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## Four new eremophilendioides from *Ligularia atroviolacea*

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### Abstract

From *Ligularia atroviolacea*, four new eremophilendioides, 8 $\beta$ -hydroxy-eremophil-3,7 (11)-dien-12,8 $\alpha$ -(14,6 $\alpha$ )-diolide (**1**), 8 $\beta$ -methoxy-eremophil-3,7(11)-dien-12,8 $\alpha$ -(14,6 $\alpha$ )-diolide (**2**), 8 $\alpha$ -hydroxy-eremophil-3,7(11)-dien-12,8 $\beta$ -(14,6 $\alpha$ )-diolide (**3**) and eremophil-3,7(11),8-trien-12,8 (14,6 $\alpha$ )-diolide (**4**), as well as a known diolide (**5**) were isolated. Their structures were elucidated on the basis of 1D and 2D NMR as well as ESI-MS spectral data.

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**Keywords:** Phytochemical examination; Sesquiterpene; Eremophilendioides; *Ligularia atroviolacea*

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*Ligularia atroviolacea* (Franch.) Hand.-Mazz. is an endemic species scattered in western Yunnan province, China [1]. Previous phytochemical studies on the genus *Ligularia* have revealed that it is a rich source of eremophilenolides. [2,3]. However, the chemical constituents of this plant have not been reported up to date. The present study on EtOAc extract of the roots of *L. atroviolacea* has led to the isolation and identification of three new eremophilendioides **1**, **2**, and **3** along with a known compound **4** (Fig. 1).

The roots of *L. atroviolacea* (Franch.) Hand.-Mazz. were collected from Lijiang, Yunnan Province in August, 2001. A voucher specimen (LSP200108-04) was deposited at Department of Traditional Chinese Medicine and Natural Drug Research, College of Pharmaceutical Science, Zhejiang University and was identified by Prof. Hua Peng.

The dried roots (5.0 kg) of *L. atroviolacea* were extracted with 95% EtOH (50 L) for three times and seven days for each time at room temperature. The extract was combined and evaporated to dryness *in vacuo*. The residue (462.0 g) was suspended in water and extracted with petroleum ether, ethyl acetate, *n*-butanol, respectively. The ethyl acetate part (89.0 g) was chromatographed on repeated silica gel columns using CHCl<sub>3</sub>–MeOH and CHCl<sub>3</sub>–Me<sub>2</sub>CO as solvent systems to afford 15 mg of **1**, 19 mg of **2**, 12 mg of **3** and 22 mg of **4**, respectively.

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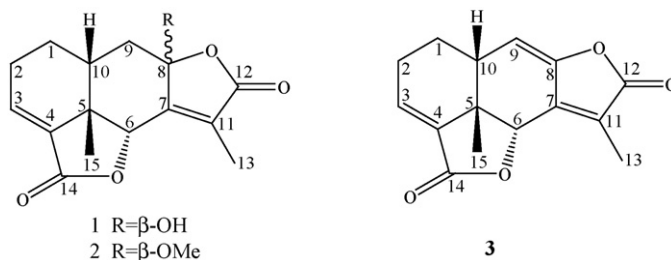
Fig. 1. Structure of compounds **1**, **2**, and **3**.

Table 1

<sup>1</sup>H NMR spectral data of compounds **1**, **2**, and **3** (TMS, δ ppm, 400 MHz)

Position	<b>1</b> (Me <sub>2</sub> CO-d <sub>6</sub> )	<b>2</b> (Me <sub>2</sub> CO)	<b>3</b> (CDCl <sub>3</sub> )
1	2.02 m, 1.66 m	2.09 m, 1.73 m	2.41 m, 1.95 m
2	2.27 m	2.40 m	2.18 m
3	6.75 (t, 3.6)	6.89 (t, 3.2)	6.81 (t, 3.6)
6	5.26 br s	5.34 br s	5.30 br s
9	2.13 m, 1.37 (t, 13.6)	2.19 m, 1.39 (t, 13.6)	5.45 (d, 2.4)
10β	2.36 m	2.30 m	2.94 m
13	2.05 br s	1.93 (d, 1.2)	2.05 br s
15	1.81 s	1.46 s	1.47 s
OMe	—	3.22 s	—

