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Two new *ent*-kaurane diterpenoids from *Isodon excisoides*

Ji Xia Zhang [a,*], Yong Xue Wang [a], Zhi An He [a], Fu Lin Yan [a], Han Dong Sun [b]

[a] *Pharmaceutical Laboratory, Xinxiang Medical University, Xinxiang 453003, China*
[b] *State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204, China*

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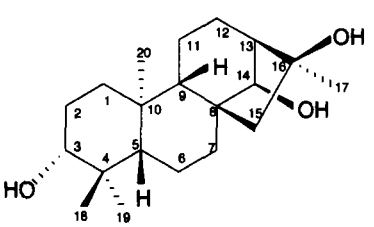
Abstract

Two new *ent*-kaurane diterpenoids taihangexcisoidesin A and B (**1** and **2**), were isolated from the EtOAc extract of the leaves of *Isodon excisoides*. Their structures were determined on the basis of spectroscopic methods.

Keywords: *Isodon excisoides*; *ent*-Kaurane; Diterpenoid; Taihangexcisoidesin A and B

Isodon species are rich in *ent*-kaurane diterpenoids, some of which have antitumor, antibacterial, and antiinflammatory activities [1,2]. To search more bioactive compounds in genus *Isodon*, two new *ent*-kaurane diterpenoids taihangexcisoidesin A and B (**1** and **2**), were isolated from the EtOAc extract of the leaves of *Isodon excisoides* (Sun ex C.H. Hu) C.Y. Wu et H.W. Li, which was collected in Taihang Mountains, Henan province. This paper presents the structural elucidation of the new compounds.



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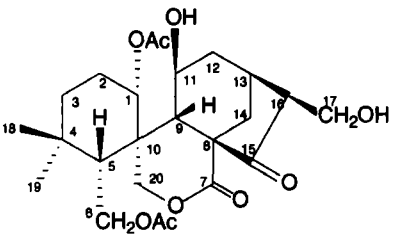

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Compound **1**, obtained as colourless needles from MeOH, has a molecular formula $C_{20}H_{34}O_3$ based on its HR-ESI-MS (*m/z* 345.2391 $[M+Na]^+$, calcd. 345.2406) and the ^1H and ^{13}C NMR data, suggesting four degrees of unsaturation. In its ^{13}C NMR (DEPT) spectrum showed the signals of four methyls, seven methylenes, five methines including two oxymethines [δ_C 78.1 (d), δ_H 3.44 (m, 1H) and δ_C 78.9 (d), δ_H 4.46 (d, 1H, J = 8.4 Hz)], and four quaternary carbons

* Corresponding author.
E-mail address: zjx@xxmu.edu.cn (J.X. Zhang).

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including one oxygenated [δ_C 79.2 (s)]. Considering the compounds isolated from the *Isodon* genus, compound **1** had a 20-non-oxygenated-*ent*-kaurane diterpene skeleton. The chemical shifts at δ_H 6.32 (d, 1H, J = 6.4 Hz), δ_H 5.98 (s, 1H) and 5.70 (br s, 1H) in the ^{1}H NMR spectrum and the absorption at 3351 and 3318 cm^{-1} in the IR spectrum suggested the existence of three hydroxyl groups. In the HMBC spectrum, the correlations were clearly observed among H-14 with C-8, C-9, C-15 and C-16, H-3 with C-1 and C-5, H_2-12, H_2-15 and H_3-17 with C-16 (Fig. 1). Meanwhile, according to the cross-peaks in the HMBC and ^{1}H-^{1}H COSY spectra, three hydroxyl groups were obviously located at C-3, C-14 and C-16, respectively.

The relative configuration of the substituents were revealed by NOESY experiments (Fig. 2). In the NOESY spectrum, there were correlations of H-3 with H-1β, H-5β and Me-18, H-14 with H-6α, H-12α, H-13α and Me-20. Thus, OH-3 and OH-14 have the α and β orientation, respectively. The β-orientation of OH-16 was suggested by the clear cross-peaks of H_3-17 with H-13α in NOESY spectrum as shown in Fig. 2. Therefore, **1** was elucidated as 3α, 14β, 16β-trihydroxy-*ent*-kaurane, and named taihangexcisoidesin A.

