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Two New Eremophilenolides from *Ligularia tongolensis*

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Abstract: Chemical investigation of *L. tongolensis* afforded two new eremophilenolides, which were identified as 3β-(2′-methylbutanoyloxy)-8βH-eremophil-7(11)-en-12, 8α (14, 6α)-diolide (**1**) and 8βH-eremophil-3, 7(11)-dien-12, 8α (14, 6α)-diolide (**2**). Their structures were established by spectroscopic methods including 2D NMR experiments.

Keywords: *Ligularia tongolensis*, Compositae, eremophilenolide, sesquiterpene.

Ligularia tongolensis has long been used as a folk medicine to reduce phlegm and relieve cough[1]. However its chemical constituents were not reported until now. From the title plant collected in Sichuan Province, we found two new eremophilenolides and their structures were elucidated as follows.

Compound **1**, colorless plates, mp 190-191℃, $[\alpha]_D^{20}$ +125.5 (*c* 0.40, $CHCl_3$). Its molecular formula was proposed as $C_{20}H_{26}O_6$ by ^{1}HNMR, ^{13}CNMR and DEPT spectra in accordance with its molecular ion peak at *m/z* 362 in EIMS and $[M+H]^+$ peak at *m/z* 363.1803 (calcd. for $[C_{20}H_{26}O_6+H]^+$ 363.1802) in HRSIMS. Its IR bands displayed the existence of a cyclic ester carbonyl (1800 cm^{-1}), a saturated γ-lactone (1767 cm^{-1}) and an unsaturated γ-lactone (1714 cm^{-1}). In the ^{1}HNMR spectrum, there were signals of two methyl groups [δ_H = 1.99 (brs, 3H), 1.54 (s, 3H)], one 2′-methylbutanoyloxy group [δ_H = 2.38 (m, 1H), 1.66 (m, 1H), 1.48 (m, 1H), 1.14 (d, 3H, J = 7.2 Hz) and 0.92 (dd, 3H, J = 7.5, 7.2 Hz)]. Except for the 2′-methylbutanoyloxy group, the ^{13}CNMR and DEPT spectra showed 15 carbon signals for 5×C, 5×CH, 3×CH_2 and 2×CH_3 (**Table 1**). The information mentioned above and biogenetic considerations suggested that **1** was an eremophilenolide sesquiterpene lactone similar to that of the known 3β-angeloyloxy-8βH-eremophil-7(11)-ene-12,8α(14,6α)-diolide[2]. The difference was only the substituent at C-3. In the HMBC spectrum of **1**, the cross peak between H-3 (δ 5.47 brs) and C-1′ (δ 175.5) confirmed the location of the 2′-methyl butanoyloxy group at C-3. Stereochemically, H-14 and H-15 are generally biogenetically β orientaions[3]. On NOE difference spectra, the irradiation of H-15 enhanced the signal H-10 (5.30%) indicating their *cis* relationship; *i.e.* A/B was a *cis*-fused arrangement, whereas the signal enhancements of H-3 and H-4 had not been observed, but the irradiation of H-3

