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ent-Atisane and *ent*-kaurane diterpenoids from *Isodon rosthornii*☆

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ABSTRACT

A new *ent*-atisanoid (**1**) and three new *ent*-kauranoids (**2**-**4**) belonging to different types, along with four known compounds were isolated from *Isodon rosthornii*. Their structures were established by means of extensive spectroscopic analysis. The absolute configuration of **1** was further determined by X-ray diffraction. Compounds **1** and **5** are the first example of atisane-type diterpenoid from this plant.

1. Introduction

Isodon is a cosmopolitan and important genus of Lamiaceae family. The use of *Isodon* species in Chinese folk medicine has a long tradition. Investigations proved *Isodon* species to be a pool of diverse structures of diterpenoids with a range of bioactivities, most of which were *ent*-kauranoids [1]. The discovery of a series of compounds with promising use in anti-inflammatory and anti-tumors, such as eriocalyxin B [2,3], pharicin B [4], oridonin [5], ponicidin [6], and adenanthin [7] further supported their folk use and brought great attention.

Isodon rosthornii, used to treat rheumatism and sore throat in Chinese folk therapy, was distributed in Sichuan and Guizhou provinces of China [8]. Previous studies on this species just led to the isolation of seven *ent*-kauranoids, some of which showed anti-bacteria activity [8–13]. For the secondary metabolites of the genus *Isodon* often differ when grows in different ecological environments, in continuation of our effort to find bioactive substances, we explored the plant indigenous to Qionglai City of Sichuan Province, which had even not been studied on the secondary metabolites. From the EtOAc section, two *ent*-atisanoids, including a new one, isorosthornin D (**1**), and six *ent*-kauranoids including a new 11,20-epoxy-*ent*-kauranoid (**2**), a new 3,20-epoxy-*ent*-kauranoid (**3**) and a new enmein-type diterpenoid (**4**) were isolated (Fig. 1). The absolute configuration of **1** were further confirmed by X-ray diffraction study. In this paper, we reported the isolation, stucture elucidation and the cytotoxic evaluation.

2. Experimental

2.1. General experimental procedures

Optical rotations were measured with a Horiba SEPA-300 polarimeter. UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. A Tenor 27 spectrophotometer was used for scanning IR spectroscopy with KBr pellets. 1D and 2D NMR spectra were recorded on Bruker AM-400 and DRX-500 spectrometers with TMS as internal standard. Unless otherwise specified, chemical shifts (δ) were expressed in ppm with reference to the solvent signals. HRESIMS was

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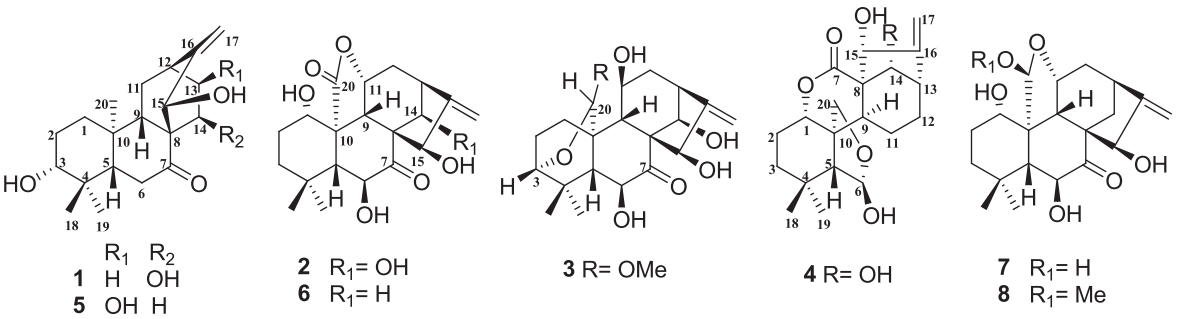

Fig. 1. The structures of compounds **1**–**8.**

performed on an API QSTAR time-of-flight spectrometer. HREIMS was performed on a Waters Auto Spec Premier P776 spectrometer. HSCCC was performed on TBE-300B. Semipreparative HPLC was performed on an Agilent 1100 HPLC with a Zorbax SB-C_{18} (9.4 mm × 25 cm) column. Column chromatography was performed with silica gel (200–300 mesh, Qing-dao Marine Chemical, Inc., Qingdao, China), Lichroprep RP-18 gel (40–63 μm, Merck, Darmstadt, Germany) and MCI gel (75–150 μm, Mitsubishi Chemical Corporation, Tokyo, Japan). Fractions were monitored by TLC, and spots were visualized by heating Si gel plates sprayed with 5% H_2SO_4 in EtOH.

