

## Two New Eremophilenolides from *Cacalia ainsliaeflora*

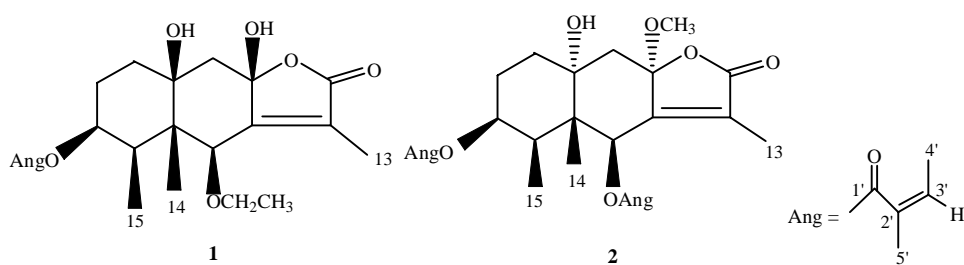
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**Abstract:** Two new eremophilenolides (3 $\beta$ -angeloyloxy-8 $\beta$ , 10 $\beta$ -dihydroxy-6 $\beta$ -ethoxyeremophilenolide (**1**) and 3 $\beta$ , 6 $\beta$ -diangeloyloxy-8 $\alpha$ -methoxy-10 $\alpha$ -hydroxyeremophilenolide (**2**) were isolated from the roots of *Cacalia ainsliaeflora*. Their structures were elucidated by spectroscopic methods.

**Keywords:** *Cacalia ainsliaeflora*, Compositae, eremophiane sesquiterpene.

The roots of *C. ainsliaeflora* (compositae) have been used as traditional Chinese medicine for invigorating the circulation of blood, curing pellagra, rheumatismal edema and as an insecticide<sup>1</sup>. Previous phytochemical studies on this plant revealed the presence of five eremophilane sesquiterpenes<sup>2</sup>. In our continuing study of bioactive compounds, two new eremophilane sesquiterpenes were isolated from the roots of *C. ainsliaeflora*.



Compound **1**, colorless gum [ $\alpha$ ]<sub>D</sub><sup>20</sup> +117.4 (*c* 0.60, CHCl<sub>3</sub>). Its IR spectrum showed absorption for typical  $\alpha$ ,  $\beta$ -unsaturated  $\gamma$ -lactone bands (1763, 1713 cm<sup>-1</sup>) and hydroxyl group (3360cm<sup>-1</sup>). The molecular formula, C<sub>22</sub>H<sub>32</sub>O<sub>7</sub>, was determined by EIMS *m/z* 408 [M]<sup>+</sup>, <sup>13</sup>C NMR and DEPT spectra. Analysis of the <sup>1</sup>H, <sup>13</sup>C NMR and DEPT of **1** (Table 1) indicated the presence of three methyl groups characteristic of an eremophilenolide [ $\delta$ 1.95 (s, H-13),  $\delta$ 1.41 (s, H-14),  $\delta$ 0.93 (d, H-15, J=6.8)], an angeloyl group, an ethoxyl group and other 12 carbon atom signals (3 $\times$ CH, 3 $\times$ CH<sub>2</sub> and 6 $\times$ C).