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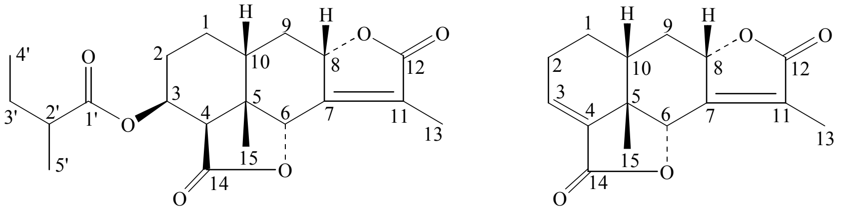
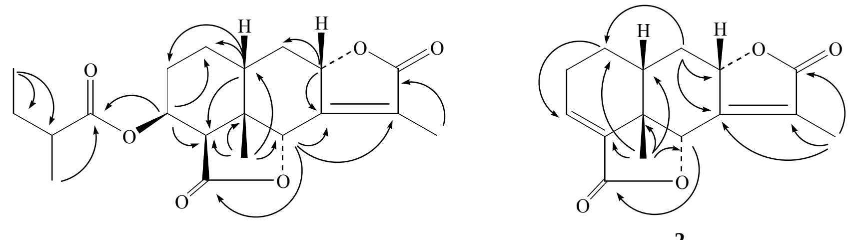
enhanced the signal H-4 (4.65%) indicating H-3 and H-4 at α-orientation, which was further confirmed by the coupling pattern of H-3α (quartet with $J_{3\alpha,2\alpha} = J_{3\alpha,2\beta} = J_{3\alpha,4\alpha}$ = 3Hz) due to the coupling of H-3α (equatorial proton) with three vicinal protons (one equatorial and two axial protons)[4]. The H-6, H-8 were identified as β-orientation from the evidence of positive NOE between H-6 and H-15 (7.73%), H-8 (4.35%). Therefore, the structure of **1** was determined as 3β-(2′-methylbutanoyloxy)-8βH-eremophil-7(11)-en-12, 8α (14, 6α)-diolide.

Figure 1 The structure of compounds **1** and **2**



1 **2**

Figure 2 The key HMBC (H to C) correlations of **1** and **2**



1 **2**

Table 1 ^{1}H-NMR (300MHz), ^{13}C-NMR (75MHz) and DEPT data of **1, 2** ($CDCl_3$, TMS, δ ppm)

No.	**1*** δ_H	**1*** δ_C	**2** δ_H	**2** δ_C
1	1.49, 2.10 m	21.0	1.74, 2.04 m	21.8
2	1.58 m	25.1	2.23, 2.33 m	22.0
3	5.47 (q, 3.0)	64.4	6.85 (dd, 3.6, 3.0)	136.9
4	2.41 (d, 3.0)	42.5	-----	129.6
5	-----	44.2	-----	44.0
6	4.98 brs	82.8	5.14 brs	81.8
7	-----	154.0	-----	155.9
8	4.72 (dd, 11.1, 3.9)	77.4	4.68 (dd, 9.3, 4.2)	77.4
9	1.54, 2.36 m	32.1	1.08, 2.23 m	33.0
10	2.17 m	34.8	2.15 m	33.6
11	-----	126.2	-----	125.4
12	-----	171.1	-----	173.4
13	1.99 brs	9.3	2.00 brs	9.4
14	-----	173.1	-----	168.3
15	1.54 s	23.2	1.42 s	27.0

*2′-methylbutanoyloxy: δ_H 2.38 (m, H-2′), 1.48/1.66 (m, H_2-3′), 0.92 (dd, 7.5, 7.2, H_3-4′), 1.14 (d, 7.2, H_3-5′); δ_C 175.5 (s, C-1′), 41.3 (d, C-2′), 26.7 (t, C-3′), 11.4 (q, C-4′), 16.4 (q, C-5′). J(Hz)

Compound **2**, colorless plates, mp 230-231℃, $[\alpha]_D^{20}$ +28.0 (*c* 0.20, $CHCl_3$). The molecular formula $C_{15}H_{16}O_4$ was deduced from its molecular ion peak at *m/z* 260 in EIMS and $[M+H]^+$ peak at *m/z* 261.1122 (calcd. for $[C_{15}H_{16}O_4+H]^+$ 261.1121) in HRSIMS as well as NMR spectra. Its spectral data were very similar to those of **1 (Table 1)** except for the presence of double bone at C-3 in **2** instead of the 2′-methylbutanoyloxy group in **1**. This was disclosed by downfield shifted signals of H-3 at δ 6.86, C-3 at δ 136.9 and C-4 at δ 129.6. In combination with the other NMR data (**Table 1**) and HMBC spectrum, the structure **2** was confirmed as 8βH-eremophil-3, 7(11)-dien-12, 8α (14, 6α)-diolide.

Acknowledgments

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