2.2. Plant material

The aerial parts of *I. rosthornii* were collected Qionglai City of Sichuan Province, China, in July 2008, and was identified by Prof. Xi-Wen Li, Kunming Institute of Botany. A voucher specimen (KIB 200809003) has been deposited in the Herbarium of the Kunming Institute of Botany, Chinese Academy of Sciences.

2.3. Extraction and Isolation

The aerial parts (10 kg) of *I. rosthornii* were shade dried, powdered, and extracted with the 70% aqueous acetone (20 L) for four times (two days for each time) at room temperature. The resulting extract was evaporated to be concentrated. Then the concentrate without acetone (7 L) was partitioned by EtOAc. The EtOAc soluble portion (485 g) was subjected to column chromatography on a silica gel column (2000 g, 100–200 mesh) and eluting with step wise gradient of $CHCl_3$-Me_2CO (1:0, 9:1, 8:2, 7:3, 6:4, 1:1) to afford five major fractions (F_1–F_5). F_2–F_4 were first subjected to column chromatography on MCI gel respectively, eluted with CH_3OH:H_2O 90:10. After that, fraction 2 was purified by repeat flash chromatography on silica gel (200-300 mesh, eluted with petroleum ether-acetone 30:1) to afford compound **6** (10 mg).

Fraction 3 (63 g) was separated by RP-18 gel column chromatography (eluted with CH_3OH:H_2O 30:70–80:20 gradient) to yield four fractions (C1–C4). C1 was subjected to HSCCC ($CHCl_3$:CH_3OH:H_2O 4:3:2) and then was rechromatographed by silica gel, eluted with $CHCl_3$:acetone 30:1 to give compound **1** (25 mg). C2 was purified by HSCCC ($CHCl_3$:MeOH:H_2O 4:3:2) and then was separated by semi-preparative HPLC with CH_3OH:H_2O 50:50 to afford compounds **2** (2 mg), **5** (2 mg), and **8** (5 mg).

Fraction 4 (85 g) was first chromatographed by Rp-18 gel column chromatography with elution of CH_3OH:H_2O (30:70–80:20 gradient) and then was subjected to HSCCC ($CHCl_3$:CH_3OH:H_2O 4:3:2). After that, silica gel column (eluted with $CHCl_3$:acetone 30:1) and semipreparative HPLC with elution of CH_3OH:H_2O (50:50) were used to yield compounds **3** (2 mg), **4** (120 mg), and **7** (3 mg).

2.4. Spectroscopic data

Isorosthornin D (**1**), colorless crystals. $[\alpha]^{21}{}_D = -24.7$ ($c = 0.68$, MeOH). UV (MeOH): 203 (3.22) nm. IR (KBr): 3427, 2928, 2851, 1694, 1679, 1089, 1071, 1031 cm^{-1}. NMR: see Tables 1 and 2. HR-ESI-MS: 357.2031 ($[M + Na]^+$, $C_{20}H_{30}O_4Na$; calc. 357.2041).

Isorosthornin E (**2**), colorless oil. $[\alpha]^{18.6}{}_D = +41.4$ ($c = 1.6$, MeOH). UV (MeOH): 204 (3.39), 289 (2.84) nm. IR (KBr): 3424, 2924, 1631, 1432, 1032 cm^{-1}. NMR: see Tables 1 and 2. HR-EI-MS: 378.1663 ($[M]^+$, $C_{20}H_{26}O_7$; calc. 378.1679).

Isorosthornin F (**3**), white powder. $[\alpha]^{26.3}{}_D = -97.5$ ($c = 0.51$, MeOH). UV (MeOH): 204 (3.39) nm. IR (KBr): 3421, 2931, 1705, 1663, 1439, 1084, 1048 cm^{-1}. NMR: see

Table 1
^{13}C NMR data of compounds **1**–**4** (in C_5D_5N, δ in ppm, *J* in Hz)[a].

