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Two New Sesquiterpenes from *Ligularia macrophylla*

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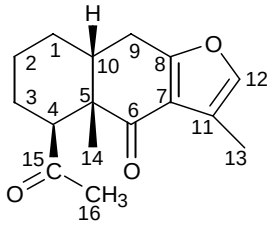
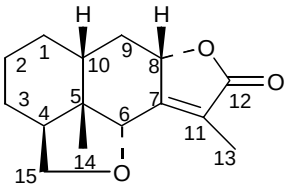
Abstract: Two new eremophilane sesquiterpenes, 15β-formic ether-6-oxo-furanoeremophilane (**1**) and 6α, 15β-epoxy eremophila-7(11)-en-8α, 12-olide (**2**) were isolation from the roots of *Ligularia macrophylla*. Their structures were deduced from spectroscopic methods and 2D NMR experiments.

Keywords: *Ligularia macrophylla*, Compositae, eremophilane sesquiterpene.

Ligularia macrophylla (Ledeb.) DC. is mainly distributed in Tianshan mountain and Aletai areas of Xingjiang province. Its root has been used traditional folk medicine for antiasthmatic, anticancer and antibacterial[1]. Here we report the roots from the south Tianshan mountain. In our currently study, two new eremophilane sesquiterpenes were isolated from the roots of *Ligularia macrophylla.*



1



2

Compound **1** is colorless needle crystals (acetone), mp: 128-130°C; $[\alpha]_D^{20}$ -40.8 (*c* 0.27, $CHCl_3$). Its IR spectrum revealed absorption bands for formic ether group (1725 cm^{-1}), α, β-unsaturated ketone group (1666 cm^{-1}) and furan ring (1563,1457,1423 cm^{-1}). Its molecular formula of $C_{16}H_{20}O_4$, was deduced from its HRESIMS quasi-molecular ion peak at *m/z* 277.1432 $[M+H]^+$ (calcd. 277.1434). The ^{13}C NMR and DEPT spectra revealed the presence of 16 carbon atoms (including 3×CH_3, 4×CH_2, 3×CH and 6×C). Due to the signals at δ 197.9 (keto carbonyl carbon), 175.1 (carboxylic ester group), 119.9, 154.4 with δ 117.3, 139.6 (two double bonds) could be observed, therefore **1** was a tricylic sesquiterpene. In the ^1H NMR spectrum of **1**, two methyls, one methoxy

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group and one olefinic proton were due to Me-13 [δ 2.08 (s, 3H)], Me-14 [δ 1.10 (s, 3H)], OMe-16 [δ 3.57 (s, 3H)] and an α proton of furan ring H-12 [δ 7.05 (s, 1H)]. The two signals at δ 2.08 and 7.05 were the characteristic signals of furanosesquiterpenes [2,3]. By comparison of the ^{13}C NMR spectrum of **1** with that of the known compound furanoeremophilane[4,5], the C-4 signal of **1** was shifted downfield to δ 43.7 ppm from 36.8 ppm and the signal of C-6 was shifted downfield to δ 197.9 ppm from 29.5 ppm. Due to the absence of the Me-15, the formic ether group had to be at C-15 and ketone group was at C-6, respectively. These conclusion was further confirmed by the HMBC correlations: H-1/ C-3, C-9; H-2/C-4, C-10; H-3/C-1, C-5, C-15; H-4/C-2, C-6, C-10, C-14; H-9/C-1, C-5, C-7; H-10/C-2, C-4, C-6, C-8, C-14; H-12/C-13; CH_3-14/C-4, C-6, C-10, C-15; OCH_3/C-15. Stereochemically, due to Me-14 and Me-15 were biogenetically β-orientated[6], besides NOE difference examination of **1** showed that H-4 had a clear NOE effect on H-9α (*ca*. 3.2%), so $COOCH_3$ should be in β-orientation. Furthermore, the Me-14 signal had a clear NOE effect on H-10 (*ca*. 3.5%), indicating H-10 should be in β-orientation. Thus the structure of **1** was determined to be 15β-formic ether-6-oxofuranoeremophilane (**1**).