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The NMR spectra (**Table 1**) were similar to those of eremophilanolides reported in the literature<sup>3,4</sup>. In the <sup>1</sup>H NMR spectrum of **1** the downfield shifted signal for H-6 ( $\delta$  4.35) indicated that the ethoxyl group located on C-6. This was supported by the long range coupling of C-6 with ethoxyl group protons and H-14 in the HMBC spectrum of **1**. The localization of the angeloyloxy moiety at the C-3 position was deduced from the HMBC spectrum in which H-3 gave a long-range coupling with C<sub>1</sub>( $\delta$ 167.1) and H-15 gave a long-range coupling with C-3 ( $\delta$ 71.9). In the <sup>1</sup>H NMR spectrum the C-14 methyl singlet at  $\delta$  1.41 was downfield from the C-15 methyl doublet ( $J=6.8\text{Hz}$ ) at  $\delta$  0.92. This suggested that **1** is an A/B cis-fused compound with 8 $\beta$ , 10 $\beta$ -hydroxy groups<sup>4,5</sup>. The NOESY cross-peak between H-4 ( $\delta$ 1.41dq) and H-9 $\alpha$  ( $\delta$ 2.28d) further confirmed a cis-eremophilane. The missing homoallylic spin-coupling between H-6 and H-13 showed that ethoxyl group at C-6 and the hydroxy at C-8 were  $\beta$ -orientation<sup>6</sup>, respectively. The coupling pattern observed for H-3 at  $\delta$  4.99(dt, $J=3.0, 1.6\text{Hz}$ ) implied that the angeloyl group at C-3 was an equatorial  $\beta$ -orientation<sup>7</sup>, and this was supported by the NOESY cross peak between H-3 $\alpha$  and H-6 $\alpha$ . Therefore compound **1** was determined as 3 $\beta$ -angeloyloxy-8 $\beta$ , 10 $\beta$ -dihydroxy-6 $\beta$ -ethoxyeremophilanolide.

**Table 1** <sup>1</sup>H (400MHz), <sup>13</sup>C NMR (100MHz) data and HMBC correlations of **1** (CD<sub>3</sub>COCD<sub>3</sub>,  $\delta$  ppm,TMS)

H	$\delta_{\text{H}}$	C	$\delta_{\text{C}}$	<sup>1</sup> H- <sup>13</sup> C long range correlation
1	1.65 (m)	1	30.0 (CH <sub>2</sub> )	H-9, H-2
	1.83 (m)	2	27.4 (CH <sub>2</sub> )	H-4, H-1
2	1.35 (m)	3	71.9 (CH)	H-15, H-4, H-2
	1.95 (m)	4	36.5 (CH)	H-6, H-14, H-2, H-15
3	4.99 (d t, 3.0, 1.6)	5	47.2 (C)	H-9, H-3, H-6, H-4, H-14, H-15
4	1.41 (dq)	6	77.9 (CH)	-OCH <sub>2</sub> -, H-4, H-14
	4.35 (s)	7	153.7 (C)	H-9, H-6, H-13
9	2.35 (d, 14.5)	8	103.7 (C)	H-9, H-6
		9	44.5 (CH <sub>2</sub> )	H-1
	2.28 (d, 14.5)	10	74.7 (C)	H-9, H-2, H-6, H-4, H-14
		11	128.9 (CH)	H- H-6, H-13
13	1.95 (s)	12	170.3 (C)	H- H-13
		13	8.7 (CH <sub>3</sub> )	
14	1.41 (s)	14	13.1 (CH <sub>3</sub> )	H-6, H-4
15	0.93 (d, 6.8)	15	12.5 (CH <sub>3</sub> )	H-4
OEt	3.28-3.64 (m)	OEt	65.8 (CH <sub>2</sub> )	H-6, CH <sub>3</sub>
	1.20 (t, 6.8)		14.9 (CH <sub>3</sub> )	-OCH <sub>2</sub> -
OAng		1'	167.1 (C)	H-3, H-5', H-3'
		2'	127.5 (C)	H-4', H-5'
3'	6.10 (qq, 7.0, 1.6)	3'	139.0 (CH)	H-4', H-5'
4'	2.00 (dq, 7.0, 1.4)	4'	20.8 (CH <sub>3</sub> )	H-3'
5'	1.91 (dq, 1.6, 1.4)	5'	15.7 (CH <sub>3</sub> )	H-3'

Compound **2**, colorless gum [ $\alpha$ ]<sub>D</sub><sup>20</sup> -109.8(c 0.56, CHCl<sub>3</sub>); Its IR spectrum showed absorption for a typical  $\alpha$ ,  $\beta$ -unsaturated  $\gamma$ -lactone bands (1771, 1712 cm<sup>-1</sup>) and hydroxyl group (3505 cm<sup>-1</sup>). The molecular formula, C<sub>26</sub>H<sub>36</sub>O<sub>8</sub>, was determined by

