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Two Cytotoxic Eremophilanolides from *Senecio tsoongianus*

Qi Jun ZHANG[1], Hui DOU[1], Qun Xiong ZHENG[1,2], Chang Xin ZHOU[1], Zhao Jun XU[1], Hua PENG[3], Yu ZHAO[1]*

[1]Department of Traditional Chinese Medicine and Natural Drug Research, College of Pharmaceutical Sciences, Zhejiang University, Hangzhou 310031
[2]Department of Food Science, Hangzhou College of Commerce, Hangzhou 310035
[3]Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204

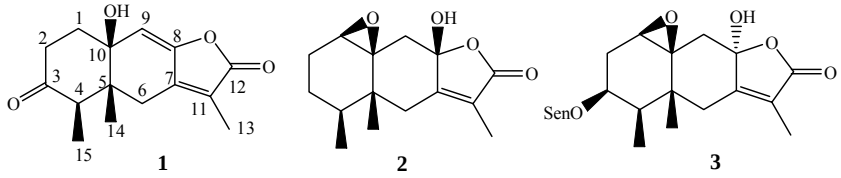
Abstract: Two new eremophilanolides, tsoongianolide E and F, were isolated from *Senecio tsoongianus*. Their structures were elucidated on the basis of NMR and MS spectra. Both of these two compounds showed *in vitro* cytotoxicity to cultured KB and A-549 cancer cell lines.

Keywords: Sesquiterpenes, eremophilanolide, *Senecio tsoongianus*.

The crude extract of *Senecio tsoongianus* Ling is found to possess cytotoxicity to KB cell with an inhibition ratio of 100% in 100 μmol/L. Previous investigations on the chemical constituents of *S. tsoongianus* have reported the presence of eremophilanolides[1]. Our further examination of this plant resulted in the isolation of other two new eremophilanolides, named as tsoongianolide E (**1**) and tsoongianolide F (**2**).

The molecular formula of $C_{15}H_{18}O_4$ for **1** was established by EIMS (*m/z* 262 $[M]^+$) and ^{13}C NMR data. Its IR spectrum exhibited absorptions for α,β-unsaturated γ-lactone (1779 cm^{-1}) and carbonyl group (1702 cm^{-1}). Accordingly, the ^{13}C NMR spectrum of **1** showed the signals for methyl substituted α,β-unsaturated lactone with an *endo*-double bond (δ 172.0, 147.5, 123.9, and 8.4), and trisubstituted double bond (δ 151.8 and 104.8). In the ^1H NMR spectrum of **1**, one methyl doublet (δ 0.72, J = 6.8 Hz) and two methyl singlets (δ 0.41, 1.67) were observed, while the only vinyl proton singlet appeared at δ 5.74, suggesting an eremophil-7(11),8-dien-8(12)-olide skeleton for **1**. Additionally, its ^{13}C NMR spectrum revealed the presence of a quaternary hydroxyl group located at C-10 (δ 78.2). From the biogenetic consideration of eremophilane derivatives isolated from *Senecio* species[1-4], Me-14 and Me-15 were both assigned to the β-configuration. The tertiary methyl signal in relative highfield for Me-14 (δ 0.41) indicated the presence of a *cis*-fused A/B ring system of **1**[5-7]. Placement of the carbonyl group at C-3 was deduced from the quartet signal for H-4 (δ 2.42,

* E-mail: dryuzhao@zju.edu.cn



1 **2** **3**

J = 6.8 Hz). Thus, the structure of **1** was elucidated as 10β-hydroxy-eremophil-7(11), 8-dien-3-oxo-8(12)-olide.

The molecular formula of $C_{15}H_{20}O_4$ for **2** was established from its EIMS (*m/z* 264 $[M]^+$) and ^{13}C NMR data. On the basis of IR absorption for unsaturated lactone (1752 cm^{-1}), characteristic ^1H NMR methyl signals (δ 1.80, 0.92, and 0.85) and ^{13}C NMR signal for a quaternary carbon (δ 98.3), a skeleton of 8-hydroxy-eremophil-7(11)-en-8(12)-olide for **2** was established[1-4]. An epoxy group was ascribed to C-1(10) due to one quaternary and one methine carbon signals germinal to oxygen (δ 63.1 and 68.6) in ^{13}C NMR spectrum and two independent AB systems for H-6 (δ 1.78, 2.44, d, *J* = 13.5 Hz) and H-9 (δ 2.22, 2.42, d, *J* = 13.5 Hz) in ^1H NMR spectrum of **2**. The β-orientation of the epoxy ring was deduced from the doublet for H-1 (δ 3.38, d, *J* = 8.0 Hz)[3]. As for the stereochemistry of OH-8, the splitting pattern for H-6 and H-9 was consistent with an 8β-hydroxy-eremophilane lactone[1-3]. Additionally, the C-9 of **2** was highfield shifted for 7.4 ppm and C-10 was downfield shifted for 7.1 ppm compared with those of **3**[3]. Thus, the structure of **2** was determined to be 1β,10β-epoxy-8β-hydroxy-eremophil-7(11)-en-8α(12)-olide.

Both compounds **1** and **2** showed *in vitro* cytotoxic activity against KB and A-549 cancer cell lines in MTT assays. The IC_{50} values of 8.6×10^{-5} mol/L and 3.6×10^{-5} mol/L were measured for compound **1** against KB and A-549 cell lines, while those of 3.2×10^{-5} mol/L and 5.7×10^{-5} mol/L were found for compound **2**, respectively [8-10].

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11. ^{13}C NMR data for compounds **1** and **2** (in $CDCl_3$): (**1**): C-1 - C-15: 33.6 t, 30.6^a t, 209.8 s, 33.6 d, 46.2 s, 30.9^a t, 147.5 s, 151.8 s, 104.8 d, 78.2 s, 123.9 s, 172.0 s, 8.4 q, 13.5 q, 14.7 q. (**2**): C-1 - C-15: 63.1 d, 29.0 t, 22.9 t, 39.4 d, 42.8 s, 29.9 t, 157.5 s, 98.3 s, 31.9 t, 68.6 s, 123.4 s, 172.0 s, 8.3 q, 14.9 q, 15.9 q. ^{a} values with the same superscript are interchangeable.
12. ^{1}H NMR data for compounds **1** and **2** (in $CDCl_3$): (**1**): 1.83 m, H-1; 1.38 m, H-1′; 2.94 m, H-2, 1.95 m, H-2′; 2.42 q (6.8), H-4; 2.54 d (13.5), H-6; 2.51 d (13.5), H-6′; 5.74 s, H-9; 1.67 s, H-13; 0.41 s, H-14, 0.72 d (6.8), H-15. (**2**): 3.38 d (8.0), H-1; 2.44 d (13.5), H-6; 1.78 d (13.5), H-6′; 2.42 d (13.5), H-9; 2.22 d (13.5), H-9′; 1.80 s, H-13; 0.85 s, H-14; 0.92 d (6.0), H-15.

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