Compound **2** was obtained from MeOH as colourless needles, showed the molecular ion peak at *m/z* 489.2083 $[M+Na]^+$ in its HR-ESI-MS, consistent with the molecular formula $C_{24}H_{34}O_9$ which was confirmed by its ^{13}C NMR spectrum presenting signals for 24 carbons of molecular formula including four carbons of two acetoxyl groups. On the basis of the characteristic lactone carbonyl signal at δ_C 170.3 (s) due to C-7 and noticeable oxygenated methylene signals [δ_C 67.6 (t), C-20; δ_H 5.08 and 4.79 (ABd, each 1H, J = 12.4 Hz), H-20a/b], compound **2** was inferred to be a 6,7-seco-7,20-olide *ent*-kauranoid. Comparison of the spectroscopic data of **2** with those of robdosin B [3] indicated that **2** was nearly identical with robdosin B except for C-16 and C-17. The exomethylene group at C-16 of robdosin B was replaced by a methine (δ_C 57.4, C-16; δ_H 3.11, m, 1H, H-16α) and a hydroxymethyl group (δ_C 59.1, C-17; δ_H 4.39, m, 2H, H_2-17) in **2**, which was approved by the HMBC spectral evidence (Fig. 1). The 16β-CH_2OH was determined by the HMBC correlations of H_2-17 with C-13 and C-15, and the NOEs of H-16α with H-13α, H_2-17 with H-12β and H-9β (Fig. 2), which was also confirmed by the obvious upshift of C-12 (δ_C 33.1 in **2**, δ_C 41.5 in robdosin B) caused by the steric compress effect between H_2-17 and H-12β [4]. The β-orientation of H-1 was proved by the NOE of H-1 with H-5β. Similarly, H-11α was confirmed by the NOE among H-11α with H-14α. Thus, compound **2** was deduced as 16(*S*)-hydroxymethyl-11β-hydroxy-1α,6-diacetoxy-6,7-seco-7,20-olide-*ent*-kaur-15-one, named taihangexcisoidesin B.

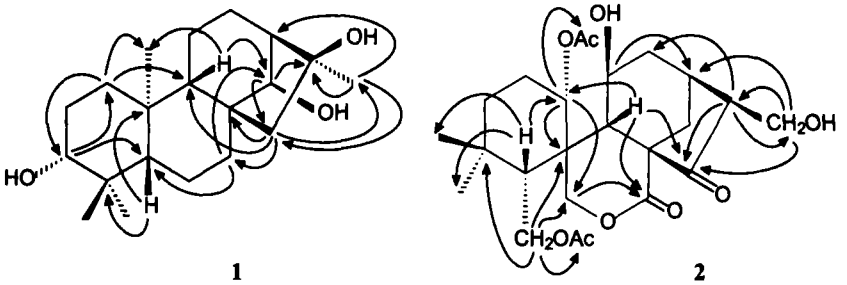

Fig. 1. Key HMBC correlations of compounds **1** and **2**.

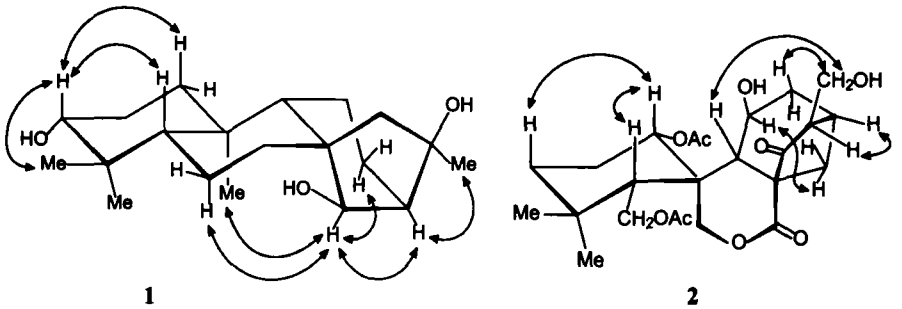

Fig. 2. Key NOESY correlations of compounds **1** and **2**.

