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Letter

Three new sesquiterpenoids from *Solanum septemlobum* with cytotoxic activities

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ABSTRACT

Three new sesquiterpenoids, attributable to eudesmane-related (**1–2**, named septemlobins A–B) and vetispirane-type (**3**, named septemlobin C), respectively, were isolated from the whole plant of *Solanum septemlobum*. Their structures were elucidated on the basis of integrated spectroscopic techniques. *In vitro*, compounds **1–3** were found to show significant cytotoxicities against three cancer cell lines (P-388, HONE-1, and HT-29), and gave IC_{50} values in the range 3.8–7.5 μM.

1. Introduction

Solanum, which is mainly distributed in tropical and temperate regions, is the most representative and largest genus of the family Solanaceae with more than 1700 species recognized currently. Many species belonging to this genus are found to show various pharmacological activities and high diversity in the secondary metabolites (Lu et al., 2011; Zhang et al., 2013; Chang et al., 2013). *Solanum septemlobum*, commonly known as "Qing-qi" in traditional Chinese medicine, is a perennial herb distributed in many areas of China, and has been used as antipyretic and antidotal agents (Xie et al., 2008).

In previous phytochemical studies on *Solanum lyratum*, a series of new sesquiterpenoids were isolated and most of them showed significant cytotoxic activities (Dai et al., 2009; Ren et al., 2009; Yue et al., 2012; Yao et al., 2013; Li et al., 2014; Nie et al., 2014). As part of serial investigations on novel and bioactive sesquiterpenoids from *Solanum* plants, great efforts of our group had been devoted to the phytochemical investigation on the whole plant of *S. septemlobum* collected in Linyi, Shandong Province, China. The $CHCl_3$ fraction of EtOH extract of this species was successively subjected to column chromatography over silica gel and Sephadex LH-20, and preparative HPTLC (high-performance thin layer chromatography) to give three new sesquiterpenoids, named septemlobins A–C (**1–3**), the structures of which were elucidated by means of extensive spectroscopic analyses. Furthermore, the new compounds were screened for cytotoxity against three tumor cell lines (P-388, HONE-1 and HT-29 cells), with IC_{50} values being in the range of 3.8–7.5 μM. Herein, we report on the isolation, structural elucidation and cytotoxicity of the three new sesquiterpenoids.

2. Results and discussion

Compound **1** was obtained as a colorless viscous oil. In the HR-FABMS, it gave a quasi-molecular ion peak at *m/z* 249.1485 $[M+H]^+$, corresponding to a molecular formula $C_{15}H_{20}O_3$. The IR spectrum showed absorption bands at 3393, 1744, 1612, 1507 and 1463 cm^{-1}, which were in accordance with hydroxyl, lactone and aromatic groups. The ^1H and ^{13}C NMR data of **1** (Table 1) indicated the presence of the following fragments: a γ,γ-dimethyl-γ-lactone ring moiety [δ_H 2.47 (1*H*, dd, *J* = 11.0, 15.6 Hz, Ha-3), 2.27 (1*H*, dd, *J* = 6.1, 15.6 Hz, Hb-3), 1.43 (3*H*, s, H-13), 1.57 (3*H*, s, H-14); δ_C 175.6, C-2; 34.3, C-3; 46.0, C-4; 86.7, C-5; 21.6, C-13; 26.9, C-14], a 1,2,3-trisubstituded benzene ring moiety [δ_H 7.14 (1*H*, br d, *J* = 7.6 Hz, H-9), 7.17 (1*H*, br t, *J* = 7.6 Hz, H-10),

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Table 1
NMR spectroscopic data for compounds **1–3**[a,b].

No.	**1**		**2**		**3**	
	δ_H	δ_H	δ_H	δ_C	δ_H	δ_C
1					2.16 (d, 14.5, Ha-1) 1.82 (d, 14.5, Hb-1)	47.1 CH_2
2		175.6 C		175.5 C		83.9 C
3	2.47 (dd, 11.0, 15.6, Ha-3) 2.27 (dd, 6.1, 15.6, Hb-3)	34.3 CH_2	2.53 (dd, 11.2, 15.6, Ha-3) 2.17 (dd, 6.3, 15.6, Hb-3)	33.6 CH_2	2.06 (m, Ha-3) 1.85 (m, Hb-3)	39.7 CH_2
4	2.53 (m)	46.0 CH	2.47 (m)	46.4 CH	2.08 (m, Ha-4) 2.04 (m, Hb-4)	33.8 CH_2
5		86.7 C		86.8 C		50.1 C
6	2.84 (m, 2*H*)	27.7 CH_2	3.37 (t, 11.8, Ha-6) 3.16 (d, 12.2, Hb-6)	26.8 CH_2		165.5 C
7		135.8 C		139.5 C	5.72 (s)	125.3 CH
8		136.6 C		138.0 C		199.4 C
9	7.14 (br d, 7.6)	130.8 CH	7.44 (br d, 7.3)	136.4 CH	2.72 (dd, 4.7, 16.8, Ha-9) 2.22 (dd, 2.1, 16.8, Hb-9)	42.9 CH_2
10	7.17 (br t, 7.6)	126.8 CH	7.38 (br t, 7.3)	127.0 CH	2.45 (m)	40.1 CH
11	7.22 (br d, 7.6)	127.3 CH	7.65 (br d, 7.3)	134.7 CH		148.6 C
12		138.7 C		134.1 C	5.04 (s, Ha-12) 4.85 (s, Hb-12)	110.1 CH_2
13	1.43 (s, 3*H*)	21.6 CH_3	1.48 (s, 3*H*)	21.9 CH_3	1.85 (s, 3*H*)	19.4 CH_3
14	1.57 (s, 3*H*)	26.9 CH_3	1.60 (s, 3*H*)	27.0 CH_3	1.93 (s, 3*H*)	20.4 CH_3
15	4.68 (s, 2*H*)	63.5 CH_2	10.09 (s)	194.0 CH	1.00 (d, 6.7, 3*H*)	15.8 CH_3
16	2.35 (s, 3*H*)	20.1 CH_3	2.41 (s, 3*H*)	19.8 CH_3		

[a] Chemical shift values were in ppm and *J* values (in Hz) were presented in parentheses.
[b] The assignments were based on HMQC, HMBC, and ^1H–^1H COSY experiments.