No.	1	2	3	4
1	27.7 (t)	80.0 (d)	27.5 (t)	76.4 (d)
2	37.5 (t)	30.4 (t)	22.5 (t)	24.3 (t)
3	77.7 (d)	41.9 (t)	76.3 (d)	37.6 (t)
4	39.3 (s)	35.6 (s)	38.2 (s)	31.2 (s)
5	52.1 (d)	53.6 (d)	58.3 (d)	55.0 (d)
6	38.5 (t)	75.6 (d)	73.0 (d)	102.0 (d)
7	212.8 (s)	208.9 (s)	210.5 (s)	173.2 (s)
8	59.8 (s)	63.5 (s)	63.8 (s)	59.1 (s)
9	44.3 (d)	51.9 (d)	54.4 (d)	40.9 (d)
10	37.0 (s)	60.2 (s)	54.3 (s)	50.9 (s)
11	28.7 (t)	75.1 (d)	64.3 (d)	19.0 (t)
12	37.3 (d)	39.1 (t)	40.1 (t)	32.7 (t)
13	38.1 (t)	46.7 (d)	48.5 (d)	46.5 (d)
14	66.1 (d)	75.5 (d)	76.8 (d)	74.4 (d)
15	67.1 (d)	73.1 (d)	74.1 (d)	75.5 (d)
16	155.8 (s)	159.0 (s)	156.6 (s)	159.7 (s)
17	108.8 (t)	110.3 (t)	108.0 (t)	109.1 (t)
18	27.8 (q)	36.3 (q)	29.6 (q)	33.1 (q)
19	15.7 (q)	23.2 (q)	24.2 (q)	23.3 (q)
20	14.7 (q)	177.6 (s)	99.6 (d)	73.3 (t)
OMe			54.3	

[a] NMR data of compounds **1**, **4** were recorded at 100 MHz; data for compounds **2** and **3** were recorded at 150 MHz. Assignments were made based on DEPT, HSQC, COSY, HMBC, and ROESY experiments.

Tables 1 and 2. HR-EI-MS: 394.2000 ([M]$^+$, $C_{21}H_{30}O_7$; calc. 394.1992).

Isorosthornin G (**4**), white powder. [α]26.3 D = −75.3 (c = 1.00, MeOH). UV (MeOH): 202 (3.15), 254 (2.37) nm. IR (KBr): 3417, 2948, 1716, 1060 cm^{-1}. NMR: see Tables 1 and 2. HR-EI-MS: 364.1891 ([M]$^+$, $C_{20}H_{28}O_6$; calc. 364.1886).

2.5. The cytotoxicity assay

The following human tumor cell lines were used: HL-60, SMMC-7721, A-549, MCF-7 and SW-480 which were obtained from ATCC (Manassas, VA, USA). All the cells were cultured in RPMI-1640 or DMEM medium (Hyclone, Logan, UT, USA), supplemented with 10% fetal bovine serum (Hyclone) at 37 °C in a humidified atmosphere with 5% CO_2. Cell viability was assessed by conducting colorimetric measurements of the amount of insoluble formazan formed in living cells based on the reduction of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) (Sigma, St. Louis, MO, USA) [14]. Briefly, 100 μL of adherent cells were seeded into each well of a 96-well cell culture plate and allowed to adhere for 12 h before drug addition, while suspended cells were seeded just before drug addition, both with an initial density of 1×10^5 cells/mL in 100 μL medium. Each tumor cell line was exposed to the test compound at various concentrations in triplicate for 48 h, with cisplatin and paclitaxel (Sigma) as positive controls. After the incubation, MTT (100 μg) was added to each well, and the incubation continued for 4 h at 37 °C. The cells were lysed with 100 μL of 20% SDS-50% DMF after removal of 100 μL medium. The optical density of the lysate was measured at 595 nm in a 96-well microtiter plate reader (Bio-Rad 680). The IC_{50} value of each compound was calculated by the Reed and Muench's method [15].

2.6. X-ray crystal structure analysis

Colorless crystals of **1** were obtained in CH_3OH. Intensity data were collected at 100 K on a Bruker APEX DUO diffractometer equipped with an APEX II CCD, using Cu $K\alpha$ radiation. Cell refinement and data reduction were performed with Bruker SAINT. The structures were solved by direct methods using SHELXS-97 [16]. Refinements were performed with SHELXL-97 using full-matrix least-squares, with anisotropic displacement parameters for all the non-hydrogen atoms. The H-atoms were placed in calculated positions and refined using a riding model. Molecular graphics were computed with PLATON. Crystallographic data (excluding structure factor tables) for the structures reported have been deposited with the Cambridge Crystallographic Data Center as supplementary publications no. CCDC 923358 for **1**. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB 1EZ, UK [fax: Int. +44(0) (1223) 336 033); e-mail: deposit@ccdc.cam.ac.uk].