Table 1
^{13}C (100 MHz) NMR spectral date of **1** and **2** in C_5D_5N (δ in ppm).

Position	δ_C		Position	δ_C	
	1	**2**		**1**	**2**
1	39.2 t	77.1 d	12	27.8 t	33.1 t
2	28.4 t	24.5 t	13	54.5 d	31.5 d
3	78.1 d	40.1 t	14	78.9 d	31.5 t
4	39.4 s	34.3 s	15	57.3 t	212.4 s
5	55.5 d	49.3 d	16	79.2 s	57.4 d
6	20.2 t	61.9 t	17	24.4 q	59.1 t
7	34.1 t	170.3 s	18	28.0 q	34.0 q
8	51.3 s	59.5 s	19	18.0 q	24.1 q
9	59.6 d	44.1 d	20	16.3 q	67.6 t
10	39.4 s	44.7 s	$O\underline{C}OCH_3$		170.4 s, 170.5 s
11	18.0 t	65.9 d	$OCO\underline{C}H_3$		21.5 q, 21.2 q

Compound **1**: $C_{20}H_{34}O_3$, colourless needles, m.p. 237–239 °C, IR ν^{KBr} (cm^{-1}): 3351, 3318, 2946, 2864, 1453, 1066, 1040, 1028, 976, 934. ^{1}H-NMR (C_5D_5N, 400 MHz, δ (ppm)): 4.46 (d, 1H, J = 8.4 Hz, H-14α), 3.44 (m, 1H, H-3β), 2.78 (d, 1H, J = 12.8 Hz, H-7a), 2.32 (br s, 1H, H-13α), 2.22 and 1.72 (d, each 1H, J = 13.6 Hz, H-15a/b), 1.88 (m, 2H, H_2-2), 1.74 (m, 1H, H-1a), 1.67 (m, 2H, H_2-12), 1.60 (m, 2H, H_2-11), 1.52 (s, 3H, Me-17), 1.45 (m, 2H, H_2-6), 1.14 (m, 1H, H-9β), 1.13 (m, 1H, H-7b), 1.20, 0.98 and 0.97 (s, each 3H, 3× Me), 0.92 (m, 1H, H-1b), 0.85 (dd, 1H, J = 11.6, 2.0 Hz, H-5β). HR-ESI-MS *m/z*: 345.2391 $[M+Na]^+$ (calcd. 345.2406). ^{13}C NMR data see Table 1.

Compound **2**: $C_{24}H_{34}O_9$, colourless needles, m.p.180–182 °C, $[\alpha]_D^{20}$ +53.8 (*c* 0.02, MeOH), IR ν^{KBr} (cm^{-1}): 3572, 3471, 3322, 2993, 2944, 2837, 2822, 1726, 1708, 1640, 1409, 1375, 1301, 1262, 1233, 1126, 1054. ^{1}H-NMR (C_5D_5N, 400 MHz, δ (ppm)): 5.57 (dd, 1H, J = 5.6, 9.6 Hz, H-1β), 5.08 and 4.79 (ABd, each 1H, J = 12.4 Hz, H-20a/b), 4.57 and 4.47 (dd, each 1H, J = 12.8, 4.0 Hz, H-6a/b), 4.41 (m, 1H, H-11α), 4.39 (m, 2H, H_2-17), 3.29 (t, 1H, J = 7.6, 3.6 Hz, H-5β), 3.11 (m, 1H, H-16α), 3.06 (d, 1H, J = 9.6 Hz, H-9β), 2.85 (br s, 1H, H-13α), 2.62 (dd, 1H, J = 12.8, 4.0 Hz, H-14a), 2.32 (d, 1H, J = 12.8 Hz, H-14b), 2.24 (m, 2H, H_2-12), 2.17 and 1.98 (s, each 3H, 2× OAc), 1.92 (m, 2H, H_2-2), 1.33 (m, 2H, H_2-3), 0.91 and 0.87 (s, each 3H, 2× Me). HR-ESI-MS *m/z*: 489.2083 $[M+Na]^+$ (calcd. 489.2101). ^{13}C NMR data see Table 1.

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