-13. In addition, according to the molecular formula of $C_{20}H_{26}O_5$, compound **2** shall has an extra degree of unsaturation, a methine, a methyl attached to the methine and a methylene, which suggested that a cyclopropane substituted by a methyl attached at C-13. The correlation of H-16 to C-12, C-13, C-14, C-15 and H-17 to C-12, C-13, C-15, C-16 in HMBC further confirmed the assumption. HMBC, HMQC and ^1H-^1H COSY also supported the above deduces. Therefore, compound **2** was elucidated as 1, 4-phenanthrenedione-2,3,4b,5,6,8a,9,10-octahydro-3,9β,10α-trihydroxy-4b,7,8-trimethyl-2-propylene, and named as Coleon T.

Experimental

General: Kofler melting points were uncorrected; IR were recorded on KBr discs with a Perkin-Elmer 577 spectrometer. UV were obtained in MeOH on UV-210A spectrometer. EIMS (positive) were measured on a VG Auto Spec-3000 spectrometer with direct inlet 70 ev or 20ev. NMR were run on a Bruker AM-400 spectrometer using TMS as internal standard; chemical shift values were reported in δ (ppm) units (CD_3COCD_3 and $CDCl_3$). Coupling constant (J) were expressed in Hz.

Plant material: The leaves of *Coleus forskohlii* were collected in Huize, Yunnan, China in 1999, and were identified by Prof. Zongyu Wang. A voucher specimen was deposited in the Herbarium of Kunming Institute of Botany, Academia Sinica.

Extraction and isolation: 2.5 kg dried leaves of *Coleus forskohlii* were extracted with 6000mL of 95% ethanol for 15 days in room temperature. The extract was decoloured with 100g active charcoal and the solvent was removed *in vacuum*. The residues were solved in H_2O-MeOH (3:1) and evaporated the MeOH. The aqueous solution was extracted with $CDCl_3$ (3x200mL), the $CDCl_3$ extract evaporated to give 60g of residues. The residues were subjected to CC silica gel, eluted with petroleum ether-acetone (from petroleum ether to petrol ether-acetone 1:1). The fractions were combined by monitoring with TLC to obtain fractions B1~B20. Then B1 (4g) was further purified repeatedly on silica gel CC with petroleum ether-acetone 10:1 to give compound **1**; B2 (8g) was chromatographed repeatedly on silica gel eluted with petroleum ether-acetone 5:1 and recrystallized repeatedly in petroleum ether-acetone 3:1 to afford compound **2**.

Table 1 The ^{13}C NMR of compound **1** and **2** (100MHz)#

Carbon	**1**	**2**	Carbon	**1**	**2**
1	35.07t	32.70t	12	154.55s	77.24d
2	30.75t	29.70t	13	117.90s	36.37s
3	126.81s	127.94s	14	188.68s	197.26s
4	126.02s	123.17s	15	30.44t	22.11d
5	45.04d	43.76d	16	74.69d	27.11t
6	70.73d	70.98d	17	20.37q	13.27q
7	67.80d	66.95d	18	14.96q	14.60q
8	141.85s	140.83s	19	19.07q	19.04q
9	147.27s	156.38s	20	20.33q	20.59q
10	37.71s	36.82s	21	64.11t	
11	184.40s	198.16s	22	15.93q	

#Compound **1** was measured in CD_3COCD_3, Compound **2** in $CDCl_3$, chemical shifts are given in ppm with TMS as internal standard.

Table 2 The ^1H NMR data of compound **1** and **2** (100MHz)#

Compound **1**		Compound **2**	
H	Chemical Shift	H	Chemical Shift
1α-H	1.44(1H, sext, J=5.10, 7.25, 12)	1α-H	1.43(1H, m)
1β-H	2.58(1H, m)	1β-H	2.05(1H, m)
2α-H	2.22(1H, m)	2α-H	2.15(m)
2β-H	2.07(1H, m)	2β-H	2.00(m)
5α-H	2.58(1H, brs)	5α-H	2.47(1H, brs)
6α-H	4.36(1H, m, J=3.60, 1.75, 1.70)	6α-H	4.31(1H, brs)
7β-H	4.68(1H, m, J=4.50, 2.40, 1.90)	7β-H	4.55 (1H, brs)
15-Ha	2.74(1H, dd, J=5.40, 13.8)	12-H	3.75(1H, brs)
15-Hb	2.46(1H, dd, J=7.53, 13.8)	15-H	2.05(m)
16-H	3.65(1H, sext, J=6.20, 7.53, 5.40)	16-Ha	0.91(1H, dd, J=3.75, 7.15)
17-H	1.05(3H, d, J=6.20)	16-Hb	1.26(1H, dd, J=3.75, 7.15)
18-H	1.82(3H, s)	17-H	1.22(3H, d, J=5.12)
19-H	1.65(3H, s)	18-H	1.76(3H, s)
20-H	1.37(3H, s)	19-H	1.62(3H, s)
6β-OH	3.86(1H, d, J=3.60)	20-H	1.39(3H, s)
7α-OH	4.18(1H, d, J=4.50)		
21-H	3.51(2H, q, J=7.00)		
22-H	1.09(3H, t, J=7.00)		

#Compound **1** was measured in CD_3COCD_3, Compound **2** in $CDCl_3$, chemical shifts are given in ppm with TMS as internal standard.