Crystallographic data for compound (**1**): $C_{20}H_{30}O_4 \cdot H_2O$, M = 352.46, orthorhombic, a = 7.19610(10) Å, b = 11.6805(2) Å, c = 21.1935(3) Å; α = 90.00°, β = 90.00°, γ = 90.00°, V = 1781.40(5) Å^3, T = 100(2) K, space group $P2_12_12_1$, Z = 4, 8453 reflections measured, 3070 independent reflections (R_{int} = 0.0330). The final R_1 values were 0.0345 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.0901 ($I > 2\sigma(I)$). The final R_1 values were 0.0345 (all data). The final $wR(F^2)$ values were 0.0901 (all data). Flack parameter = −0.01(14).

3. Results and discussion

The EtOAc extract was subjected to repeated column chromatography to afford eight diterpenoids, including four new ones which were named as isorosthornins D–G (Fig. 1).

Table 2
^{1}H NMR spectroscopic data (in C_5D_5N, δ in ppm, J in Hz) of compounds **1**–**4**[a].

No.	1	2	3	4
1a	1.81 (m)	4.10 (dd, 10.5, 3.5)	2.52 (overlapped)	4.85 (overlapped)
1b			1.11 (m)	
2a	1.55 (m)	2.43 (m)	1.97 (m)	1.84 (m)
2b	0.98 (overlapped)	1.84 (overlapped)	1.80 (dd, 13.7, 11.5)	
3a	3.77 (dd, 11.0, 4.8)	1.59 (m)	3.40 (m)	1.32 (m)
3b		1.33 (overlapped)		1.25 (m)
5	1.53 (m)	1.84 (overlapped)	1.66 (d, 12.8)	2.26 (s)
6	2.63 (br s)	5.19 (br s)	4.90 (d, 12.8)	5.79 (s)
9	2.53 (m)	4.15 (d, 5.5)	2.80 (br s)	4.02 (dd, 13.0, 6.6)
11a	1.73 (m)	6.04(dd, 7.8, 5.5)	4.87 (overlapped)	2.22 (m)
11b	1.45 (m)			1.65 (m)
12a	2.55 (m)	2.73 (m)	2.54 (overlapped)	2.44 (m)
12b		2.08 (dd, 15.0, 7.8)	2.34 (d, 10.4)	1.86 (overlapped)
13a	2.30 (ddd, 13.0, 9.0, 3.8)	3.04 (d, 7.8)	3.13 (br s)	2.06 (d, 8.0)
13b	1.85 (overlapped)			
14	4.79 (dd,9.0, 3.8)	5.14 (br s)	4.84 (br s)	4.87 (overlapped)
15	5.77 (s)	6.51 (s)	6.46 (d, 9.7)	6.39 (s)
17a	5.52 (s)	5.70 (s)	5.66 (s)	5.67 (s)
17b	5.23 (s)	5.32 (s)	5.41 (s)	5.25 (s)
18	1.04 (s)	1.34 (s)	1.12 (s)	1.06 (s)
19	0.97 (s)	1.90 (s)	1.61 (s)	1.02 (s)
20a	1.11 (s)		5.66 (overlapped)	4.77 (d, 8.0)
20b				4.28 (d, 8.0)
OMe			3.46 (s)	

[a] NMR data for compounds **1** and **4** were recorded at 500 MHz, and data of compounds **2** and **3** were recorded at 600 MHz; Assignments were made based on DEPT, HSQC, COSY, HMBC, and ROESY experiments.

The structures of the known compounds were determined by comparing spectroscopic data with literature values and were identified as isorubesin E (**5**) [17], jianshirubesin D (**6**) [18], rubescensin W (**7**) [19], and jianshirubesin E (**8**) [18].

