



Two new diterpenoids from *Isodon serra*

Fu Lin Yan^{a,*}, Lai Bin Zhang^a, Ji Xia Zhang^a, Han Dong Sun^b

^a Pharmacy College, Xinxiang Medical University, Xinxiang 453003, China

^b Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204, China

Received 13 June 2007

Abstract

From the aerial part of *Isodon serra*, two new ent-6,7-seco-kaurane-type diterpenoids, 15 α ,20 β -dihydroxy-6 β -methoxy-6,7-seco-6,20-epoxy-1,7-olide-ent-kaur-16-ene (1) and 6 α ,15 α -dihydroxy-20-aldehyde-6,7-seco-6,11 α -epoxy-1,7-olide-ent-kaur-16-ene (2) were isolated. Their structures were elucidated by spectroscopic means.

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Keywords: Labiatae; *Isodon serra*; ent-6,7-seco-Kaurane diterpenoid

Isodon serra (Labiatae) is widely distributed in China and has various bioactivities. It has been used for the treatment of acute jaundice hepatitis and acute cholecystitis in folk medicine [1]. Further investigation of this plant material led to the isolation of two new ent-6,7-seco-kaurane-type diterpenoids. Their structures were elucidated by spectroscopic techniques (1D NMR, 2D NMR, HR-MS and IR).

Compound 1, obtained as colorless needles, mp 196–197 °C, $[\alpha]_D^{23} -141.0$ (c 0.19, CH₃OH). HRESIMS showed $[M + Na]^+$ at m/z 401.1939 (calcd. 401.1940), indicating a molecular formula of C₂₁H₃₀O₆. The IR spectrum exhibited the presence of a lactone carbonyl group (1717 cm⁻¹) and hydroxyl groups (3359 cm⁻¹). The NMR spectra of compound 1 suggested a diterpenoid skeleton. The ¹³C NMR (DEPT) spectrum (Table 1) showed 21 carbon signals, consisting of three Me (including an oxygenated one), six CH₂ (including an olefinic one), seven CH (including four oxygenated ones), a lactone carbonyl group and four quaternary C-atoms. The ¹H NMR spectrum (Table 1) indicated the presence of a methoxyl group (δ 3.33) and a terminal double bond (δ 5.04, 5.14). On examination of the HMQC and HMBC spectra of compound 1, the methoxyl group at δ_C 55.2(q) (δ_H 3.33) was located at C-6 based on the HMBC correlation of OCH₃ with C-6. On the other hand, the positions of hydroxyl groups were determined by the HMBC correlations between the H-15 (δ 5.12) and C-7 (δ 176.7), C-9 (δ 31.4), C-14 (δ 33.7), C-17 (δ 108.9); H-20 (δ 5.60) and C-1 (δ 76.0), C-6 (δ 104.9), C-9 (δ 31.4), C-10 (δ 49.4).

The relative stereochemistry of 1 was confirmed by NOESY experiment. In its NOESY spectrum, H-15 (δ 5.12, s) showed a strong correlation with H-13 (δ 2.70, m) and H-14 (δ 1.78, 1.82, m); H-20 (δ 5.60, s) with H-2 (δ 1.86, 1.95, m) and H-19 (δ 0.96, s). It showed that the H-15 was in β -orientation and H-20 was in α -orientation. Based on the above spectral analysis and by comparison of its spectral data with the literatural values of similar structure [2,3], the

* Corresponding author.

E-mail address: yanfulin03@xxmu.edu.cn (F.L. Yan).