Compound **2** was obtained as colorless needle crystals (acetone), mp: 185-186°C, $[\alpha]_D^{20}$+50, (*c* 0.36, $CHCl_3$). Its IR spectrum revealed absorption bands of a typical α, β-unsaturated γ-lactone (1743, 1676 cm^{-1}) and ether group (1141, 1097 cm^{-1}). The molecular formula $C_{15}H_{20}O_3$ of **2** was deduced from its HRESIMS at *m/z* 249.1748 $[M+H]^+$ (calcd. 249.1485). Analysis of the ^{1}H, ^{13}C and DEPT NMR of **2**, indicated the presence of 15 carbon atoms (including 2×CH_3, 5×CH_2, 4×CH and 4×C), with 6 degree of unsaturation. The signals of C-7 (δ 158.5), C-8 (δ 78.7), C-11 (δ 125.7), C-12 (δ 172.1) and C-13 (δ 8.5) showed compoud **2** was a tetracylic sesquiterpene with an α, β-unsaturated γ-lactone[7]. In the ^{1}H NMR the signal of δ 4.49 (s, 1H) was belong to H-6

Table 1 ^{1}H (300MHz), ^{13}C NMR (75MHz) and DEPT data of **1** and **2*** ($CDCl_3$, δppm, J_{Hz})

No	Compound **1**			Compound **2**		
	δ_H	δ_C	DEPT	δ_H	δ_C	DEPT
1	1.52 (m)	26.0	CH_2	1.29 (m)	21.8	CH_2
2	1.38 (m)	21.0	CH_2	1.34 (m)	21.4	CH_2
3	1.69 (m)	29.3	CH_2	1.56 (m)	25.0	CH_2
4	2.05 (m)	43.7	CH	1.64 (m)	33.5	CH
5		48.6	C		45.3	C
6		197.9	C	4.49 (d, *J* =1.2)	82.8	CH
7		119.9	C		158.5	C
8		154.4	C	4.61 (t, *J* = 7.5)	78.7	CH
9α	2.54 (d,*J* = 18.0)	27.7	CH_2	1.86 (m)	37.2	CH_2
9β	3.10 (dd,*J* = 18.0, 5.4)			1.96 (m)		
10β	2.81 (m)	38.2	CH	2.16 (m)	38.8	CH
11		117.3	C		125.7	C
12	7.05 (s)	139.6	CH		172.1	C
13	2.08 (s)	9.2	CH_3	1.99 (d, *J* =1.2)	8.5	CH_3
14	1.10 (s)	31.0	CH_3	1.15 (s)	18.9	CH_3
15α		175.1	C	3.89 (m)	69.9	CH_2
15β				3.53 (m)		
OCH_3	3.57(s)	51.3	CH_3			

* The proton assignments for **1** and **2** by 1D and 2D NMR

because C-6 connected with –O-CH_2- group, its chemical shift appeared to downfield. According to the above signals, we compared the reported data in literatures[6,7], the structure of eremophilanodiolides was very similar to that of **2**, the significant differences were the chemical shifts of C-4 and C-15 (**Table 1**). The **2** featured an additional –CH_2-O-(δ_C 69.9, $\delta_{H\alpha}$3.89, t; $\delta_{H\beta}$ 3.53, t) at C-4 and C-6 instead of lactone group (δ_C 174.7). Its HMBC experiment showed the following connections: H-6/C-4, C-8, C-10, C-14; H-4/C-2, C-6, C-10, C-14, C-15. Thus, –CH_2-O- group should connect between C-4 and C-6. NOE difference measurements of **2** indicated that Me-14 signal had evidently NOE effect on H-6, H-8 and H-10, respectively; Besides, H-4 had evidently NOE effect on H-9α (*ca*. 5.45%). From the above spectral evidence, the structure and stereochemistry of the compound **2** should be represented by 6α, 15β-epoxyeremophila-7(11)-en-8α, 12-olide (**2**).

Acknowledgments

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