Compound **1** was obtained as colorless crystals. Its molecular formula was established as $C_{20}H_{30}O_4$ by HR-ESI-MS data (*m/z* 357.2031 $[M + Na]^+$, calcd. 357.2041), indicating of six degrees of unsaturation. Absorption bands at 3427, 1694, and 1679 cm^{-1} in the IR spectrum accounted for the presence of OH, C═O, and C═CH_2 groups. In the ^{13}C NMR and DEPT spectra, 20 carbon signals were observed: including three methyls, six methylenes (including an olefinic one), six methines (including three oxygenated ones), and five quaternary carbons (including a carbonyl one and an olefinic one). Considering main diterpenoids, *ent*-kauranoids from *Isodon* species, compound **1** was first assumed to be a 20-non-oxygenated-*ent*-kauranoid, while HMBC correlations observed from H-9 (δ_H 2.53) and H_2-17 (δ_H 5.52 and 5.23) to C-12 (δ_C 37.3) suggested it a rearranged 16(13 → 12)-*abeo*-*ent*-kaurane skeleton (*ent*-atisane skeleton) [20]. With the ^1H-^1H COSY, HSQC and HMBC spectra, the planar structure of **1** was elucidated. The HMBC correlations from H_3-18 (δ_H 1.04) to C-3 (δ_C 77.7), from H_2-17 to C-15 (δ_C 67.1), H-9 and H-15 (δ_H 5.77) to C-14 (δ_C 66.1) proved the linkage of OH groups to C-3, C-14 and C-15, respectively. The HMBC correlations from H-5 (δ_H 1.53) and H-9 to C-7 (δ_C 212.8) permitted the location of the carbonyl carbon at C-7 (Fig. 2). Therefore, **1** was presumed to be 3,14,15-trihydroxy-*ent*-atis-16-en-7-one.

The ROESY correlations helped assign the relative configuration of **1**. Correlations of H-3/H-1β/H-5β, H-14/H_3-20/H-13α and H-15/H-13β confirmed H-3, H-14 and H-15 to be β, α, and α-oriented, respectively (Fig. 2). To determine the absolute configuration of **1**, a single crystal of **1** was analyzed by X-ray crystallography. Bearing on four oxygen atoms in the molecular, the final refinement on Cu *Kα* data resulted in a Flack parameter of −0.01 (14), allowing an unambiguous assignment of the complete absolute configuration of **1** as shown in its formula (Fig. 3) [21]. All chiral centers, C-3, C-5, C-8, C-9, C-10, C-12, C-14 and C-15 were determined as *R*, *S*, *S*, *R*, *S*, *R*, *R* and *R*, respectively. Therefore, compound **1** was determined to be 3α,14β,15β-trihydroxy-*ent*-atis-16-en-7-one, named as isorothornin D (**1**).

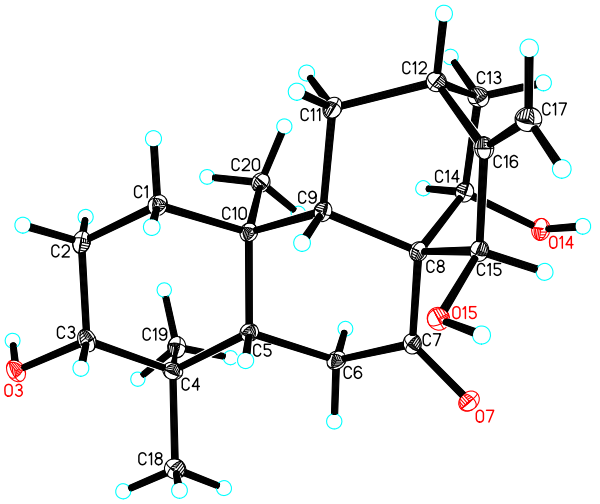

Fig. 3. X-ray crystal structure of **1**.

The molecular formula of **2** was determined as $C_{20}H_{26}O_7$ on the basis of the HREIMS data. Analysis of the spectroscopic data of **2** revealed it a 11,20-epoxy-*ent*-kauranoid, with extreme similarity to **6** [18]. The only difference was an additional OH substituted at C-14 in **2** which was deduced by the HMBC correlations from H-14 (δ_H 5.14) to C-9 (δ_C 51.9), C-12 (δ_C 39.1), and C-16 (δ_C 159.0). The HMBC correlations from H_2-3 (δ_H 1.59 and 1.33), H-5 (δ_H 1.84), and H-9 (δ_H 4.15) to C-1 (δ_C 80.0), from H-6 (δ_H 5.19) to C-5 (δ_C 53.6) and C-8 (δ_C 63.5), and from H-15 (δ_H 6.51) to C-16 and C-17 (δ_C 110.3) confirmed the connections of other three OH groups to C-1, C-6, and C-15, respectively, the same as those in **6**. The HMBC correlations from H-5, H-9, and H-15 to the ketone carbonyl (δ_C 208.9), from H-1 (δ_H 4.10), H-5, and H-9 to the lactone carbonyl (δ_C 177.6) permitted the location of the ketone and lactone carbonyls at C-7 and C-20, respectively.

