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Six new sesquiterpenes from *Cacalia ainsliaeflora*

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Five new eremophilane sesquiterpenes, 3β,6β-diangeloyloxy-8β,10β-dihydroxyeremophilenolide (**1**); 6β-acetoxy-3β-angeloyloxy-8β,10β-dihydroxyeremophilenolide (**2**); 3β-angeloyloxy-6β-methoxyeremophil-7(11),9(10)-dien-8α,12-olide (**3**), 3β-angeloyloxy-8-oxo-eremophil-6(7)-en-12-oic acid (**4**); 3β-angeloyloxy-10β-hydroxy-8-oxo-eremophil-6(7)-en-12-oic acid (**5**), and a novel nor-eremophilane derivative, 3β-angeloyloxy-10β-hydroxy-8-oxo-eremophil-6(7)-en (**6**), were isolated from the roots of *Cacalia ainsliaeflora*. Their structures were elucidated by spectroscopic methods, including 2DNMR. Compounds **1** and **2** were assayed against P388 and A549 Carcinoma cell lines. No positive activities were observed.

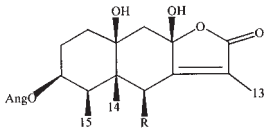
1. Introduction

The genus *Cacalia* (Compositae), belonging to the tribe Senecioneae, is known to be a source of sesquiterpenes (Kuroyanagi et al. 1985; EI-Emary et al. 1980; Zhang et al. 1998). Many sesquiterpenes have been reported to exhibit antitumor and anti-histamine activities (Lin et al. 1998; Tobinaga et al. 1983). The petrol-Et_2O-MeOH (1 : 1 : 1) extract of the roots of *Cacalia ainsliaeflora* were rich in eremophilane sesquiterpenes. In previous papers, we reported thirteen eremophilane sesquiterpenes from *C. ainsliaeflora* (Mao and Jia 2002; Mao et al. 2003). As part of our ongoing search for pharmacologically interesting substances from *Cacalia* species, we investigated the chemical constituents of the roots of *C. ainsliaeflora*. Here we describe the isolation and structure elucidation of five new eremophilane sesquiterpenes and a novel nor-eremophilane derivative.

2. Investigations, results and discussion

The IR spectra of compounds **1**–**3** indicated the typical α,β-unsaturated γ-lactone (1767, 1716 cm^{-1}). The ^1H NMR and ^{13}C NMR spectra were similar to those of eremophilenolides reported previously (Mao et al. 2003; Zhang et al. 1998; Sugama et al. 1985; Massiot et al. 1990; Aclinou et al. 1991). The molecular formula of **1** was assigned as $C_{25}H_{34}O_8$ by HRESI-MS m/z 485.2144 ($[M + Na]^+$, 485.2146 of calcd), ^{13}C and DEPT-NMR. In the ^1H NMR spectra the downfield shifted signal H-6 (δ 5.83) indicated that an angeloyl group was located on C-6. The localization of two angeloyloxy moieties at C-3 and C-6 was deduced from the HMBC spectrum. In the ^1H NMR spectrum the H-14 methyl singlet at δ 1.35 was downfield from the H-15 methyl doublet at δ 1.02, This suggested that **1** was an A/B *cis*-fused compound with 8β,10β-hydroxy group (Massiot et al. 1990; Naya et al. 1978). The missing homoallylic spin-coupling between H-6 and H-13 showed that the angeloyl group at C-6 was β-equatorial (Naya et al. 1975; Moriyama and Takahashi 1976). The coupling pattern observed for H-3 at δ 5.01 (dt, J = 3.0, 2.0 Hz) implied that the angeloyl group at C-3 was β-equatorial (Sugama et al. 1985; Zhao et al. 1992). Thus compound **1** was determined as 3β,6β-diangeloyloxy-8β,10β-dihydroxyeremophilenolide.