Compound **1**: $[\alpha]_D^{25}$ 58.75° (MeOH), mp: 117~119°C, UV λ_{max}^{MeOH}: 213 nm; IR: 3367, 2978, 2923, 2887, 2830, 1657, 1639, 1607, 1428, 1400, 1375, 1337, 1305, 1285, 1267, 1213, 1160, 1148, 1128, 1085, 1073, 1043, 1017, 1000, 979 cm-1; MS(*m/z*, %): 390(37, M^+), 374(10, M^+-CH_3-H^+), 344(29, M^+-C_2H_5OH), 326(12, 344-H_2O), 311(15, 326-CH_3), 300(80, 374-C_4H_9OH), 283(11), 271(9), 257(6), 84(5), 73(100); ^{13}CNMR data see table 1, ^{1}HNMR data see **Table 2**.

Compound **2**: $[\alpha]_D^{25}$ 225.56° (MeOH), mp: 171~173°C, white needles (petrol ether-acetone), UV λ_{max}^{MeOH}: 237.5 nm; IR: 3512, 2934, 1699, 1673, 1609, 1401, 1378, 1315, 1281, 1214, 1174, 1137, 1098, 1030, 996, 915, 768, 736 cm-1; MS(*m/z*, %): 346(6, M^+), 330(26, M^+-CH_4), 328(100, M^+-H_2O), 313(28, 328-CH_3), 310(76, M^+-$2H_2O$), 299(36), 295(61, M^+-$2H_2O$-CH_3), 282(21), 277(23), 267(21), 257(15), 249(17), 234(12), 217(9), 205(7), 179(7), 149(7), 133(3), 122(5), 109(7), 95(9), 83(3), 69(3); ^{13}C NMR data: see table 1, ^1H NMR data: see table 2.

Table 3 Correlation of ^1H NMR and HMBC of compound **1**

HMBC		**H-H COSY**	
H	Correlative C	H	Correlative H
1α-H	C-1, C-2, C-5, C-9, C-10, C-20	1α-H	1β-H, 2β-H, 2α-H
1β-H	C-2, C-3, C-5, C-9, C-10, C-20	1β-H	1α-H, 2β-H, 2α-H
2α-H	C-2	2α-H	1α-H, 1β-H, 2β-H
2β-H	C-1, C-2	2β-H	1α-H, 1β-H, 18-H, 2α-H
5α-H	C-2, C-3, C-4, C-5, C-6, C-9, C-10	5α-H	6-H, 19-H, 18-H
6α-H	C-7, C-8, C-10	6α-H	5α-H, 6β-OH, 7β-H
7β-H	C-5, C-6, C-8, C-9, C-14	7β-H	6α-H, 7α-OH
15-Ha	C-12, C-13, C-14, C-16, C-17	15-Ha	15-Hb, 16-H
15-Hb	C-12, C-13, C-14, C-16, C-17	15-Hb	15-Ha, 16-H
16-H	C-13, C-15, C-21	16-H	15-Ha, 15-Hb, 17-H
17-H	C-16	17-H	16-H
18-H	C-3, C-4, C-5	18-H	2α-H, 2β-H, 5α-H, 19-H
19-H	C-2, C-3, C-4, C-5	19-H	1β-H, 18-H
20-H	C-1, C-5, C-9, C-10	20-H	1β-H, 2β-H, 2α-H
6β-OH	C-5, C-6, C-7	6β-OH	6α-H
7α-OH	C-6, C-7, C-8	7α-OH	7β-H
21-H	C-16, C-22	21-H	22-H
22-H	C-21	22-H	21-H

Table 4 Correlation of ^1H NMR and HMBC of compound **2**

HMBC		**H-H COSY**	
H	Correlative C	H	Correlative H
1α-H	C-2, C-9, C-10, C-20	1α-H	1β-H, 2α-H, 2β-H
1β-H	C-2, C-3, C-5, C-9, C-10, C-20	1β-H	1α-H, 2α-H, 2β-H
2α-H	C-1	2α-H	1α-H, 2β-H
2β-H	C-3, C-4, C-10	2β-H	1α-H, 2α-H
5α-H	C-3, C-4	5α-H	6α-H, 18-H, 19-H
6α-H	C-4, C-5, C-7, C-8, C-10	6α-H	5α-H, 7β-H
7β-H	C-5, C-6, C-8, C-9, C-14	7β-H	6α-H
12-H	C-9, C-13, C-14, C-16	12-H	no correlation
16-Hb	C-12, C-13, C-14 , C-15, C-17	15-H	16-Ha, 16-Hb
16-Ha	C-13, C-14 , C-15, C-17	16-Ha	16-Hb, 15-H
17-H	C-12, C-13, C-15, C-16	16-Hb	16-Ha, 15-H
18-H	C-3, C-4, C-5	17-H	15-H
19-H	C-2, C-3, C-4	18-H	2α-H,2β-H,5α-H, 19-H
20-H	C-1, C-5, C-9, C-10	19-H	18-H, 5α-H
		20-H	1β-H, 2α-H

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