

A new diterpenoid from *Isodon lophanthoides* var. *gerardianus*

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A new diterpenoid, 11,12-dihydroxyabieta-7-oxo-8,11,13-trien-15-ol, along with two known diterpenoids were isolated from the roots of *Isodon lophanthoides* var. *gerardianus*. The structures of the three compounds were elucidated by spectroscopic methods and literatures.

Keywords: *Isodon lophanthoides* var. *gerardianus*, diterpenoid

Isodon lophanthoides var. *gerardianus* is widely distributed in South and Southeast Asia.¹ It is a famous folk medicine for treatment of enteritis, jaundice, hepatitis, laryngo-pharyngitis, leprosy and ascariasis in South China.² A number of abietane diterpenoids have been isolated from this species.^{3–5} In this study, we investigated the aerial parts of this plant, and we isolated three abietane diterpenoids, a new 11,12-dihydroxyabieta-7-oxo-8,11,13-trien-15-ol (**1**), and two known 16-acetoxy-7 α -methoxyroyleanone (**2**),⁶ and horminone (**3**),⁷ and characterised their structures through spectroscopic methods.

Compound **1** was revealed to have the molecular formula C₂₀H₂₆O₄ by HR-ESIMS [M + Na]⁺ ion at *m/z* 353.1725. The UV absorption at 333 and 284 nm indicated the presence of the benzene ring. IR absorption implied the presence of hydroxyl (3424 cm⁻¹) group. The ¹H and ¹³C NMR data (Table) revealed the presence of 20 carbon signals, which were sorted by a DEPT experiment into 5 methyls, 3 methylenes, 2 olefinic methines and 10 quaternary carbon signals. A hydroxyl group (δ_c 76.7), a double-bond conjugated with a carbonyl carbon (δ_c 175.2, 123.3, and 185.7), and an aromatic ring signals (δ_c 121.5, 138.8, 147.0, 142.5, 129.3, and 114.7) were also observed respectively. The unsaturation degree of **8** and the previously described data above suggested that it was an abietane diterpenoid with an aromatic ring. The partial structure (C-1–C-3) was deduced from detailed analyses of 2D NMR data (¹H–¹H COSY) of **1** (Fig. 2). The HMBC crosspeaks (Fig. 2) of H₃-19 to C-3, 4, 5, and 18 indicated the connection among C-3, 5, 18, and 19 through C-4. HMBC correlations for H₃-20 to C-1, 5, 9, and 10 indicated connection among C-1, 5, 9, and 20 through C-10. On the other hands, HMBC correlations for H-6 to C-4, 5, 7, and 8 supported the connectivity of the double-bond conjugated with the carbonyl carbon. And the

substituted of the benzene ring were confirmed by the HMBC correlations of H-14 with C-7, 8, and 15. Furthermore, the connection between C-13 and 15 was deduced from HMBC correlations of H₃-16 to C-13, 15 and 17. Since the abietane diterpenoids isolated from the genus *Isodon* possess an *ent*-configuration,^{3–5} the absolute stereochemistry of **1** was tentatively assigned an abietane configuration. The structure of **1** was established as 11,12-dihydroxyabieta-7-oxo-8,11,13-trien-15-ol (Fig. 1). Compound **2** was obtained as yellow needles. Its data of melting point and rotation, m.p. 184–185 °C and $[\alpha]_D^{16} + 13.0^\circ$ (C 0.5, MeOH) were the same as the values for 16-acetoxy-7 α -methoxyroyleanone⁶ and the NMR spectra of **2** were also similar to this compound.⁶ Consequently **2** was determined to be 16-acetoxy-7 α -methoxyroyleanone. Compound **3** had m.p. 175–177 °C, $[\alpha]_D^{19} - 133^\circ$ (C 1.2, CHCl₃), and comparison of the NMR spectra with the literature,⁷ showed that **3** was horminone. However, the rotations are those of the normal abietane series.

Experimental

The melting points of the natural products were determined on an XRC-1 apparatus and were uncorrected. Optical rotations were carried out on a Perkin-Elmer model 241 polarimeter. UV spectra were obtained using a Shimadzu UV-2401A. IR spectra were recorded as KBr pellets on a Perkin-Elmer 599B spectrophotometer. MS were determined on a Bruker Daltonics Apex III mass spectrometer. NMR spectra were measured on Bruker DRX-400 spectrometers with TMS as int. standard and CDCl₃ as solvent. Silica gel (80–100, and 200–300 mesh) were used for column chromatography and silica gel GF254 for TLC (Qingdao Marine Chemical Co., China). Sephadex LH-20 (GE), reversed-phase C-18 silica gel (60 mesh, Merck). Agilent 1220 LC equipped with a Welchrom C-18 column (4.6 × 250 mm) was used for HPLC analysis and a semi-preparative Welchrom C-18 column (10 × 250 mm) was used in sample preparation.