Compound **2** was obtained as colorless gum. The molecular formula, $C_{22}H_{30}O_8$, was determined by EIMS m/z 362 $[M-CH_3COOH]^+$, ^{13}C and DEPT-NMR. The ^1H and



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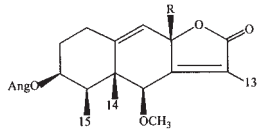
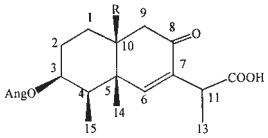
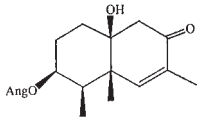
2 R = OAc



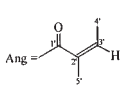
3 R = H
3a R = OH



4 R = H
5 R = OH



6



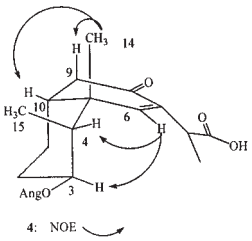


Table 1: ^{1}H NMR data of compounds 1–6 ($CDCl_3$, 400 MHz)

H	1	2	3	4	5	6
1	2.02 m	2.00 m	2.47 m	2.10 m	2.38 m	2.24 m
	1.66 m	1.65 m	2.04 m	1.95 m	2.12 m	2.00 m
2	1.85 m	1.83 m	1.61 m	1.73 m	1.85 m	1.83 m
	1.38 m	1.40 m	1.30 m	1.25 m	1.71	1.68 m
3	5.01 dt (3.0, 2.0)	5.00 dt (3.0, 1.6)	5.05 dt (3.0, 2.8)	4.90 dt (5.4, 3.9)	4.96 dt (3.0, 2.8)	4.98 dt (3.3, 3.1)
4	1.48 dq	1.46 dq	1.90 dq	1.53 dq	1.65 dq	1.60 dq
6	5.83 s	5.70 s	3.98 brs	6.63 brs	6.59 brs	6.66 d (2.1)
8			5.16 brs			
9	2.33 d (14.7)	2.35 d (14.5)	5.59 brs	2.64 dd (17.5, 4.8)	2.85 d (16.5)	2.90 d (16.7)
	2.25 d (14.7)	2.28 d (14.5)		2.38 dd (17.5, 4.8)	2.51 d (16.5)	2.55 d (16.7)
10				2.10 m		
11				3.58 q (7.2)	3.57 q (7.0)	
13	1.98 s	1.94 s	1.99 s	1.34 d (7.1)	1.25 d (7.0)	2.34 s
14	1.35 s	1.33 s	1.14 s	1.24 s	1.32 s	1.24 s
15	1.02 d (7.0)	0.99 d (6.8)	1.17 d (7.1)	1.00 d (7.0)	1.14 d (7.0)	1.03 d (7.2)
OMe			3.43 s			
OAc		2.10 s				
OAng	2.00 dq (6 H)	2.00 dq (7.2, 1.4)	6.08 qq (7.4, 1.4)	6.09 brq (7.2)	6.08 brq (7.1)	6.09 brq (7.0)
	1.91 brd (1.6, 6 H)	1.91 dq (1.5, 1.4)	2.01 brd (7.4)	1.99 dq (7.2, 1.2)	1.95 brd (7.1)	2.03 dq (7.0, 1.5)
	6.10 qq, 6.18 qq	6.10 qq (7.2, 1.5)	1.92 brd (1.3)	1.90 brs	1.89 brs	1.94 brd (1.4)

^{13}C NMR (Table 1 and 2) spectra were very similar to those of **1** except for the presence of an acetoxyl group in **2** in contrast to the angeloyl group present in **1**. The upfield shifted signal H-6 (δ 5.70 s) indicated that the acetoxyl group was located on C-6. Thus, the structure of **2** was determined to be 6β-acetoxy-3β-angeloyloxy-8β,10β-dihydroxyeremophilenolide.

The NMR data of **3** were similar to those of compound **3a** reported in our previous paper (Mao and Jia 2002). At variance with the ^{1}H and ^{13}C NMR of **3a**, the spectrum of **3** has an additional downfield shifted H-8 (δ 5.16) and a oxygen-bearing methine carbon (δ 77.8) agreed. The signals of H-9 (δ 5.59), H-6 (δ 3.98), and the corresponding carbons are shifted upfield. There is not semiketal quaternary sp^3 carbon signal (δ 104.1) in the ^{13}C NMR spectrum. Consequently, compound **3** was determined to be 3β-angeloyloxy-6β-methoxyeremophil-7(11),9(10)-dien-8α,12-olide.