Compound **1** was obtained as colorless needles, mp 193–195 °C,  $[\alpha]_D^{20} = +45.0$  (*c* 0.40, Me<sub>2</sub>CO). Its molecular formula, C<sub>15</sub>H<sub>16</sub>O<sub>5</sub>, was determined by the ESI-MS, <sup>13</sup>C NMR and DEPT data. Its IR bands indicated the presence of a hydroxyl (3284 cm<sup>-1</sup>), a saturated γ-lactone (1772 cm<sup>-1</sup>) and an α, β-unsaturated-γ-lactone (1720, 1668 cm<sup>-1</sup>). In the <sup>1</sup>H NMR spectrum, there were two methyl groups [δ 2.05 (br s, 3H), 1.81 (s, 3H)] displayed (Table 1). Furthermore, the <sup>13</sup>C NMR and DEPT spectra of **1** showed 15 carbons including two methyls, three methylenes, three methines and seven quaternary carbons, which revealed that compound **1** was an eremophilolide-type sesquiterpene and its NMR data were similar to those of a known compound named 8β-H-eremophil-3, 7(11)-dien-12,8α(14,6α)-diolide (**4**) [4]. However, their substituents at C-8 are different. A quaternary carbon signal at δ 103.6 was observed, replacing the C-8 methine signal at δ 81.8 (d) in the <sup>13</sup>C NMR spectrum in the case of **4**. Furthermore, H-8 methine signal at δ 4.68 (1H) in the <sup>1</sup>H NMR spectrum of compound **4** was absent in the case of **1**. This suggested that **1** was an OH-8 derivative of **4**. From the biogenetic point of view, Me-14 and Me-15 of **5** should be β-oriented [5]. Furthermore, NOE measurements for **1** indicated that the Me-15 was spatially close to H-6 and 8-OH which could be exchanged by D<sub>2</sub>O. All these suggested the presence of an 8β-OH in **1**. Thus, compound **1** was assigned as 8β-hydroxyeremophil-3,7(11)-dien-12,8α(14,6α)-diolide.

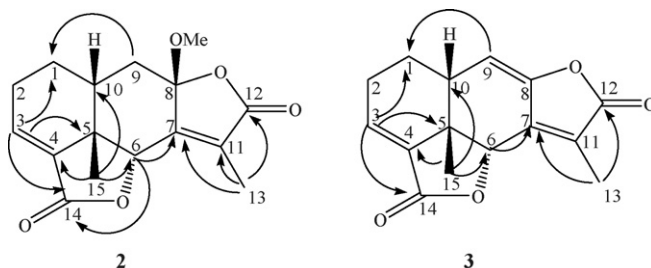
Compound **2** was obtained as colorless plates, mp 167–169 °C,  $[\alpha]_D^{20} = +41.0$  (*c* 0.25, CHCl<sub>3</sub>), with molecular formula C<sub>16</sub>H<sub>18</sub>O<sub>5</sub> deduced from the ESI-MS, <sup>13</sup>C NMR and DEPT spectra. Its IR spectrum showed the absorptions for a saturated γ-lactone (1777 cm<sup>-1</sup>) and an α,β-unsaturated-γ-lactone (1741, 1679 cm<sup>-1</sup>). The NMR data of **2** showed close resemblance to those of **1** except for a methoxy group, as suggested by signals at δ 3.22 (s, 3H) and δ 50.8 (q) in the <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra, respectively (Tables 1 and 2). In the HMBC spectrum of **2**, the cross peak between the methoxyl group (δ 3.22, s) and C-8 (δ 105.2) suggested the location of methoxyl group at C-8 (Fig. 2). Therefore, the structure of compound **2** was determined as 8β-methoxyeremophil-3,7(11)-dien-12, 8α(14,6α)-diolide.

Compound **3** was obtained as colorless needles, mp 233–235 °C,  $[\alpha]_D^{20} = +29.0$  (*c* 0.30, CHCl<sub>3</sub>). UV λ<sub>max</sub> (CHCl<sub>3</sub>) nm: 224, 279. Its molecular formula was proposed as C<sub>15</sub>H<sub>16</sub>O<sub>4</sub> by its <sup>1</sup>H, <sup>13</sup>C NMR and DEPT spectra in accordance with its [M + H]<sup>+</sup> peak 259 in ESI-MS. The NMR spectral data of **3** were very similar to those of **1** (Tables 1 and 2) except for the presence of the double bond at C-8 in **3** instead of the hydroxyl group in **1**. This was indicated by the downfield shifted signals of H-9 (δ 5.45, d, *J* = 2.4 Hz), C-8 (δ 141.7) and C-9 (δ 107.7). Hence, compound **3** was assigned as eremophil-3,7(11),8-trien-12,8(14, 6α)-diolide.

Table 2

 $^{13}\text{C}$  NMR spectral data of compounds **1**, **2** and **3** ( $\delta$  ppm, 100 MHz)

Position	<b>1</b> ( $\text{C}_3\text{D}_6\text{O}$ )	<b>2</b> ( $\text{CDCl}_3$ )	<b>3</b> ( $\text{CDCl}_3$ )
1	22.1 t	21.5 t	22.4 t
2	22.3 t	21.7 t	23.4 t
3	137.7 d	137.0 d	137.2 d
4	130.5 s	129.7 s	129.9 s
5	44.6 s	44.0 s	41.4 s
6	82.8 d	82.1 d	82.2 d
7	155.3 s	152.2 s	148.1 s
8	103.6 s	105.2 s	141.7 s
9	37.2 t	35.2 t	107.7 d
10	34.4 d	32.9 d	36.4 d
11	126.1 s	128.7 s	127.2 s
12	169.0 s	168.5 s	168.5 s
13	8.9 q	9.1 q	9.3 q
14	171.2 s	170.5 s	169.8 s
15	26.9 q	26.8 q	26.5 q
OMe	–	50.8 q	–

Fig. 2. Key HMBC correlations of compounds **2** and **3**.

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