The ROESY experiment verified that the relative configuration of H-1, H-6, H-11, and H-15 of compound **2** were β-, α-, β-, α-oriented, respectively, identical to compound **6** (Fig. 4) [18]. The correlations of H-14/H-12α verified H-14 to be α-oriented. Thus, compound **2** was elucidated

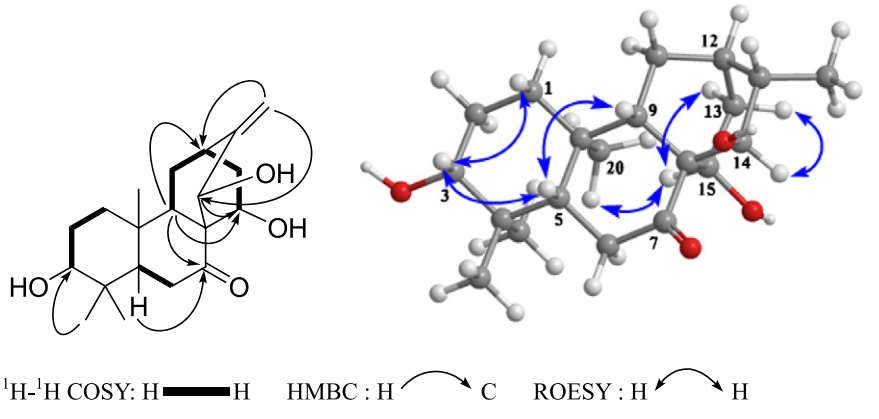

Fig. 2. ^1H–^1H COSY, selected HMBC and key ROESY correlations of **1.**

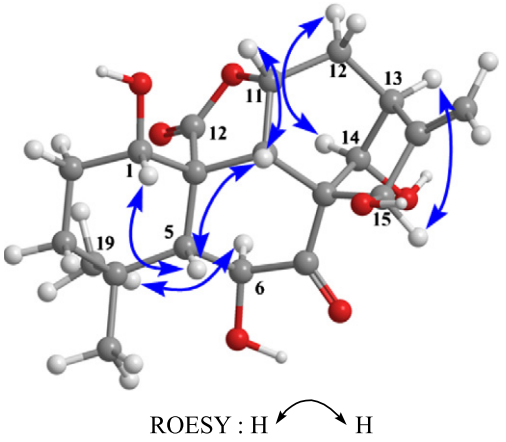

Fig. 4. Key ROESY correlations of **2**.

as 1α,6β,14β,15β-tetrahydroxy-11α,20-olide-*ent*-kaur-16-en-7-one, named as isorothornin E (**2**).

The HREIMS of compound **3** suggested the molecular formula of $C_{21}H_{30}O_7$, indicative of seven degrees of unsaturation. The absorption bands at 3421, 1705, and 1663 cm^{-1} in its IR spectrum revealed the existence of OH, C═O, and C═C groups. In its ^{13}C NMR and DEPT spectra (Table 1), 21 carbon signals were observed, which were assigned to three methyls (including an oxygenated one), four methylenes (including an olefinic one), nine methines (including six oxygenated ones), and five quaternary carbons (including a carbonyl one and an olefinic one). These data suggested **3** to be a 20-oxygenated *ent*-kauranoid which was further proved by the 2D NMR spectra. The HMBC correlations from H-3 (δ_H 3.40) to C-20 (δ_C 99.6) confirmed **3** to be a 3,20-epoxy-*ent*-kauranoid; correlations from OMe (δ_H 3.46) to C-20 permitted the connection of OMe to C-20 directly; correlations from H-6 (δ_H 4.90) to C-4 (δ_C 38.2) and C-5 (δ_C 58.3), from H-11 (δ_H 4.87) to C-13 (δ_C 48.5) and C-8 (δ_C 63.8), from H-14 (δ_H 4.84) to C-9 (δ_C 54.4) and C-16 (δ_C 156.6), and from H_2-17 (δ_H 5.66 and 5.41) to C-15 (δ_C 74.1) verified the linkage of OH groups to C-6, C-11, C-14 and C-15, respectively; correlations from H-5 (δ_H 1.66) and H-15 (δ_H 6.46) to C-7 (δ_C 210.5) permitted the location of the carbonyl carbon at C-7 (Fig. 5). Consequently, compound **3** was assigned as 6,11,14,15-tetrahydroxy-20-methoxy-3,20-epoxy-*ent*-kaur-16-en-7-one.