The IR spectrum of **4** indicated the presence of a typical α,β-unsaturated ketone (1675 cm^{-1}) and carboxyl group (1710, 1736 cm^{-1}). The molecular formula, $C_{20}H_{28}O_5$, was determined by HRESIMS m/z 477.2474 ($[M + 1]^+$, 477.2483 of calcd), ^{13}C and DEPT-NMR. The NMR data were similar to those reported in the literature (Sugama et al. 1985; Yoko et al. 2001). The ^{1}H, ^{13}C NMR and DEPT-NMR indicated the presence of three methyl groups [δ 1.34 (d, J = 7.1, H-13), δ 1.24 (s, H-14), δ 1.00 (d, J = 7.0, H-15)], an angeloyl group and an olefin [δ 6.63 (brs, H-6), δ 154.6 (C-6)], an oxygen-bearing methine [δ 4.90 (dt, J = 5.4, 3.9 Hz, H-3), δ 73.0 (C-3)] and a carbonyl group [δ 197.9 (C-8)]. The signal of H-9 was double doublets [δ 2.38 (dd, J = 17.5, 4.8 Hz, H-9α), δ 2.64 (dd, J = 17.5, 4.8 Hz, H-9β)] due to the coupling $J_{9\alpha.9\beta}$ and $J_{9.10}$. These spectra data therefore agreed with the proposed structure **4**. In the HMBC experiment the

Table 2: ^{13}C NMR data of compounds 1–6 ($CDCl_3$, 100 MHz)

C	1	2	3	4	5	6
1	30.0 (CH_2)	30.1 (CH_2)	27.4 (CH_2)	24.6 (CH_2)	25.4 (CH_2)	27.1 (CH_2)
2	27.2 (CH_2)	27.2 (CH_2)	31.4 (CH_2)	25.8 (CH_2)	33.3 (CH_2)	30.1 (CH_2)
3	71.9 (CH)	71.9 (CH)	74.0 (CH)	73.0 (CH)	73.6 (CH)	72.0 (CH)
4	36.6 (CH)	36.5 (CH)	46.4 (CH)	41.2 (CH)	43.3 (CH)	41.8 (CH)
5	47.1 (C)	46.9 (C)	50.2 (C)	39.9 (C)	45.2 (C)	55.1 (C)
6	70.3 (CH)	71.2 (CH)	87.3 (CH)	154.6 (CH)	154.2 (CH)	152.5 (CH)
7	151.5 (C)	151.3 (C)	148.7 (C)	136.6 (C)	137.1 (C)	141.5 (C)
8	103.2 (C)	103.2 (C)	77.8 (CH)	197.9 (C)	197.1 (C)	197.3 (C)
9	43.2 (CH_2)	43.2 (CH_2)	117.8 (CH_2)	39.7 (CH_2)	48.6 (CH_2)	41.5 (CH_2)
10	74.1 (C)	74.2 (C)	156.9 (C)	36.2 (CH)	74.5 (C)	81.3 (C)
11	129.0 (CH)	129.0 (CH)	121.9 (CH)	38.6 (CH)	38.2 (CH)	
12	171.1 (C)	171.2 (C)	174.0 (C)	178.4 (C)	175.6 (C)	
13	8.8 (CH_3)	8.7 (CH_3)	8.6 (CH_3)	15.8 (CH_3)	16.4 (CH_3)	8.7 (CH_3)
14	12.9 (CH_3)	12.7 (CH_3)	14.5 (CH_3)	24.6 (CH_3)	18.8 (CH_3)	14.9 (C H_3)
15	12.7 (CH_3)	12.6 (CH_3)	15.1 (CH_3)	8.8 (CH_3)	11.4 (CH_3)	13.6 (CH_3)
OMe			57.7 (CH_3)			
OAc		170.3 (C)				
		20.8 (CH_3)				
OAng	167.1, 166.3	167.1 (C)	167.4 (C)	167.3 (C)	167.4 (C)	167.7 (C)
	141.5, 139.2	139.2 (CH)	139.8 (CH)	138.0 (CH)	138.0 (CH)	138.6 (CH)
	127.4, 126.5	127.5 (C)	127.7 (C)	128.0 (C)	129.0 (C)	127.7 (C)
	20.8, 20.6	20.7 (CH_3)	20.6 (CH_3)	20.7 (CH_3)	20.9 (CH_3)	20.9 (CH_3)
	15.8, 15.7	15.7 (CH_3)	15.7 (CH_3)	15.8 (CH_3)	15.8 (CH_3)	15.7 (CH_3)