7.22 (1*H*, br d, *J* = 7.6 Hz, H-11); δ_C 135.8 C-7; 136.6, C-8; 130.8, C-9; 126.8, C-10; 127.3, C-11; 138.7, C-12], a hydroxymethyl group [δ_H 4.68 (2*H*, s, H_2-15); δ_C 63.5, C-15], along with a methyl group [δ_H 2.35 (3*H*, s, H_3-16); δ_C 20.1, C-16]. In the HMBC spectrum, the correlations were observed from H-16 at δ 2.35 to C-8 at δ 136.6, from H-15 at δ 4.68 to C-12 at δ 138.7, and from H-4 at δ 2.53 to C-6 at δ 27.7 and C-7 at δ 135.8. This proved that the methyl, hydroxymethyl and γ,γ-dimethyl-γ-lactone groups were connected to the benzene ring at C-8, C-12 and C-7, respectively. The relative configuration of **1** was determined from NOESY experiment (Fig. 3). NOEs from H-4 to Hb-3 and H_3-14, as well as from H_3-13 and H_2-6 indicated that Hb-3, H-4 and H_3-14 were co-facial and β-oriented, while Ha-3 and H_3-13 were on the opposite side of the molecular plane and thus α-oriented. Based on above analyses, the structure of **1** was established as shown in Fig. 1.

Compound **2** was isolated and purified as a colorless viscous oil, and the molecular formula was determined as $C_{15}H_{18}O_3$ by HR-FABMS, which showed a quasi-molecular ion at *m/z* 247.1338 $[M+H]^+$. Comparison of its ^1H and ^{13}C NMR data (Table 1) with those of **1** showed that **2** had many features in common with **1**. The differences in their NMR spectra were accounted for by the absence of the hydroxymethyl group in **1** and presences of one aldehyde group (δ_H 10.09, 1*H*, s, H-15; δ_C 194.0, C-15) in **2**. With the aid of the NOESY data, it was readily confirmed **2** had the same relative configuration at C-4 as **1**. Accordingly, compound **2** was formulated as shown in Fig. 1.

Compound **3** was isolated as a colorless viscous oil, and the molecular formula was determined to be $C_{15}H_{22}O_2$ by HR-FABMS, which displayed a quasi-molecular ion peak at *m/z* 235.1692 $[M+H]^+$. The IR spectrum showed absorption bands at 3350 and 1659 cm^{-1}, which were assignable to hydroxyl and α,β-unsaturated ketone groups (Coxon et al., 1974). The ^1H NMR spectrum (Table 1) revealed the presence of the following fragments: two tertiary methyl group [δ_H 1.85 (3*H*, s, H-13); 1.93 (3*H*, s, H-14)], one secondary methyl group [δ_H 1.00 (3*H*, d, *J* = 6.7 Hz, H-15)], a tri-substituted double bond moiety [δ_H 5.72 (1*H*, s, H-7)], a terminal double bond unit [δ_H 5.04 (1*H*, s, Ha-12), 4.85 (1*H*, s, Hb-12)]. The ^{13}C NMR spectrum (Table 1) displayed 15 carbon resonances, which were consistent with one oxygenated quaternary carbon (δ_C 83.9, C-2), one carbonyl carbon (δ_C 199.4, C-8), four olefinic carbons (δ_C 165.5, C-6; 125.3, C-7; 148.6, C-11; 110.1, C-12), as well as three methyls, four sp^3 hybridized methylenes, one sp^3 hybridized methane and one sp^3 hybridized quaternary carbon by DEPT and HMQC analyses. These signal patterns indicated **3** could be a sesquiterpenoid with a vetispirane-type skeleton (Anderson et al., 1977). In the HMBC experiment (Fig. 2), the long-range correlations from H_3-14 at δ_H 1.93 to C-6 at δ_C 165.5 and C-7 at δ_C 125.3, as well as from H-7 at δ_H 5.72 to C-6 at

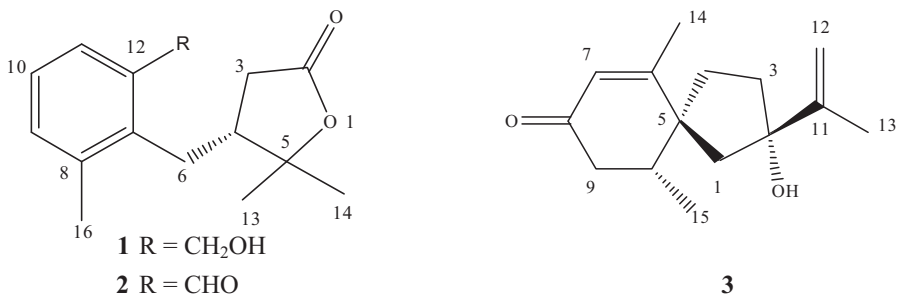

Fig. 1. The structures of new sesquiterpenoids isolated from *Solanum septemlobum*.