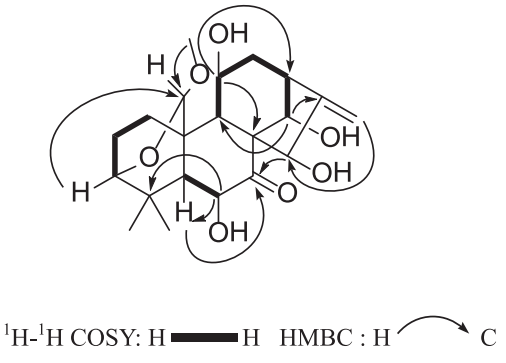

Fig. 5. ^{1}H–^{1}H COSY, selected HMBC of **3**.

The relative configuration of **3** was derived by the ROESY spectrum. The correlations of H-3/H-1β/H-5β, H-6/H_3-19α/H-20, H-11/H-12α/H-OMe, H-14/H-20, and H-15/H-13α confirmed H-3, H-6, H-11, H-14 and H-15 to be β-, α-, α-, α-, and α-oriented, respectively. The R^* configuration of C-20 was determined by the correlations from H-20 to H_3-19α and H-2α. As a result, **3** was characterized as 20(R^*)-6β,11β,14β,15β-tetrahydroxy-20-methoxy-3α,20-epoxy-*ent*-kaur-16-en-7-one, named as isorothornin F (**3**).

Compound **4** was obtained as white amorphous powders. The HREIMS of **4** exhibited a $[M]^+$ peak at 364.1891, which suggested the molecular formula of $C_{20}H_{28}O_6$, indicating of seven degrees of unsaturation. Its IR spectrum had absorption bands at 3417, 1716 and 1060 cm^{-1}, accounting for the presence of OH, C═O, and C═C groups. In its ^{13}C NMR and DEPT spectra (Table 1), 20 carbon signals were observed, which were assigned to two methyls, six methylenes (including an olefinic one and an oxygenated one), seven methines (including four oxygenated ones), and five quaternary carbons (including a carbonyl one and an olefinic). These data indicated that **4** was a 6,7-*seco*-1,7-olide-*ent*-kauranoid, similar to epinodosinol [22,23]. The only difference verified by the ^{1}H-^{1}H COSY, HSQC, and HMBC spectra was the connection of OH to C-14 instead of the one substituted at C-11 in epinodosinol. The ROESY spectrum supported the same relative configurations of H-1, H-6 and H-15 with epinodosinol. The configuration of H-14 was determined to be β-oriented by the ROESY correlation of H-14/H-13β. Hence, **4** was elucidated as 6β,14α,15α-trihydroxy-6,7-*seco*-6,20-epoxy-1α,7-olide-*ent*-kaur-16-ene, named as isorothornin G (**4**).

To the best of our knowledge, compounds **1** and **5** are the first example of atisane-type diterpenoids from this plant. Furthermore, those sub-types of *ent*-kauranoids, 11,20-epoxy-*ent*-kauranoid (**2** and **6-8**), 3,20-epoxy-*ent*-kauranoid (**3**) and enmein-type *ent*-kauranoid (**4**) were also isolated from *Isodon rosthornii* for the first time.

Considering the folk use of the *Isodon* genus, these isolates except **2** and **3** were tested for in vitro cytotoxicity against A-549, HL-60, MCF-7, SMMC-7721, and SW-480 human cancer cell lines using the MTT method [14]. Compound **6** showed significant inhibitory activity against HL-60 cell line (Table 3).

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Table 3
IC_{50} values (μM) of diterpenoids from *I. rosthornii* for human tumor cell lines.

Compound[a]	HL-60	SMMC-7721	A-549	MCF-7	SW480
6	5.00	>40	30.11	16.22	22.62
DDP[b]	2.0	16.2	17.5	17.8	12.8
Paclitaxel[b]	<0.008	<0.008	1.36	<0.008	0.04

[a] Other selected ones not listed in the table were inactive (IC_{50} > 40 μM) for all cell lines.
[b] DDP (cisplatin) and paclitaxel were used as positive controls.

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