long-range correlation between H-3 and $C_{1'}$ (δ 167.1), and between C-12 and H-13, H-11(δ 3.58 brq, J = 7.2 Hz) indicated the angeloyloxy moiety at C-3, a carboxyl group at C-11, respectively. The coupling pattern observed for H-3 at δ 4.90 (dt, J = 5.4, 3.9 Hz) implied that the angeloyl group at C-3 was β-equatorial (Sugama et al. 1985; Zhao et al. 1992), and this was supported by the NOESY cross peak between H-3 and H-4α. The NOESY cross-peak between H-4 and H-9α (δ 2.38 dd), H-10 and H-14, H-6 and H-3α further confirmed a *cis*-eremophilane. Therefore compound **4** was determined as 3β-angeloyloxy-8-oxo-eremophil-6(7)-en-12-oic acid.

The molecular formula of **5**, $C_{20}H_{28}O_6$, was determined by EIMS m/z: 364 $[M]^+$(2), ^{13}C and DEPT-NMR. The NMR and IR data of **5** were similar to those of **4** except for a hydroxy-bearing quaternary carbon (δ 74.5) in **5** instead of a methine (δ 36.2, CH) in **4**. The downfield shift of the H-14 methyl singlet (δ 1.32) and an oxygen-bearing quaternary carbons (δ 74.5) obviously required a β-orientated hydroxyl at C-10 (Massiot et al. 1990; Naya et al. 1978). Thus, the structure of **5** was determined to be 3β-angeloyloxy-10β-hydroxy-8-oxo-eremophil-6(7)-en-12-oic acid.

The molecular formula of compound **6**, $C_{18}H_{26}O_4$, was determined by HRESIMS m/z: 329.1709 $[M + Na]^+$ (329.1723 of calcd), ^{13}C NMR and DEPT-NMR. The NMR data of **6** were similar to those of **5** except for the signals of H-11, C-11 and C-12 were missing and the presence of a methyl singlet at δ 2.32 in **6** instead of the methyl doublet at δ 1.25 (d, J = 7.0 Hz) in **5**. These data suggested that the methyl (δ 2.32) was located at C-7. The ^1H-^1H COSY and HMBC experiments supported the structure of **6**.

Compounds **1** and **2** were tested for *in vitro* anticancer activities against P388 (mouse leukemia) and A-549 (human pulmonary adenocarcinoma). No positive activities were observed.

3. Experimental

3.1. Apparatus

Optical rotations were taken on a JASCO-20 auto recording polarimeter; IR spectra were measured on a Nicolet 170SX FT-IR instrument; EI-MS were obtained on a VG-ZAB-HS mass spectrometer. HRESIMS were recorded on a Bruker APEX II mass spectrometer; ^1H NMR, ^{13}C NMR and 2D-NMR spectra were recorded on a Bruker AM-400 FT-NMR spectrometer using TMS as the internal standard.

3.2. Plant material

The roots of *C. ainsliaeflora* (Franch) Hand-Mazz were collected in August 2000 in Hubei Province, P. R. of China. The plant was identified by Prof. Z. N. Zhao of the Wuhan Institute of Botany of Chinese Academy of Sciences, where a voucher specimen 99801 is deposited.