HRESIMS  $m/z$  477.2474 ( $[M+1]^+$ , calcd. 477.2483). The NMR spectra (Table 2) of **2** were similar to those of **1** and eremophilenolides reported in the literature<sup>3,4</sup>. The position of the methoxy group at C-8 was supported by the downfield shifts of the semiketal quaternary  $sp^3$  carbon C-8 signal at  $\delta_c$  104.1 in the  $^{13}C$  NMR spectrum and the long-range coupling of C-8 with methoxyl group protons in the HMBC spectrum. In the  $^1H$  NMR spectrum of **2**, the C-15 methyl doublet ( $J=7.2$ Hz) at  $\delta$ 1.16 was downfield of the C-14 methyl singlet at  $\delta$  1.07 and there was homoallylic coupling ( $J=1.3$ Hz) between the H-6 $\alpha$  and Me-13 protons. These data indicate that **2** was an A/B trans-fused compound with 6 $\beta$ -OAng, 8 $\alpha$ -OCH<sub>3</sub> and 10 $\alpha$ -OH<sup>4,5</sup>. Therefore, the structure of **2** was determined to be 3 $\beta$ , 6 $\beta$ -dangeloyloxy-8 $\alpha$ -methoxy-10 $\alpha$ -hydroxyeremophilenolide.

**Table 2**  $^1H$  (400MHz),  $^{13}C$  NMR(100MHz) data and HMBC correlations of **2** (CD<sub>3</sub>COCD<sub>3</sub>,  $\delta$ ppm,TMS.)

H	$\delta_H$	C	$\delta_C$	$^1H$ - $^{13}C$ long range correlation
1	2.65 (m)	1	34.5 (CH <sub>2</sub> )	H-9, H-3, H-2
	2.05 (m)	2	21.5 (CH <sub>2</sub> )	H-3, H-4, H-1
2	2.35 (m)	3	71.0 (CH)	H-15, H-4, H-2, H-1
	1.60 (m)	4	35.4 (CH)	H-6, H-14, H-15, H-3
3	5.06 (ddd, 2.6,4.3,4.3)	5	49.5 (C)	H-9, H-6, H-4, H-14, H-15
4	1.85 (m)	6	70.8 (CH)	H-4, H-14
6	5.83 (d, 1.3)	7	153.9 (C)	H-9, H-6
9	2.27 (d, 13.7)	8	104.1 (C)	-OCH <sub>3</sub> , H-9, H-6
	1.95 (d, 13.7)	9	47.8 (CH <sub>2</sub> )	H-1
		10	72.9 (C)	H-9, H-2, H-6, H-14
		11	128.1 (CH)	H- H-6, H-13
		12	170.9 (C)	H- H-13
13	1.84(d, 1.3)	13	8.0 (CH <sub>3</sub> )	
14	1.07 (s)	14	9.8 (CH <sub>3</sub> )	H-6, H-4
15	1.16 (d, 7.2)	15	14.3 (CH <sub>3</sub> )	H-3
OMe	3.29 (s)	OMe	50.6 (CH <sub>3</sub> )	
OAng		1',1''	166.9, 166.3 (C)	(C1',H-3), (C1'',H-6)
		2',2''	141.4,137.7 (CH)	H-4',H-4'', H-5',H-5''
3', 3''	6.27 (qq), 6.02 (qq)	3',3''	126.7,126.4 (C)	H-4',H-4'', H-5',H-5''
4', 4''	2.07 (dq), 1.95 (dq)	4',4''	20.5, 20.4 (CH <sub>3</sub> )	H-3',H-3''
5', 5''	2.00 (dq), 1.87 (brs)	5',5''	15.9, 15.6 (CH <sub>3</sub> )	H-3', H-3''

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