Table 1

¹H NMR (400 MHz), ¹³C NMR (100 MHz), DEPT and HMBC data of compounds 1 and 2

1				2			
No.	δ _H	δ _C	HMBC	No.	δ _H	δ _C	HMBC
1	4.44 (dd, <i>J</i> = 6.0, 11.6 Hz)	76.0 d	H-9, 20	1	4.50 (dd, <i>J</i> = 4.8, 8.4 Hz)	77.3 d	H-3,5,9
2	1.86, 1.95 m	23.7 t	H-1, 3, 5	2	1.76, 1.98 m	25.6 t	H-3
3	1.20 m	37.7 t	H-1, 2, 18, 19	3	1.41, 2.69 m	39.8 t	H-2,18,19
4		31.3 s	H-2, 5, 18, 19	4		33.4 s	H-2,3,5,18,19
5	2.02 s	54.2 d	H-2, 6, 18, 19	5	1.92 s	50.4 d	H-6,9,18,19
6	4.53 s	104.9 d	H-5, 20	6	5.93 s	92.2 d	H-5,11
7		176.7 s	H-14, 15	7		173.8 s	H-2,14
8		52.3 s	H-9, 13	8		49.8 s	H-9,13,14,15
9	2.75 (dd, <i>J</i> = 5.6, 12.4 Hz)	31.4 d	H-1, 12, 14, 15, 20	9	3.59 (d, <i>J</i> = 11.6 Hz)	33.2 d	H-12,14,15
10		49.4 s	H-5, 6, 9, 18, 19, 20	10		50.7 s	H-2,5,6,9
11	1.24, 1.75 m	19.4 t	H-9, 13	11	4.30 (dt, <i>J</i> = 8.4, 11.6 Hz)	62.9 d	H-6,9,12,13,14
12	2.16, 2.19 m	31.8 t	H-9, 14	12	1.42, 2.72 m	40.8 t	H-9,13,14
13	2.70 m	37.2 d	H-12, 14, 17	13	2.83 m	37.3 d	H-12,14,17
14	1.78, 1.82 m	33.7 t	H-9, 12,15	14	1.15, 1.70 m	32.3 t	H-9,12,15
15	5.12 s	77.9 d	H-9, 13, 14, 17	15	5.85 s	80.2 d	H-9,13,14,17
16		157.7 s	H-12, 14, 15, 17	16		158.8 s	H-15,17
17	5.14, 5.64 s	108.9 t	H-13, 15	17	5.57, 5.58 brs	109.5 t	H-15
18	0.98 s	33.2 q	H-3, 5, 19	18	0.94 s	30.4 q	H-2,3,5,19
19	0.96 s	23.6 q	H-3, 5, 18	19	1.13 s	21.9 q	H-3,5,18
20	5.60 s	102.0 d	H-1, 5, 6, 9	20	10.71 s	203.1 d	H-5,9
21	3.33 s	55.2 q	H-6				

structure of compound 1 was established as 15α, 20β-dihydroxy-6β-methoxy-6,7-seco-6,20-epoxy-1,7-olide-ent-kaur-16-ene (Fig. 1).

Compound 2, obtained as colorless needles, mp 221–222 °C, $[\alpha]_D^{23} -11$ (c 0.12, CH₃OH). HRESIMS showed $[M + Na]^+$ at *m/z* 385.1627 (calcd. 385.1625), indicating a molecular formula of C₂₀H₂₆O₆. The IR spectrum exhibited the presence of a lactone carbonyl group (1705 cm⁻¹), an aldehyde group (1733 cm⁻¹) and hydroxyl groups (3392 cm⁻¹). The ¹³C NMR (DEPT) spectrum of 2 (Table 1) exhibited 20 signals: two Me, five CH₂ (including an olefinic one), eight CH (including four oxygenated ones and one aldehyde), a lactone carbonyl group and four quaternary C-atoms, respectively. The ¹H NMR spectrum (Table 1) indicated the presence of a aldehyde group (δ 10.71) and a terminal double bond (δ 5.57, 5.58). Considering the structures of diterpenoids previously isolated from the genus isodon [4], along with one characteristic lactone-type C=O signal at δ_C 173.8 (s) assignable to C-7, and a terminal double bond signal at δ_C 109.5 (t) and 158.8 (s) assignable to C-17 and C-16, as well as four oxygenated CH (δ_C 62.9, 77.3, 80.2, 92.3), compound 2 was assigned an 6,7-seco-1,7-olide-kauranoid structure [5]. On examination of the HMQC and HMBC spectra of compound 2, the moiety structure of 6,11-epoxy was determined by the HMBC correlations between the H-6 (δ 5.93) and C-11 (δ 62.9), C-10 (δ 50.7), C-5 (δ 50.4). On the other hand, the positions of hydroxyl groups were determined by the HMBC correlations between the H-6 (δ 5.93) and C-11 (δ 62.9), C-10 (δ

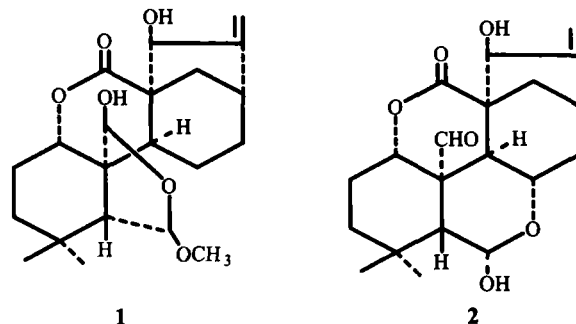


Fig. 1. The structures of compounds 1 and 2.

50.7), C-5 (δ 50.4); H-15 (δ 5.85) and C-17 (δ 109.5), C-14 (δ 32.3), C-9 (δ 33.2). This was also supported by the observed cross peaks in its ^1H – ^1H COSY spectrum between H-6 (δ 5.93, s) and H-5 (δ 1.92, s) and 6-OH (δ 8.80, s) as well as H-9 (δ 3.59, d) and H-11 (δ 4.30, dt).

The observed NOESY correlations from β -oriented H-5 to both H-6 and H-11, established that the H-6 and H-11 were in β -orientation; H-15 no correlations with H-9, it showed that the H-15 was in β -orientation.

Based on the above evidence, the structure of compound **2** was elucidated as 6α , 15α -dihydroxy-20-aldehyde-6,7-seco-6,11 α -epoxy-1,7-olide-ent-kaur-16-ene (Fig. 1).

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