3.3. Extraction and isolation

The air-dried roots of the plant (1 kg) were pulverized and extracted with petrol–Et_2O-MeOH (1 : 1 : 1) four times at room temperature. The extract (46 g) was obtained after concentration in reduced pressure. Then the extract was subjected to column chromatography over Silica gel (200–300 mesh, 1200 g), and elution with a gradient of petrol-EtOAc (40 : 1, 30 : 1, 20 : 1, 10 : 1, 8 : 1, 6 : 1, 4 : 1 and 1 : 1; 2500 ml for each eluent). Based on the differences exhibited by TLC, six fractions [A (40 : 1 and 30 : 1), B (20 : 1 and 10 : 1), C (8 : 1), D (6 : 1), E (4 : 1) and F (1 : 1)] were obtained. Fraction B (3 g) was chromatographed on Silica gel (240 g) and eluted with petrol-EtOAc (15 : 1 → 4 : 1, 350 ml for each eluent) yielding **6** (10 : 1, 8 mg), which was purified by preparative TLC with petrol-Acetone (4 : 1). Fraction C (2 g) was chromatographed on silica gel (160 g) and eluted with petrol-acetone (8 : 1 → 4 : 1, 350 ml for each eluent) yielding **2** (6 : 1, 11 mg) and **3** (4 : 1, 15 mg); fraction D (3.5 g) was subjected to CC on Silica gel H (240 g), and elution with petrol-acetone (10 : 1 → 2 : 1, 300 ml for each eluent) to afford **5** (6 : 1, 12 mg) and **1** (5 : 1, 20 mg). Fraction E (2.5 g) on CC over Silica gel H (200 g), and elution with petrol-acetone (8 : 1 → 1 : 1, 300 ml for each eluent) afforded **4** (4 : 1, 10 mg), which was purified by preparative TLC with petrol-$C_6H_5CH_3$-Acetone (1 : 3 : 1).

3.4. Compounds identified

3.4.1. 3β,6β-Diangeloyloxy-8β,10β-dihydroxyeremophilenolide (**1**)

Colorless gum, $C_{25}H_{34}O_8$, $[\alpha]_D^{20}$ + 100.8° (c 0.56, $CHCl_3$); IR: ν_{max}^{KBr} = 3548, 3337, 2953, 1767, 1716, 1646, 1456, 1387, 1229, 1152, 1037 cm^{-1}; ^1H and ^{13}C NMR: Tables 1 and 2; HRESIMS m/z (rel.int.): 463.2319 $[M + 1]^+$, 485.2144 $[M + Na]^+$ (485.2146 of calcd).

3.4.2. 6β-Acetoxy-3β-angeloyloxy-8β,10β-dihydroxyeremophilenolide (**2**)

Colorless gum, $C_{22}H_{30}O_8$, $[\alpha]_D^{20}$ + 125.2° (c 1.00, $CHCl_3$); IR: ν_{max}^{KBr} = 3526, 3311, 2953, 1765, 1714, 1647, 1456, 1387, 1229, 1157, 1035 cm^{-1}; ^1H and ^{13}C NMR: Tables 1 and 2; EIMS m/z (rel.int.): 362 $[M-CH_3COOH]^+$ (2), 344 $[M-CH_3COOH-H_2O]^+$ (4), 322 (2), 304 (1), 280 (2), 262 (45), 244 (30), 162 (5), 140 (6), 124 (7), 83 (100).

3.4.3. 3β-Angeloyloxy-6β-methoxyeremophil-7(11),9(10)-dien-8α,12-olide (**3**)

Colorless gum, $C_{21}H_{28}O_5$, $[\alpha]_D^{20}$ − 64.0° (c 0.15, $CHCl_3$); IR: ν_{max}^{KBr} = 2938, 1755, 1713, 1647, 1452, 1234, 1146, 1097 cm^{-1}; ^1H and ^{13}C NMR: Tables 1 and 2; HRESIMS m/z: 361.2010 $[M + H]^+$ (361.2010 of calcd); EIMS m/z: 360 $[M]^+$ (28), 328 (1), 260 (46), 228 (23), 217 (100), 185 (11), 83 (100).

3.4.4. 3β-Angeloyloxy-8-oxo-eremophil-6(7)-en-12-oic acid (**4**)

Colorless gum, $C_{20}H_{28}O_5$, $[\alpha]_D^{20}$ + 10.8° (c 0.55, $CHCl_3$); IR: ν_{max}^{KBr} = 2974, 2934, 1736, 1710, 1675, 1457, 1383, 1157 cm^{-1}; ^1H and ^{13}C NMR: Tables 1 and 2; HRESIMS m/z: 371.1832 $[M + Na]^+$ (371.1829 of calcd); EIMS m/z: 348 $[M]^+$ (2), 275 (2), 248 (35), 230 (17), 204 (37), 148 (33), 83 (100).