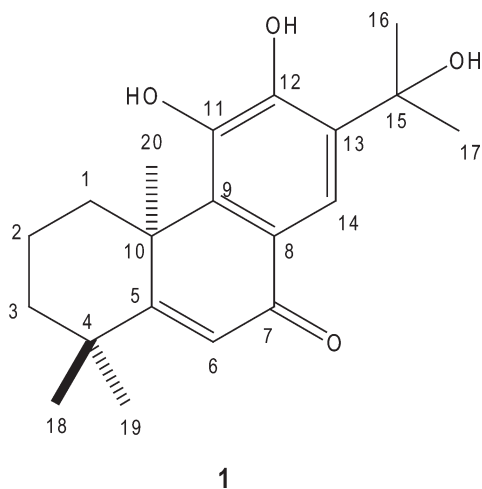


Fig. 1 Chemical structure of compound **1**.

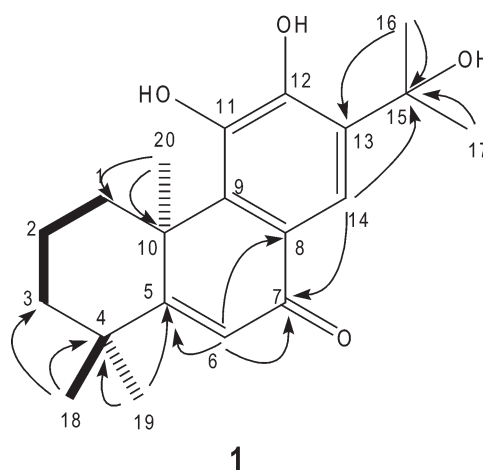


Fig. 2 The key ¹H–¹H COSY (H–H) and HMBC (H→C) correlations of **1**.

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Plant Material

The roots of *Isodon lophanthoides* var. *gerardianus* were purchased from Wanshoulu Chinese medicine market in Xi'an, P.R. China, in June 2011. A voucher specimen (No. 20110601) is deposited in Xi'an Medical University, Xian, Shaanxi., P.R. China.

The plant material was identified by Prof. Suo You-Rui, Northwest Institute of Plateau Biology, Chinese Academy of Sciences.

Extraction and isolation

Air-dried roots of *I. lophanthoides* (0.5 kg) were extracted by 75% ethanol three times (each 3 days and 20 L) at room temperature. The extracts were condensed *in vacuo* to afford crude residue (165 g) which was suspended in H₂O. The aqueous suspension was subsequently partitioned successively with EtOAc to afford EtOAc fraction (68 g), which was subjected to column chromatography on silica gel using a step gradient elution of CHCl₃-MeOH. The fractions obtained from CHCl₃-MeOH (2:1) elution were combined and subjected to repeated column chromatography and further purified by HPLC to yield pure compounds **1** (7 mg), **2** (3 mg), and **3** (3 mg).

11,12-Dihydroxyabieta-7-oxo-8,11,13-trien-15-ol (1): White solid. m.p. 166–168 °C. $[\alpha]_D^{19}$ + 42.0° (C 0.31, MeOH). UV (MeOH) λ_{max} (log ϵ) 406 (4.31), 333 (4.15), 284 (3.51), 251 (3.01) nm. IR (KBr) ν_{max} cm⁻¹: 3424, 2967, 2928, 1658, 1623, 1562, 1467, 1374, 1154, 1004. HR-ESIMS: revealed $[M + Na]^+$ ion at m/z 353.1725 (calcd 353.1728 for C₂₀H₂₆O₄). ¹H and ¹³C NMR: see Table 1.

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Table 1 ¹H and ¹³C NMR data (in CDCl₃) for compound **1** (δ in ppm, J in Hz)

No	δ_C^a	δ_H J/Hz ^b	No	δ_C^a	δ_H J/Hz ^b
1 α	34.0 (t)	1.45 ^c	10	42.2 (s)	
1 β		3.34 ^c	11	147.0 (s)	
2 α	18.6(t)	1.60 ^c	12	142.5 (s)	
2 β		1.94 ^c	13	129.3 (s)	
3 α	40.5 (t)	1.67 ^c	14	114.7(d)	7.58 (1H, s)
3 β		1.42 ^c	15	76.7 (s)	
4	38.1 (s)		16	30.3 (q)	1.67 (s)
5	175.2 (s)		17	30.4 (q)	1.65 (s)
6	123.3 (d)	6.43 (1H, s)	18	33.1 (q)	1.95 (s)
7	185.7 (s)		19	24.5 (q)	1.69 (s)
8	121.5 (s)		20	30.4 (q)	1.96 (s)
9	138.8 (s)				

^aAt 125 MHz; ^bat 500 MHz; ^coverlap.

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