3.4.5. 3β-Angeloyloxy-10β-hydroxy-8-oxo-eremophil-6(7)-en-12-oic acid (**5**)

Colorless gum, $C_{20}H_{28}O_6$, $[\alpha]_D^{20}$ + 33.8° (c 0.68, $CHCl_3$); IR: ν_{max}^{KBr} = 3461, 2976, 2947, 1711, 1677, 1457, 1384, 1161, 1041 cm^{-1}; ^1H and ^{13}C NMR: Tables 1 and 2; EIMS m/z: 364 $[M]^+$ (2), 346 $[M-H_2O]^+$ (2), 302 (4), 264 (10), 246 (52), 228 (32), 188 (10), 173 (7), 137 (8), 83 (100).

3.4.6. 3β-Angeloyloxy-10β-hydroxy-8-oxo-eremophil-6(7)-en (**6**)

Colorless gum, $C_{18}H_{26}O_4$, $[\alpha]_D^{20}$ + 80° (c 0.20, $CHCl_3$); IR: ν_{max}^{KBr} = 3476, 2944, 2880, 1760, 1712, 1664, 1454, 1384, 1159, 1038 cm^{-1}; ^1H and ^{13}C NMR: Tables 1 and 2; HRESIMS m/z: 329.1709 $[M + Na]^+$ (329.1723 of calcd); EIMS m/z: 306 $[M]^+$ (1), 262 (1), 223 (2), 206 (35), 191 (13), 163 (77), 83 (100).

3.5. Antitumor activity assays

The *in vitro* antitumor activity assays were carried out following the methods of Kamura et al. (1996).

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References

Aclinou P, Benkouider A, Massiot G et al. (1991) Eremophilenolides from *Hertia cheirifolia*. Phytochemistry 30: 2083–2084.

EI-Emary NA, Takemoto T, Kusano G (1980) New sesquiterpenes from the roots of *Cacalia auriculata.* Planta Med 38: 161–164.

Kamura T, Komori C, Lee Y et al. (1996) Cytotoxic activities of *Solanum* steroidal glycosides. Biol Pharm Bull 19: 564–566.

Kuroyanagi M, Naito H, Noro T et al. (1985) Furanoeremophilane-type sesquiterpenes from *Cacalia adenostyloids.* Chem Pharm Bull 33: 4792–4797.

Lin YL, Qu JC, Chen CF et al. (1998) Eremophilanes from *Petasites formosanus* KITAMURA. Chem Pharm Bull 46: 1807–1809.

Mao MJ and Jia ZJ (2002) Eremophilane sesquiterpenes from *Cacalia ainsliaeflora*. Planta Med 68: 55–59.

Mao MJ, Yang ZD, Jia ZJ (2003) New eremophilane sesquiterpenes from *Cacalia ainsliaeflora*. Planta Med 69: 745–749.

Massiot G, Nuzillard JM, Olivier L et al. (1990) Eremophilenolides from *Hertia cheirifolia*. Phytochemistry 29: 2207–2210.

Moriyama Y, Takahashi T (1976) New sesquiterpene lactones of eremophilane-type from *Ligularia fauriei* (F_R.) K_{OIDZ}. Bull Chem Soc Japan 49: 3196–3199.

Naya K, Kanazawa R, Sawada M (1975) The photosensitized oxygenation of furanoeremophilanes. I. The isomeric hydroperoxides from petasalbin and their transformations to lactones. Bull Chem Soc Japan 48: 3220–3225.

Naya K, Matsuura T, Makiyama H et al. (1978) The conversion of furanoeremophilanes to epieremophilenolides. Heterocycles 10: 177–184.

Sugama K, Hayashi K, Mitsuhashi H (1985) Eremophilenolides from *Petasites japonicus.* Phytochemistry 24: 1531–1535.

Tobinaga S, Takeuchi N, Kasama T et al. (1983) Anti-histaminic and anti-allergic principles of *Petasites japonicus* Maxim. Chem Pharm Bull 31: 745–748.

Yoko G, Yasuo K, Tomoki N et al. (2001) Allelopathic sesquiterpenoids from rhizomes of *Petasites japonicus* ssp. *giganteus* Kitam, Phytochemistry 57: 109–113.

Zhang SM, Zhao GL, Li R et al. (1998) Eremophilane sesquiterpenes from *Cacalia roborowskii*. Phytochemistry 48: 519–524.

Zhao Y, Jia ZJ, Tan RX et al. (1992) Eremophilanolides from the roots of *Ligularia veitchiana*. Phytochemistry 31: 2785–2787.